Abstract
Book

22nd

State of the Art
Symposium

22nd State of the Art Symposium
«Addressing Patients' Needs –
Finding the Right Treatment for the Individual Patient»

Dear Colleagues,

It is with great pleasure that we invite you to this year's «State of the Art» symposium on Multiple Sclerosis (MS), organised by the Swiss MS Society and its Scientific Advisory Board. MS remains an incurable disease. But thanks to tremendous efforts in research the range of treatment options available for people is ever widening.

MS affects every person differently and it is important to choose the right treatment with and for every patient. A podium discussion, moderated by **Sven Schippling** will focus on this issue. First **Peter Rieckmann** and **Tjalf Ziemssen** will discuss standards of treatment and care as well as the role of MS specialists and people with MS in treatment measures and MS management strategies. Neuropsychiatric issues in MS will be addressed in a talk by **Pasquale Calabrese**, and **Gregor Hasler** will pay particular attention to the topic of resilience. **«MS Medications 2020 – Update on Safety Aspects»** is the title of **Andrew Chans** presentation. He will discuss conceptual and practical considerations of treatment-related complications.

MS Researcher Poster Viewing: During the coffee and lunch breaks you will have the opportunity to view posters of researchers currently funded by the Swiss MS Society, to network and to discuss the latest research findings.

The afternoon session with two sets of parallel workshops will address specific topics relevant to daily practice. **Jürgen Pannek** will address difficult issues in neuro-urology, a topic important to the quality of life of people with MS. **Philipp do Canto** will give you a legal perspective into data sharing. This issue is crucial in advancing precision medicine. In the workshop **«How to deal with Hypes and Dr. Google»** you have the chance to distinguish between trends and myths that are currently flooding the web. The SAB experts **Christian Kamm** and **Stefanie Müller** will try and make sense of it all. Sport and exercise are proven to be beneficial, but how can one motivate patients to exercise? **Jens Bansi** will present the newest approaches.

In the name of the organisers and speakers, we sincerely hope that the programme meets your interest and that you will be able to be a part of this years' «State of the Art» and participate in the discussions.

Jürg Kesselring

Jürg Kesselring
Honorary President of the Swiss MS Society

General Information

Date

Saturday, January 25th, 2020, 10.00 – 16.00

Venue

KKL Luzern, Europaplatz 1, CH-6005 Lucerne
www.kkl-luzern.ch

Programme Committee

Lutz Achtnichts, Aarau
Andrew Chan, Bern
Cristina Granziera, Basel
Jürg Kesselring, Valens
Sven Schippling, Zurich

Organisation

Swiss Multiple Sclerosis Society and its Scientific Advisory Board

Contact

Swiss Multiple Sclerosis Society, Josefstrasse 129, CH-8031 Zurich
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Credits

The Swiss Neurological Society awards 5 credit points.

Contacts

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Rehabilitation Centre Valens

Sven Schippling, Zurich

University Hospital Zurich

Department of Neurology

Speakers (Lectures)

Pasquale Calabrese, Basel

University of Basel

Neuropsychology and Behavioral Neurology Unit

Andrew Chan, Bern

University Hospital Bern

Department of Neurology

Gregor Hasler, Fribourg

University of Fribourg

Freiburger Netzwerk für Psychische Gesundheit

Peter Rieckmann, Bischofswiesen (DE)

Medical Park Loipl & University of Erlangen

Centrum for Clinical Neuroplasticity

Tjalf Ziemssen, Dresden (DE)

University Clinic Carl Gustav Carus Dresden

Center of Clinical Neuroscience

Speakers (Workshops)

Jens Bansi, Valens

Clinics of Valens

Rehabilitation Centre Valens

Philipp do Canto, Zurich

Public Sector Law, Zurich & Brussels

Attorney at Law

Christian Kamm, Lucerne

Lucerne Cantonal Hospital

Neurocenter

Stefanie Müller, St. Gallen

St. Gallen Cantonal Hospital

Neurologic Clinic

Jürgen Pannek, Nottwil

Swiss Paraplegic Centre

Neurourology

MS Researcher Poster Presentations

Jens Bansi, Valens

Clinics of Valens

Rehabilitation Centre Valens

Sonja Beckmann & Heidi Petry, Zurich

University Hospital Zurich

Center of Clinical Nursing Science

Bernhard F. Décard, Basel

University Hospital Basel

Neurologic Clinic and Policlinic

Christian Kamm, Lucerne

Lucerne Cantonal Hospital

Neurocenter

Marco Kaufmann, Zurich

University of Zurich

Epidemiology, Biostatistics and Prevention
Institute

Giuseppe Locatelli, Bern

University of Bern

Theodor Kocher Institute

Nicholas Sanderson, Basel

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Department of Biomedicine

Nanco van der Maas, Biel

Institut für Physiotherapieforschung

Fachgruppe Physiotherapie bei Multipler Sklerose

Viktor von Wyl, Zurich

University of Zurich

Epidemiology, Biostatistics and Prevention
Institute

Programme

«Addressing Patients' Needs – Finding the Right Treatment for the Individual Patient»

Chairpersons	**Session 1:** Jürg Kesselring, Valens Lutz Achtnichts, Aarau
	Session 2: Cristina Granziera, Basel Sven Schippling, Zurich
09.30 – 10.00	Welcome with Coffee and Gipfeli
10.00 – 10.15	Christoph Lotter, Zurich **Welcome from the Swiss MS Society**
10.15 – 10.40	Peter Rieckmann, Bischofswiesen (DE) **MS in the 21st Century**
10.40 – 11.05	Pasquale Calabrese, Basel **Addressing Neuropsychiatric Issues in MS**
11.05 – 11.30	Tjalf Ziemssen, Dresden (DE) **MS Management goes Digital**
11.30 – 11.50	Coffee Break with MS Researcher Poster Presentation*
11.50 – 12.15	Andrew Chan, Bern **MS Medications 2020 – Update on Safety Aspects**
12.15 – 12.40	Gregor Hasler, Fribourg **Resilience – Benefits for Persons with MS**
12.40 – 13.00	**Podium Discussion on Finding the Right Treatment for the Individual Patient** with Peter Rieckmann, Bischofswiesen (DE); Pasquale Calabrese, Basel; Tjalf Ziemssen, Dresden (DE); Andrew Chan, Bern; Gregor Hasler, Fribourg. Moderation: Sven Schippling, Zurich
13.00 – 14.15	Lunch with MS Researcher Poster Presentation*
14.15 – 15.00	**Workshops A and B**
15.00 – 15.15	Coffee Break
15.15 – 16.00	**Workshops C and D**
16.00	Farewell Apero

* MS Researcher Poster Presentation – During the coffee and lunch breaks you will have the opportunity to view selected posters from MS research projects that have been financially supported by the Swiss MS Society.

Peter Rieckmann

MS in the 21st Century

The «MS in the 21st Century» initiative was established with the purpose of (1) defining how multiple sclerosis (MS) treatment and standards of care should look in the 21st century; (2) developing a minimum standard of care across the globe; and (3) motivating the broad MS community to align standards of care and challenge the current treatment paradigm.

The aim was to develop a consensus statement to reach and influence the broader MS community. We constructed seven overall principles that support vision of «full access to personalized treatment, with reimbursement, to achieve freedom from disease». These principles include personalized care, patient engagement, commitment to research, regulatory body education and reimbursement issues, new endpoints in clinical trials, more therapy options, and MS centers of excellence.

Within a framework of regular meetings of both person with MS (PwMS) and health care providers (HCP) and intensive work flow on new initiatives we managed to publish several manuscripts in peer-reviewed journals, achieve high visibility at several international conferences, and presence in social media and webpages. This allowed us to reach an ever broader community and focus on the urgent need to improve communication tools for better standards of MS care: «myMS priorities» and «myMS commitments» are now available in several languages and can be used by PwMS to optimize consultations with HCP. A validation trial to test the usability of these tools in real world scenarios and future clinical trials is currently underway.

Peter Rieckmann, Bischofswiesen (DE)
Medical Park Loipl & University of Erlangen
Centrum for Clinical Neuroplasticity

Pasquale Calabrese

Addressing Neuropsychiatric Issues in MS

Neuropsychiatric disturbances (e.g. depression, anxiety) are reported in up to 60% of patients with multiple sclerosis (MS) and are among the main contributors to the morbidity and mortality associated with MS. Although these abnormalities generally present subsequent to neurological diagnosis, they may even herald a first clinical presentation of MS or may be concomitant to the neurological symptoms.

The spectrum of neuropsychiatric conditions encountered includes disorders of affect and behaviour, and psychotic and anxiety disorders. Although psychiatric comorbidity can be difficult to diagnose, it is generally responsive to treatment, conferring benefits in functional status, quality of life and overall disease burden.

In this talk I will discuss the most common neuropsychiatric syndromes that occur in MS, describe the clinical symptoms and management strategies for these conditions and speculate about their aetiology in light of recent neuropsychoimmunological findings.

The process of assisting a patient with MS starts with understanding chronicity from the patient's perspective and its effect on the health care relationship. By learning the impact that chronic illness has on the individual and recognizing the factors involved with adapting to chronic illness, the health care professionals can reach this understanding. An appreciation of the coping strategies commonly used by patients with chronic illnesses helps in selecting the appropriate counseling methods to foster psychological health.

Pasquale Calabrese, Basel
University of Basel
Neuropsychology and Behavioral Neurology Unit

Tjalf Ziemssen

MS Management goes Digital – Master programme

Background —— Multiple Sclerosis (MS) can lead to a wide range of neurological deficits and is often not diagnosed in time. However, since early therapy has an inhibitory effect on the progression of MS, timely diagnosis and treatment is important. In this context, a structured training of MS specialists is a significant part of the fight against MS.

Goals —— MS specialists should be familiar with the detailed scientifically sound diagnosis or differential diagnosis in case of suspected chronic inflammatory diseases of the central nervous system (CNS) with a focus on MS. In addition, they should know the «state of the art management» of chronic inflammatory CNS diseases. This includes treatment measures and strategies for the individual patient as well as detailed and close monitoring of disease activity and disability. MS specialists should also be able to interpret scientific publications and clinical studies on chronic inflammatory CNS diseases and apply them in direct patient care.

Methods —— A panel of experts developed a variety of modules focusing on basics, clinical and diagnostic aspects, studies and statistics, therapy and rehabilitation as well as monitoring and documentation of MS. In addition to the traditional transfer of knowledge through lectures and tutorials by experienced MS experts, the contents are to be conveyed with a particularly high practical share. For this purpose, preceptorships in specially selected centres, excursions and regular journal clubs as well as digital case conferences are intended to serve the direct practical implementation of the learned content on site.

Results —— The master´s program «Multiple Sclerosis Management» has been created. After the accreditation, it will start at the Dresden International University (DIU) in 2020 and will last four semesters. The program is mostly implemented digitally via adobe connect and will be held in German and English.

Conclusions —— For the first time a single disease complex is topic of a master course. The program with a strong practical relevance offers an unprecedented, structured and practice-oriented training for different disciplines at the highest level. After the successful establishment of the program in Germany, it will also be offered internationally.

Tjalf Ziemssen, Dresden (DE)
University Clinic Carl Gustav Carus Dresden
Center of Clinical Neuroscience

Andrew Chan

MS Medications 2020 – Update on Safety Aspects

The treatment armamentarium for MS is steadily increasing, and also in the year 2020 will see novel substances for different phenotypes, including chronic progressive disease.

Despite postulated selective mechanisms of action on specific pathophysiological pathways, especially real life use of modern agents has revealed unanticipated, potentially severe adverse drug reactions. In addition to general safety considerations of classical immunosuppressants also more selective immune therapies may harbour adverse substance specific on- and off-target effects. This situation can further be complicated by multiple therapy switches, and for many substances long term effects are unknown. In addition, individual risk factors such as age and specific risks in vulnerable patient groups (children, pregnant women) add to complexity.

In this presentation, conceptual and practical considerations of treatment-related complications will be discussed. However, optimal choice for individual patients does not only depend on benefit-risk considerations of single substances but has to be integrated with practical considerations, e.g. risk perception, treatment adherence and monitoring requirements.

Andrew Chan, Bern
University Hospital Bern
Department of Neurology

Gregor Hasler

Resilience – Benefits for Persons with MS

The experience of stress symptoms has been gradually increasing in the last decades. This increase occurs most prominently after puberty. Chronic diseases such as MS represent the most distressing conditions in adult life.

This talk will describe factors and strategies to improve stress resiliency. Among them are strategies concerning the self, including self-efficacy expectations and self-determination, that are crucial for individuals with chronic medical conditions. In addition, I will explain the relevant aspects of social relationships that are associated with resiliency.

Finally, nutrition and a healthy gut are increasingly the focus of stress research. Some of the new findings are particularly important for patients with MS.

Gregor Hasler, Fribourg
University of Fribourg,
Freiburger Netzwerk für Psychische Gesundheit

Podium Discussion: «Finding the Right Treatment for the Individual Patient»

MS affects every person differently, and it is important to choose the right treatment with and for every patient. With the vast range of available medications, this has become a challenging task for the treating neurologists. In this podium discussion the speakers of the morning lectures will elaborate on the most important questions concerning on how to find the right treatment for the individual patient.

Andrew Chan, Bern;
Tjalf Ziemssen, Dresden (DE);
Pasquale Calabrese, Basel;
Peter Rieckmann, Bischofswiesen (DE);
Gregor Hasler, Fribourg.

The discussion will be moderated by Sven Schippling, Zurich.

Workshops

Clinical Case Management
These workshops focus on aspects relevant to the daily management
of MS patients.

14.15 – 15.00   **Workshop A: «Neuro-Urology – how to Address Difficult Issues»**
Jürgen Pannek, Nottwil
Urologic symptoms, like incontinence, urinary tract infection or chronic retention,
frequently impair the quality of life (QoL) of the affected persons. Individuals with
MS suffer from several non-urologic problems like fatigue or spasticity, interfering
with standard bladder management. Therefore, each case has to be evaluated in-
dividually, and treatment should aim at preserving renal function as well as QoL.

**Workshop B: «Towards Precision Medicine – a Legal Perspective on Health
Data Sharing»**
Philipp do Canto, Zurich
In precision medicine, patient data for research become paramount. The Euro-
pean Data Protection Regulation and recent scandals raised public concern on
privacy. However, patients seem more inclined to participate in data sharing
and studies, especially regarding rare and complex diseases such as MS. Secure
data banks as well as best practices are crucial to further innovation based on
health data.

15.00 – 15.15   Coffee Break

15.15 – 16.00   **Workshop C: «How to deal with Hypes and Dr. Google»**
Christian Kamm, Lucerne & Stefanie Müller, St. Gallen
When experiencing symptoms of illness, patients often consult «Dr. Google»
before seeing a doctor. They seek information about their diagnosis and the
therapeutic options on the net and discuss in forums. We will try to distinguish
trends from myths and will support this with current studies.

Workshop D: «Sport and Activity – how to Motivate Patients to Exercise»
Jens Bansi, Valens
Exercise is part of a multidisciplinary rehabilitation approach to improve disability
in persons with MS. The primary aims of rehabilitation are to increase levels of
activity and participation leading to increased independence of the participants.
This workshop discusses new approaches and the resulting relevance for standar-
dized exercise training programs during rehabilitation.

16.00   Farewell Apero

Jürgen Pannek

Workshop A

Neuro-Urology – how to Address Difficult Issues

The physiological function of the lower urinary tract (LUT) is storage and controlled evacuation of urine. The LUT is controlled by spinal, supraspinal and cerebral networks. MS frequently leads to damage of at least one of the components, causing neurogenic LUT dysfunction (NLUTD). Depending on the location of the lesion, various forms of NLUTD can occur. Depending on the type of dysfunction, NLUTD can affect the upper urinary tract with the risk of renal failure, and can impair Quality of Life. Especially detrusor overactivity and detrusor-sphincter-dyssynergia are risk factors for renal damage. Therefore, NLUTD treatment should not be based on symptoms alone, but on urodynamic testing. Urologic symptoms, like incontinence, urinary tract infection or chronic retention, frequently impair the quality of life (QoL) of the affected persons. Individuals with MS suffer from several non-urologic problems like e.g. fatigue, impaired dexterity, or spasticity, interfering with standard bladder management. Therefore, each case has to be evaluated individually, and treatment should aim at preserving renal function as well as quality of life. Cooperation with physical therapists as well as the use of new, non- or minimal invasive techniques for neuromodulation, can vastly improve both subjective and objective outcomes.

Jürgen Pannek, Nottwil
Swiss Paraplegic Centre
Neurourology

Philipp do Canto

Towards Precision Medicine – a Legal Perspective on Health Data Sharing

In precision medicine, patient data for research become paramount. The European Data Protection Regulation (GDPR) and recent scandals raised public concern on privacy. However, patients seem more inclined to participate in data sharing and studies, especially regarding rare and complex diseases such as MS. Secure data banks as well as best practices are crucial to further innovation based on health data. This workshop provides an overview on the Swiss legal landscape related to health data.

With the transformation of global health care into a precision medicine environment, access to data and management of big data, especially genetic data, has become paramount in the industry, clinics and in research.

Data science generates value even in citizen centered research projects such as the «Swiss MS Registry» (SMSR). The SMSR utilizes a citizen science approach by involving persons with MS both as study subjects and as experts of the disease. Further features are the flexible study design that allows participation at different commitment levels, access

to own data for participants, and the broad involvement of scientists and health care providers from different disciplines.

As recent studies in the US demonstrate, patients seem more inclined than the general public to participate in data sharing and scientific studies, especially when it comes to rare or complex diseases such as MS.

On the downside however, scandals involving abuse of private data in clinics have raised public awareness on data security and privacy. General public and the media are becoming increasingly concerned regarding use of personal health data by the industry and clinics. The enactment of the European Data Protection Regulation (GDPR) and the risk of sanctions contribute to a rather confusing picture.

The public discussion is indeed dominated by the GDPR, however other laws – and exceptions for scientific research – are applicable specifically to Switzerland. The rules range from general medical secrecy to the Federal Data Protection Act and the detailed provisions of the Human Research Ordinance.

In this workshop we give an overview on the Swiss legal landscape with a specific focus on clinics and researchers. An update on the projects on General Consent and the revision of the Federal Human Research Act is also due. As a conclusion, the establishment of secure data banks and networks, such as the infrastructure of the Swiss Personalized Health Network, as well as building trust through best practices is crucial to further innovation based on health data.

Philipp do Canto, Zurich
Public Sector Law, Zurich & Brussels
Attorney at Law

Notes

Stefanie Müller & Christian Kamm

Workshop C

How to deal with Hypes and Dr. Google

The internet with its manifold offers has become an indispensable part of our lives. If patients experience symptoms of illness, they often consult «Dr. Google» before seeing a doctor. They search for information about their diagnosis and therapeutic options in the net and discuss their problems in partly anonymous forums. Internet searches can lead to unnecessary uncertainty, the medical layperson can often not distinguish serious from dubious content. Many doctors are sceptical about this, also because the quality of the information found is often not questioned by patients.

However, there are also benefits in using the internet and doctors must learn how to deal with this medium. They must point out to patients where they can find reliable online information.

It is well known that many of our MS patients use complementary and alternative treatments or follow health trends ranging from dietary supplements and vitamins to radical diets. Some products can be ordered directly from the respective websites. However, the internet usually does not offer competent and especially not personal advice. The number of unreported cases is high. Many patients do not mention the intake of non-school medical preparations for fear that their treating physician would not take them seriously. It is hardly possible for doctors to keep up to date with all the trends circulating on the net.

We will try to distinguish meaningful trends from myths and support this with current studies.

Stefanie Müller, St. Gallen
St. Gallen Cantonal Hospital
Neurologic Clinic

Christian Kamm, Lucerne
Lucerne Cantonal Hospital
Neurocenter
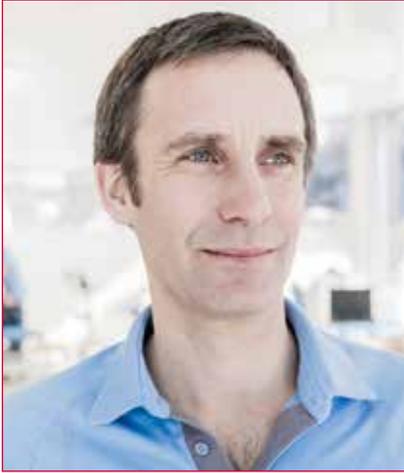
Jens Bansi

Sport and Activity – how to Motivate Patients to Exercise

Background —— Increased levels of physical activity are associated with risk reductions in several neurodegenerative disorders including Multiple Sclerosis. Moreover, exercise is known to improve the physical capacity and to reduce commonly observed symptoms, such as motoric, cognitive and affective impairments. Exercise therefore has become an efficient strategy within rehabilitative programs and is part of a goal-orientated multidisciplinary approach to improve disability and participation in persons with multiple sclerosis (pwMS). Recent studies report that exercise training might have beneficial effects on cognitive functions in pwMS, yet the overall magnitude and heterogeneity of this effect and the possible moderators (e.g. exercise type, intensity) remain unclear.

The primary aims of rehabilitation are therefore to increase levels of activity and participation leading to increased independence of the participants. Evidence shows that exercise training in pwMS then has the potential to target and improve many components outlined in the ICF model. New approaches focus acute high – intensive intervals (HIIT) and progressive exercise bouts that significantly impact cardiorespiratory fitness and lead to induction of neuroplasticity and the recovery of motor and cognitive functions.

Methods —— This workshop addresses the following issues:

(a) The role of exercise and training intensities during multidisciplinary neurorehabilitation with pwMS and their impacts on cardiorespiratory fitness on cognition, fatigue and immune functions;

(b) Discussion of new approaches (high-intensive exercise, modifiable risk factors via diet) and the resulting relevance for standardized exercise training programs during rehabilitation in pwMS;

(c) Identification of the main triggers to quantify exercise intensities during rehabilitation.

Jens Bansi, Valens
Clinics of Valens
Rehabilitation Centre Valens

Integral offer for MS patients

Bernese Clinic Montana is one of Switzerland's biggest stationary rehabilitation centres for people suffering from MS. It scores with an excellent medical expertise, an integral therapeutic approach and a wide range of therapies from physiotherapy over neuropsychology to a modern immune therapy designed to meet the individual needs of every MS patient. Furthermore, the location of the Clinic contributes to the wellbeing of its patients with its sunny and healthy climate.

For further information: bernerklinik.ch

SW!SS
REHA

MS Researcher
Poster Presentations

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

A selection of current projects will be
displayed at the KKL during the coffee and
lunch breaks of the State of the Art Symposi-
um. Do not miss out on the opportunity of
viewing these posters and discussing
the projects with the researchers.

Jens Bansi

TRAINUVIMAB – Influence of High-Intensity Interval Training on Quality of Life and Performance of Daily Activities in Multiple Sclerosis

Background —— Persons with multiple sclerosis (pwMS) report lower health-related quality of life (HRQoL) as compared to general and other chronic disease populations, while disability status is mainly driven by physical impairments and motor functions. High-intensity interval training (HIIT) has been shown to improve physical measures (muscle strength, cardiovascular fitness) more effectively than moderate training in pwMS.

Purpose —— To determine the influence of HIIT vs. moderate training over three weeks on HRQoL and motor and process performance of activities of daily living in pwMS with moderate to severe disability status (EDSS: 3.0-6.0).

Methods —— The intervention group cycled at 95–100% of HRmax (80–100 rpm) during 5× 1.5-min high-intensity intervals with 2 min of unloaded cycling in between, whereas the control group cycled for 24 minutes at 65% of HRmax (60–70 rpm). Performance of daily activities was quantified by the assessment of motor and processing skills (AMPS). The HRQoL was assessed using the patient-reported outcome measurement information system (PROMIS) short form Global-10. Effects of between-subject and within-subject factor measurement time-points (baseline vs. post intervention) have been analyzed by ANCOVA. Baseline measures were used as covariates.

Results —— No significant group interaction for either outcome measure was observed. However, physical HRQoL improved significantly only in the intervention group (p=.0001). Mental HRQoL improved significantly in both groups (intervention: p=.017; control: p=.001). While there is a significant improvement of motor performance of daily activities only in the intervention group (p=.025), no changes are observed in the processing performance in either group.

Conclusion —— HIIT over three weeks seems to have a stronger impact on physical characteristics than moderate training in pwMS which is shown by significant improvements in Global Physical Health and motor performance.

Jens Bansi, Valens
Clinics of Valens
Rehabilitation Centre Valens

Sonja Beckmann & Heidi Petry

Improving the Delivery of Care for MS Patients and Caregivers – Evaluation of the MS-Nurse Consultation Services at the USZ

Multidisciplinary teams are key to provide care for persons with MS and their families. Advanced Practice Nurses (APN) have been part of the treatment team at the University Hospital Zurich (USZ) since 2010. The specialized nurses with a Master's degree offer counselling in the MS nurse consultation services (MS-NuC). The aim of this project was to evaluate this innovative care model.

Research questions:
1) What are experiences of persons with MS, families, and healthcare professionals with the MS-NuC?
2) What is the evolution of the MS-NuC from 2011 until 2018 in view of patient characteristics, consultations, and patient outcomes?
3) What are differences in structure, process and outcome variables between the counseling provided by the MS-NuC and physicians?
4) What are the team characteristics and practice pattern of the APN in the MS-NuC?

The project followed the PEPPA evaluation matrix and included quantitative and qualitative methods for data collection and analysis.

The main results were:
1) Patients and families expressed the need of professional and emotional support. Although they valued «expertise and empathy» by the treatment team, «unfavorable processes and structures» such as changing physicians or the absence of a contact person were perceived as negative.
2) The number of patients in MS-NuC increased continuously and peaked in 2017 (n=376). Mean duration of consultations was 90 minutes, mostly covering drug management. The main symptoms experienced were fatigue (21-29%) and sensitivity disorders (17-26%).
3) People with MS were very satisfied with the counselling provided by the APN. Compared to consultation by physicians, MS-NuC patients were significantly younger, less likely to receive IV pension, had a higher workload, a shorter period of illness and a better quality of life. Quality of life was most limited in the category «mood».
4) Most common APN core competencies were «counselling and coaching of people with MS and their relatives». Less pronounced were «consultation of professionals» and «leadership», which corresponds to the role profile as designated.

The results provided a very good basis to implement first changes such as modification of the opening hours and thus extended the availability of the MS-NuC, creation of a leaflet with contact details of relevant specialists, optimization of work processes and cooperation among healthcare professionals. The initial feedback on the changes by persons with MS, families and professionals showed high satisfaction with the adjustments in clinical routine. Additional measures are planned to further improve the provision and the quality of care for people with MS at the USZ.

Sonja Beckmann & Heidi Petry, Zurich
University Hospital Zurich
Center of Clinical Nursing Science

Nanco van der Maas

Reliability and Validity of the 12-Level Modified Manual Muscle Test for Persons mit MS

Objective —— To evaluate the reliability and content validity of a new 12-level modified manual muscle test (mMMT) for persons with multiple sclerosis (MS), which considered spasticity while testing.

Background —— In MS, weakness is mostly associated with spasticity that may interfere with traditional manual muscle testing. mMMT considers spasticity and may provide a less biased outcome.

Design/Methods —— This was a single-center, prospective cross-sectional and longitudinal study with a test-retest design. Six testers examined 28 patients with MS. They tested the dorsiflexion of the foot as well as the hip and elbow flexion. The inter- and intra-rater reliability was evaluated using a one-way random effects ANOVA model. Additionally, we calculated the correlations between the mMMT and the isometric maximal muscle strength assessed by a hand-held dynamometer.

To describe motor fatigue, patients were tested at enrolment with the Fatigue Scale for Motor and Cognitive Functions. The pretest and posttest fatigue was measured with a numeric rating scale.

We used the Modified Tardieu Scale for the evaluation of spasticity. The influence of fatigue and spasticity was evaluated exploratively by using plots and in subgroups using a linear mixed effects model for each test separately.

Results —— The targeted prespecified Intra Class Correlation (ICC) margin of 0.7 for the interrater reliability was not reached. The pooled overall value of the intra-rater reliability of the mMMT (ICC=0.77 [0.65, 0.86]) passed the limit for good reliability. The mMMT demonstrated a weak to moderate, positive, monotonous correlation with isometric maximal muscle strength.

22 of 28 patients showed a severe motor fatigue at enrolment. Many patients showed a post-test increase in fatigue. However, we did not find any influence of fatigue on the test results.

High spasticity was only observed in the foot. Hence the subgroup (high and low spasticity) analyses were restricted to the mMMT foot and mMMT overall. Although 18 patients showed an increase in spasticity, we did not find an influence of spasticity. As the mMMT takes spasticity into account, this finding is in accordance with our expectations.

Conclusions —— This study demonstrated that the mMMT can be a reliable outcome measurement tool to test muscle function in an MS patient when the mMMT is applied by one therapist. Furthermore, it seems that the concept of testing considering spasticity is valid.

Nanco van der Maas, Biel
Institut für Physiotherapieforschung
Fachgruppe Physiotherapie bei Multipler Sklerose

Nanco van der Maas

Reliability of the Manual Muscle Test of the Neurostatus EDSS

Objective —— To evaluate the reliability of the manual muscle test of the Neurostatus Expanded Disability Status Scale (NEDSS).

Background —— For the validation of a new modified manual muscle test for persons with multiple sclerosis (MS), the reliability of the manual muscle tests of the NEDSS was used as a criterion and evaluated. The influence of fatigue and spasticity on the reliability was explored.

Design/Methods —— This was a single-center, prospective cross-sectional and longitudinal study with a test-retest design. Six testers examined 28 patients with MS, testing the dorsiflexion muscles of the foot as well as the hip and elbow flexion. The inter- and intra-rater reliability was evaluated using a one-way random effects ANOVA model.

The influence of fatigue and spasticity was evaluated exploratively by using plots and in subgroups using a linear mixed effects model (LME) for each test separately. We used the Modified Tardieu Scale (MTS) for the evaluation of spasticity and a numeric rating scale for the evaluation of fatigue.

Results —— The interrater reliability was mainly moderate. The Intra-class Correlation Coefficient (ICC) of the overall interrater reliability was 0.52 [0.30, 0.72]. Highest values were observed for the left foot (ICC=0.86). Lowest values were found for the right elbow (ICC=0.00).

High spasticity was only observed for the foot. Hence the subgroup (high and low spasticity) analyses were restricted to the foot and to the overall value. The ICC for these groups was generally higher in patients with low spasticity than in patients with high spasticity. However, the statistical evidence of our results is not strong enough to conclude that there is a difference between these subgroups.

The pooled overall value for the intra-rater reliability is ICC=0.74 [0.59, 0.83]. The plots of the overall ratings of the muscle test against the sum scores of the MTS as well as the LME analysis did not indicate an influence of spasticity on the intra-tester reliability.

22 of 28 patients showed a severe motor fatigue at enrolment. Many patients showed a post-test increase in fatigue. Despite these findings, we did not find an influence of fatigue on the test results.

Conclusions —— The study demonstrated that this muscle test can only be a reliable outcome tool when the test is applied by one tester. Fatigue didn't influence the reliability. Spasticity might influence the intertester reliability and needs further evaluation.

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Prospective Stratification of Infectious Risks in Multiple Sclerosis (InRIMS) Study – a progress report

Background —— Long-term use of highly effective immunotherapies for multiple sclerosis (MS) may be compromised by the occurrence of secondary immunodeficiencies and consecutive infectious side effects. To date, there is sparse real-world data that helps to stratify the risk for serious infections in treated MS patients. Screening tools for prospective risk stratification regarding serious infections can help to minimize life threatening adverse events and increase safety as well as quality of life of MS patients under immuno-modulatory treatment. The main objective of this study is to identify factors that increase the susceptibility for infections and establish a questionnaire-based infection score that allows a prospective stratification for infectious risks in MS patients.

Methods —— On the basis of a validated infection questionnaire and diary from the large population-based Airway Infection Susceptibility (AWIS) study with 12'839 randomly selected individuals, we developed a new questionnaire tool with additional MS-specific items (MS-AWIS questionnaire and infection diary). InRIMS is a monocentric, prospective, observational and comparative study, which includes regularly followed MS patients from the Swiss MS Cohort Study (SMSC) and SUMMIT study. At baseline patients are asked to fill out the MS-AWIS questionnaire at their regular clinical SMSC or SUMMIT visit.

We hypothesize that an infection score, which is calculated on the basis of this MS-AWIS questionnaire correlates with the frequency and severity of infections, prospectively measured by using monthly MS-AWIS infection diaries during the following two years. Based on the published data from the AWIS study we calculated a sample size of 254 patients to assess for this primary endpoint. InRIMS will also evaluate routinely collected laboratory data and compare the prevalence of infections in our MS cohort with the original population-based AWIS study cohort.

Results —— InRIMS study was initiated mid-September 2019; by end of October 2019 we included already 69 patients. We will perform an interim analysis of the MS-AWIS questionnaires at baseline and demonstrate preliminary data at our poster presentation.

Discussion —— In this early study phase the recruitment is ahead of schedule, underlining the broad patients' acceptance to investigate research subjects with direct impact on patients' daily life. We hope that the results of our study will enable the treating neurologists to improve the counselling of MS patients in clinical practice and help to personalize the selection of immunotherapies, dosage and treatment frequency as well as prophy-lactic measures (e.g. vaccinations or immunoglobulin substitution therapy) according to the individual risk of infectious side effects.

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Factors influencing Patient Satisfaction with the First Diagnostic Consultation in MS: a Swiss Multiple Sclerosis Registry Study

Background —— Patient satisfaction is predictive of adherence, malpractice litigation, and doctor-switching. Satisfaction with the first diagnostic consultation (FDC) in persons with multiple sclerosis (PwMS) has rarely been studied. Our aim was to investigate which factors of the FDC influence patient satisfaction and which topics PwMS thought were missing.

Methods —— The Swiss Multiple Sclerosis Registry (SMSR) is a nationwide patient-centered survey study in Switzerland. Participants complete a baseline assessment online or on paper and subsequently fill in follow-up questionnaires every six months.

We added a specific survey addressing the FDC to the first regular 6-month follow-up questionnaire for patients with initially relapsing MS diagnosed after 1995. The FDC-survey contained 14 questions covering the formal setting of the FDC (place, participants, duration) as well as the communication of diagnosis, discussed topics, presentation of disease-modifying treatments (DMT) and the process of treatment decisions. The satisfaction of the participants with the FDC was assessed on a five-point Likert-Scale ranging from very unsatisfied (=1) to very satisfied (=5). We fitted ordered logistic regression models on satisfaction with FDC, with socio-demographic and FDC features as explanatory factors.

Results —— 386 PwMS diagnosed after 1995 were included. 54% of participants were satisfied with the FDC, 22% were neutral, and 24% were not satisfied. In multivariable ordered logistic regression, good satisfaction (defined as a score of ≥4) with the FDC was associated with a conversation of at least 20 minutes (multivariable Odds Ratio [95% confidence interval 3.9 [2.42;6.27]), covering many MS relevant topics (1.35 [1.19;1.54] per additional topic), the presence of a close relative or a significant other (1.74 [1.03;2.94]), and shared decision making with regard to future DMT (3.39 [1.74;6.59]). By contrast, not receiving a specific diagnosis was a main driver for low patient satisfaction (defined as a score of ≤2) with the FDC (0.29 [0.15;0.55]). Main missing topics concerned life consequences (reported by 6.7%), psychological aspects (6.2%), how to obtain support and further information regarding therapies and prognosis of MS (5.2%).

Conclusions —— A conversation of more than 20 minutes covering many MS relevant topics, a clear communication of the diagnosis, the presence of a close relative or a significant other, as well as a shared decision making approach enhanced patient satisfaction with the FDC in PwMS.

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A Framework for Estimating the Burden of Chronic Diseases: Design and Application in the Context of Multiple Sclerosis

Background —— When population-based databases are unavailable, nationwide assessments of the disease burden of multiple sclerosis (MS) resort to clinical, administrative or convenience-sampled data sources, which may produce results of limited external validity. Our aim was to develop a framework for estimating measures of occurrence of chronic diseases, and more broadly disease burden, that mitigate these limitations, and to apply this framework to estimate the prevalence of multiple sclerosis (MS) in Switzerland.

Methods —— We developed a 7-step framework which implements the combination of several data sources together with a resampling and critical appraisal approach. The framework was applied to estimate the MS prevalence for 2016 in Switzerland, for which four distinct data sources (Swiss MS Registry, Swiss National MS Treatment Registry, MediService Database, and Swiss MS Cohort Study) were combined. Results were reviewed by disease experts and compared to earlier Swiss estimates and current prevalence estimates from other countries.

Results —— We estimate that in the year 2016 between 14'650 and 15'700 persons with MS have been living in Switzerland, yielding a period prevalence of 174–187/100'000 inhabitants. Compared to the last estimate in 1986, we detected a substantial increase of MS diagnoses which coincides with a higher number of diagnoses in women below the age of 65.

Conclusions —— Internationally, Switzerland is a high-prevalence country for MS, although estimates were somewhat lower than recent evaluations of Northern European countries. In addition, we corroborate previous reports that the prevalence increase coincides with a higher number of MS diagnoses among women. The proposed framework has wide applicability and the potential to place estimates of disease occurrence and burden with imperfect data availability on more solid grounds.

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Ageing with Multiple Sclerosis: The Role of Calendar Age and Disease Duration for Disease Outcomes and Co-Morbidity Occurrence in the Swiss Multiple Sclerosis Registry

Background —— Older age impacts Multiple Sclerosis (MS) disease course and pathology. With rising age, the risk of comorbidities exerting reinforcing effects on pre-existing MS symptoms increases. Our goal was to study the independent influences of «ageing» and «MS disease duration» (since first symptom onset) on the disability burden in a cross-section of the Swiss MS Registry.

Methods —— Using data from 1'360 persons with MS (PwMS), distribution of disability milestones (EDSS 4-6.5, n=289 (21.3%); or EDSS ≥7, n=123 (9.0%)) and self-reported occurrence of co-morbidity (cancer, n=26 (1.9%); hypertension; n=152 (11.2%); diabetes type 2, n=37 (2.7%); cardiovascular problems, n=40 (2.9%)) was compared in two dimensions across six age decades (18-29, 30-39, 40-49, 50-59, 60-69, 70+) and four MS duration strata (0-9, 10-19, 20-29, 30+ years). Multivariable logistic regression models adjusted for sex, MS subtype at diagnosis, BMI, smoking status (never, previously, current), and current disease-modifying treatment were applied. Age and MS duration were included jointly as linear variables. In a model extension, these parameters were replaced by continuous, cubic splines.

Results —— 73.5% were female, the median [interquartile range] age was 48 years [39-57], and 10.4% had a primary progressive MS at diagnosis. Achieving disability milestones was independently and positively associated with age and disease duration. The odds of an EDSS 4-6.5 increased by 4% per age category (Odds Ratio (OR) 1.04 [95% confidence interval 1.02;1.06]) and by 4% (OR 1.04 [1.02;1.05]) per disease duration category, without dominance of either factor. The odds of an EDSS ≥7 also independently increased by 2% (OR 1.02 [1.00;1.04]) per age category and by 7% (OR 1.07 [1.05;1.10]) per disease duration category. By contrast, age was the main driver for cardiovascular problems with 5% (OR 1.05 [1.02;1.09]), hypertension 8% (OR 1.08 [1.06;1.11]), diabetes 8% (OR 1.08 [1.04;1.12]), and cancer 5% (OR 1.05 [1.00;1.09]) frequency increase per category, respectively, whereas point estimates for MS duration did not reach statistical significance.

Conclusions —— Reaching specific EDSS milestones was associated with both calendar age and MS disease duration. The occurrence of four major comorbidities was mainly associated with calendar age, but not with MS disease duration. With the increased life expectancy of PwMS, this harbors implications for both prevention and treatment strategies of co-morbidities in PwMS, for instance to avoid polypharmacy.

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Cell–Binding Antibodies in the CSF of Patients with Multiple Sclerosis

Oligoclonal bands of intrathecally synthesised antibodies are a characteristic feature of MS. Extensive efforts to determine the antigen specificity of these antbodies have mostly not been fruitful. We have tried to advance this search by the following step-wise approach:

1. We focus on antibodies that bind to extracellular epitopes of live, neural- or glia-derived cell lines.
2. We screen CSF from cohorts of patients and controls for antibodies that bind to these cell lines.
3. From positive samples, we sort single B cells into wells, expand them with cytokines, and re-screen the antibody, containing supernatants.
4. From positive wells we clone the immunoglobulin genes and re-express them recombinantly.
5. We re-screen the recombinant antibodies and from positive candidates we identify the target antigen.

From a total of 260 donors with MS and a similar number of controls, from two independent, blinded cohorts from Basel and Graz, we found no cell lines that were bound by IgG in an MS-associated pattern. We found one neuroectoderman tumour cell line that was bound by IgM from 10-15 % of CSF samples from donors with MS, but only one control. The donors whose CSF contains anti-neuroectodermal antibodies include patients with relapsing-remitting, as well as progressive disease types. The cell types that were not bound preferentially by antibodies from donors with MS included glioma and astrocytoma cell lines, as well as iPS-derived neuron and astrocyte-like cells.

Focussing on the neuroectodermal cell reactivity, we have prepared five monoclonal antibodies from B cells from positive CSF samples. One of these matches the binding pattern of the CSF cohorts, i.e., binds with high affinity to live neuroectodermal cell lines, and not to the other cell lines tested.

We are now in the process of identifying the target antigens of the five monoclonal antibodies using a combination of immunoprecipitation and mass spectrometry, and bioinformatic comparison of the transcriptomes of the cell lines that are bound by the antibodies versus cell lines that are not bound.

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Mechanisms of Macrophage Invasion and Role of IGF-1 in Myeloid Inflammation in an MS Animal Model

Multiple Sclerosis (MS) is a chronic inflammatory disease of the Central Nervous System (CNS), characterized by leukocyte infiltration and tissue destruction. Microglia/macrophages are the main cell type found in demyelinating lesions of both MS patients and mice suffering from experimental autoimmune encephalomyelitis (EAE), an animal model for MS. Due to their remarkable phenotypic plasticity and developmental heterogeneity, these phagocytes guide disease development both as damaging and repairing forces.

While resident phagocytes regulate homeostasis and inflammation in the parenchyma and at CNS barriers, **invading macrophages infiltrate the CNS initially as pro-inflammatory cells evolving over time to anti-inflammatory players**. The molecular mechanism driving this phenotype switch, as well as the invading CNS gateways still remain unclear, thus hindering the design of novel therapeutic strategies.

Our research aims at unravelling (I) the **invasion gateways** used by polarized and non-polarized phagocytes inside the CNS parenchyma and (II) the **molecular mechanisms** regulating resident and invading phagocyte functions.

To reach these objectives, we employ a combination of intravital imaging and primary in vitro models of CNS barriers, such as blood brain barrier (BBB) and blood cerebrospinal fluid barrier (BCSFB). To address the role of resident and infiltrating myeloid cells during EAE, we focus on the key role of the master regulator Insulin-Like Growth Factor 1 (IGF1) and its receptor (IGF1-R).

Altogether, our study aims at foreseeing targeted interventions altering the balance between destructive and protective phagocytes in the inflamed CNS.

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We thank you for your participation and wish you a safe journey home.

See you next year at the
23rd State of the Art Symposium,
Saturday, January 23rd, 2021.

Best regards
Swiss Multiple Sclerosis Society

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