



WORLD NEUROLOGY

THE OFFICIAL NEWSLETTER OF THE WORLD FEDERATION OF NEUROLOGY

PRESIDENT'S COLUMN

WFN Neurological Community Update

WFN president reviews neurology development around the world, IGAP, World Brain Day, WCN, and other key topics.

WOLFGANG GRISOLD

Welcome to the first issue of World Neurology in 2024. We hope you had a relaxing, festive holiday season, and we look forward to the new year. 2024 will be another positive year for neurology, and we as the neurological community of the WFN will have many opportunities to foster and support neurology.

Globally, neurology is developing well. This statement can be supported by developments in neuroscience and global developments. General neurology as well as the subspecialties are thriving; examples are stroke and worldwide stroke services, epilepsy, and new drugs for epilepsy, movement disorders, and MS. The new possibilities not only to diagnose, but also

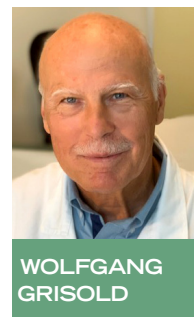
to treat some of the genetic diseases is an incredible advance, and breaks previous dogmas on therapy limitations and prognosis of some neurological diseases.

Regarding global development, important are the activities of the WHO. Worldwide, the WHO has 194 member states. Several WHO departments take care of present and emerging health problems of the world. The classification of neurological disorders still needs separation from mental disorders and requires a universal and globally accepted classification, which can be the basis for universally applied stable and more devoted structures.

A positive example for the development of classification is stroke and ICD-11, where the WHO ICD-11 classification will allow further

implementation of stroke services worldwide. Despite this amazing success story, we must continue to develop the prevention as well as chronic care, disability, and palliative care in stroke patients on the other side of the spectrum.

The WHO has implemented a "brain health unit" that fosters and supports the implementation and development of neurology. One key development is the IGAP, which is based on policy and advocacy, therapy, prevention, innovation, research, and public health. This concept was accepted by all member states at the World Health Assembly in 2022. Despite its strong support for neurology and



WOLFGANG GRISOLD

ultimately persons with neurological diseases, the echo and acceptance at the regional and country level still needs more powerful inputs.

Presently, the WHO is developing a **tool kit** for the implementation of IGAP, addressing all stakeholders. The WFN uses its channels of distribution to member societies, uses information at talks and presentations, has information on IGAP on its website, and has emphasized the IGAP and cooperation with the WHO at the World Congress of Neurology (WCN) 2023 and will continue to do so.

We want to emphasize this important IGAP activity for several reasons:

see **PRESIDENT'S COLUMN** page 3

Palliative Care for Stroke Patients

Report from the joint session of the WFN and the World Stroke Organization (WSO) at the WSO Congress in Toronto.

BY WOLFGANG GRISOLD

The Congress of the World Stroke Organization took place in October 2023 in Toronto.

In addition to the traditional joint session of the WFN and WSO at the World Congresses of Neurology, since 2022 the WSO and WFN have established joint sessions at the WSO Congresses.

Last year's topic was education; this year's topic was palliative care in stroke patients.

Speakers were:

Chairs:

Kiechl (Austria)/Grisold(Austria)

Speakers:

Gillian Mead (UK)

Stefan Kiechl (Austria)

Wolfgang Grisold (Austria): WFN.

David Oliver (UK).

Prof. Kiechl presented epidemiological data on stroke worldwide. The large number of strokes as the most frequent neurological disease and the high mortality within five years after stroke were discussed. The Austrian stroke system, which is quite elaborate from the

acute phase toward rehabilitation, was explained, and the role of palliative care discussed.

On behalf of the WFN, we discussed the worldwide availability of guidelines and recommendations for palliative care in stroke, as well as principles including the WHO recommendations and the ethical principles of autonomy, beneficence, non-maleficence, and justice (Jansen 2022). A comparison with other palliative paradigms is important (Steigleder, Kollmar, and Ostgathe 2019) and for

see **PALLIATIVE CARE** page 4

INSIDE

**26TH WORLD CONGRESS
OF NEUROLOGY PLENARY
SPEAKERS**

PAGE 5

**PUBLICATION COMMITTEE AND
HISTORY OF NEUROSCIENCES
SPECIALTY GROUP**

PAGE 6

**LEVERAGING TECHNOLOGY IN
RESOURCE POOR SETTINGS:
NOT AN IMPROBABLE DREAM**

PAGE 9

**IMPROVING BRAIN HEALTH IN
HONDURAS**

PAGE 10



WORLD FEDERATION OF NEUROLOGY

Editors-in-Chief

Steven L. Lewis (Editor)
Walter Struhal (Co-editor)
WFN London Office
Bedford House @ Fulham Green
69-79 Fulham High Street
London SW6 3JW
United Kingdom
Tel.: +44 (0)20 3542 1657/1658
e-mail: info@wfneurology.org

WFN OFFICERS

President Wolfgang Grisold (Austria)
First Vice President Guy Rouleau (Canada)
Secretary General Steven Lewis (USA)
Treasurer Morris Freedman (Canada)

ELECTED TRUSTEES

Alla Guekht (Russia)
Chandrashekhar Meshram (India)

REGIONAL DIRECTORS

Youssef Al Said (Pan-Arab)
Carlayne Jackson (North America)
Paul Boon (Europe)
Renato Verdugo (Latin America)
Beomseok Jeon (Asian-Oceania)
Augustina Charway-Felli (Africa)

EDITOR OF THE JOURNAL OF THE NEUROLOGICAL SCIENCES
John England (USA)



WORLD NEUROLOGY, an official publication of the World Federation of Neurology, provides reports from the leadership of the WFN, its member societies, neurologists around the globe, and news from the cutting-edge of clinical neurology. Content for *World Neurology* is provided by the World Federation of Neurology and Ascend Media.

Disclaimer: Articles in *World Neurology* represent the authors' personal views and do not necessarily represent the opinions of the editors, trustees, or leadership of the World Federation of Neurology or the publisher. The World Federation of Neurology and Ascend Media will not assume responsibility for damages, loss, or claims of any kind arising from or related to the information contained in this publication, including any claims related to products, drugs, or services.

Editorial Correspondence: Send editorial correspondence to *World Neurology*, Dr. Lewis at steven.lewis@wfneurology.org or Dr. Struhal at walter.struhal@wfneurology.org.

World Neurology, ISSN: 0899-9465, is published bimonthly by Ascend Media, 401 SW Ward Road, Suite 210, Lee's Summit, MO 64081
Phone +1-913-344-1300 Fax: +1-913-344-1497

©2024 World Federation of Neurology



PUBLISHING PARTNER

Ascend Media
President and CEO
Blair Johnson

Vice President of Content
Rhonda Wickham

Director of eMedia
Jena Brooks

Graphic Design
Tim Nord

Senior Project Director
Amanda Nevala

FROM THE EDITORS

BY STEVEN L. LEWIS, MD, EDITOR,
AND WALTER STRUHAL, MD, CO-EDITOR

We'd like to welcome all readers to the February 2024 issue of *World Neurology*, the first issue of 2024. The issue begins with the President's Column. Dr. Wolfgang Grisold, WFN president, provides an overview of the many activities being planned, organized, and supported by the World Federation of Neurology (WFN) for 2024 and beyond. In this issue, you will also find a summary of the many outstanding plenary sessions presented during the World Congress of Neurology (WCN) 2023, with a foreword by Dr. Guy Rouleau, WFN vice president.

Dr. Chandrashekhar Meshram, WFN elected trustee, provides a summary of the WFN Publications Committee and History of Neurosciences Specialty Group. This issue's History column is devoted to a book titled *The History of Stroke* by Dr. Jan van Gijn. Dr. Jan Stam provides the book review.

Dr. Duc Nguyen, a neurology trainee from Vietnam, summarizes his remarkable experience as the first recipient of an WFN and Indian Academy of Neurology Asian Departmental Visit provided at the Postgraduate Institute of Medical Education & Research in Chandigarh, India. Dr. Prisca-Rolande Bassolé, a young neurologist from Dakar, Senegal, reviews her attendance at the WCN2023 supported



STEVEN L. LEWIS, MD



WALTER STRUHAL, MD

by a WFN Junior Traveling Fellowship. Dr. Bindu and Medha Menon describe their foundation's activities aimed at using technology to mitigate the impact of epilepsy in their region of India.

Dr. Grisold provides a report of the Joint Session of the WFN and the World Stroke Organization (WSO) that occurred October 2023 at the WSO Congress in Toronto. The session was devoted to the concept of palliative care for stroke patients. Dr. Orla Hilton updates us on the Global Research Coalition and the call for collaboration in global research initiatives

devoted to global brain health.

Dr. Cassandra Kniffin Arnold and Joanna Amberger report on the Online Mendelian Inheritance in Man (OMIM) database, with a foreword to this important initiative by Dr. Martin Krenn. Dr. Marco Tulio Medina reports on the recent anniversary celebration of the creation of the Neurology Postgraduate Program at the Universidad Nacional Autónoma de Honduras (UNAH), which one of the World Neurology editors (SLL) had the privilege and honor of participating in.

Finally, Dr. Fabrizio Benedetti reviews the current pharmacological and toxicological concepts underlying the important phenomena of placebo/nocebo and the brain.

In this first issue of 2024, we want to thank all readers for their interest in the WFN and *World Neurology*. We look forward to sharing additional information with you about the WFN, neurology, and neurologists around the world in future issues of *World Neurology*.

In this first issue of 2024, we want to thank all readers for their interest in the WFN and *World Neurology*. We look forward to sharing additional information with you about the WFN, neurology, and neurologists around the world in future issues of *World Neurology*.

WFN JUNIOR TRAVELING FELLOWSHIP 2023

Report of My Attendance at the WCN2023

BY PRISCA-ROLANDE BASSOLÉ, MD

I am a young African neurologist and researcher working in Dakar, Senegal.

I am grateful to the World Federation of Neurology for granting me a traveling fellowship to attend the XXVI World Congress of Neurology 2023, in Montreal.

I had the opportunity to refresh my knowledge and share work of my Neurosciences Department on epilepsy (e-Poster 402) and sleep disorders (e-Poster 400) with colleagues from other countries.

I also had the privilege of following in the footsteps of the eminent Prof. Wilder Penfield, a pioneer in the "functional localization" of brain areas, during a historic discovery at the McGill Neuro Hospital of Montreal.

It was a rewarding experience and a great place for networking.

Thank you to the WFN for promoting continuing education by helping junior neurologists attend these neuroscientific events.



PRESIDENT’S COLUMN

continued from page 1

1. It promotes neurology at all levels and everywhere (“Semper et unique”).
2. It provides a well-structured concept on the establishment and needs of neurology, which can be adapted and used according to the individual local needs. This may differ according to the income status of countries.

The call to all member societies is to familiarize members and health systems with the IGAP, put it on the agenda of your society meetings, and try to promote it within your networks, including health authorities and other stakeholders.

The mission of IGAP and the role for the development of neurology is enormous. We want to remind readers of the important role of the ILAE and the WFN in its development. We share this common effort, and as stakeholders, we have to avoid competitive altruism. The common goal is implementation of neurology and improvement of the large number of persons affected with acute and chronicneurologic disorders, disability, and be on the forefront to prevent disease.

From the other tasks and programs of the WHO, such as **brain health**, fight meningitis and tuberculosis, and implementation of rehabilitation, we would like to remind readers of the WHO essential medicine list (EML), which we covered in the last issue of World Neurology in 2023. Successfully, more medications, one for epilepsy and two for MS, were added to the **EML list**. The EML is a dedicated WHO effort to make drugs available in all countries of the world. In some countries, there is a lack of registered drugs, deficits in registration, procurement, distribution, and affordability.

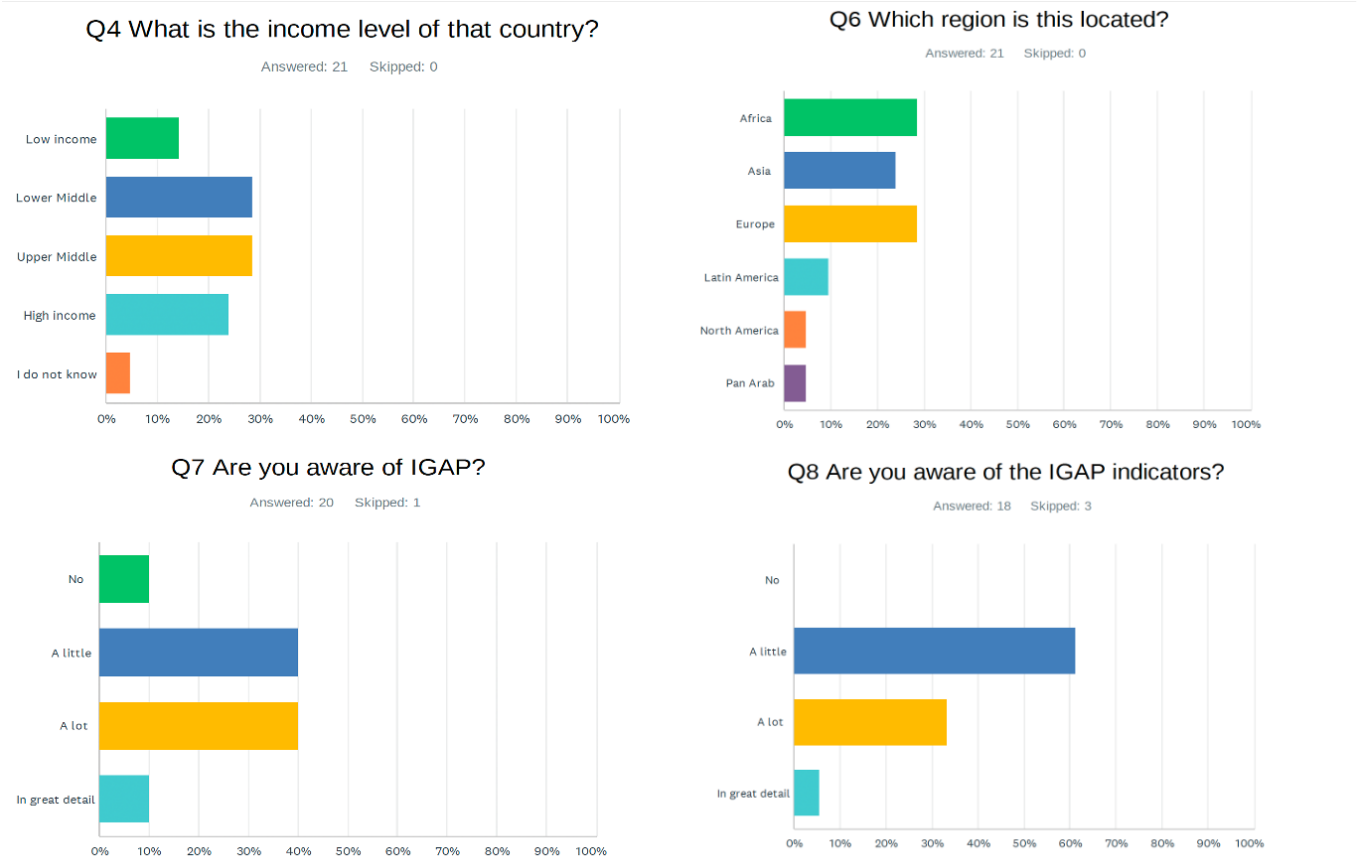
World Brain Day (WBD)

The **WBD** has become an annual event for the WFN community. It celebrates the day of WFN’s founding in 1957, chooses a yearly topic, and collaborates with topic-related societies and regions.

This year, we will continue supporting

AWARENESS OF IGAP BY WFN MEMBERS

(JUNE 2023, UNPUBLISHED WFN)



A 2023 WFN survey of WFN member societies assessing knowledge and content of the IGAP, revealed a disconcerting low level and awareness. Activities and publications of the WFN are aimed to increase the awareness and practical implementation of IGAP (Displayed Q 4-8) (London Office: C. Hunte)

the important topic of brain health, and focus on brain health and prevention. The activities will be chaired by D. Dodick and T. Wijeratne, the WFN regions, and will receive professional help from the marketing firm Yakkety Yak.

Prevention in neurology is a powerful and often underestimated tool to prevent neurological diseases and has a wide range of interventions, from vaccination, to pharmacology, nutrition, and lifestyle modifications. As with diagnosis and treatment, all types of prevention need to be added to neurological curricula.

Communication: Meetings/ Congresses and Education

Communication with the WFN’s member

societies is important. Please follow our website and social media. We also have a new medium called the **WFN Service Page**, which will be published every three months in the *Journal of the Neurological Sciences (JNS)*. This will increase the reach of the WFN. We also encourage you to publish material from your society and your regions in World Neurology. If you consider publishing in a journal, please consider the *JNS* and *eNS* as official journals of the WFN.

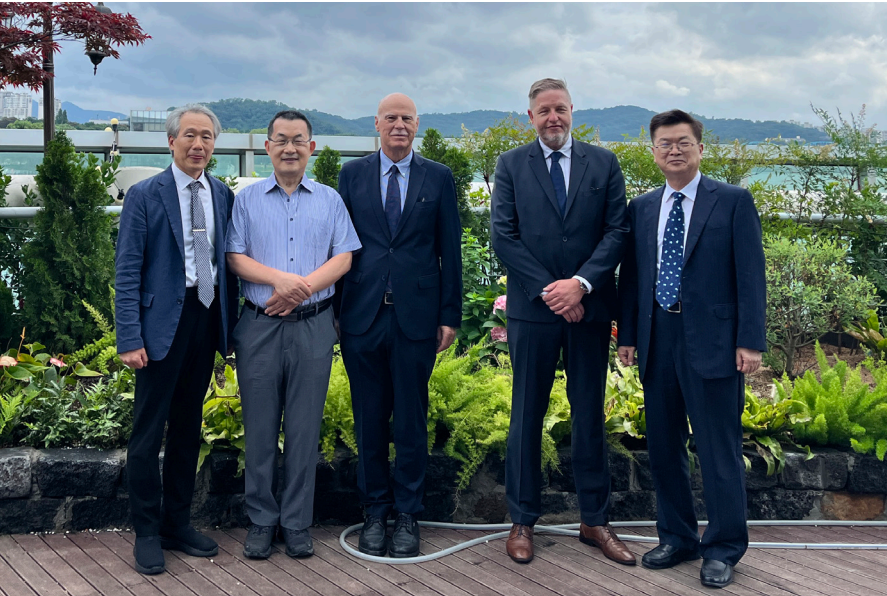
Congresses such as the WCN 2023 always leave impressions and produce new insights, either at the meeting or in discussions and informal gatherings. We are happy to report we had a large number of persons participating virtually at this

congress. This served two main purposes: to reach countries worldwide, who are unable to travel for financial and other reasons, and to increase the worldwide spread of neurology. One hundred and thirty two countries participated.

There is material on the WFN website from the WCN 2023 in Montreal. Also, please note the summary of the plenary sessions, the coffee talks, and all abstracts are now published in the **JNS**.

The next WCN will be in Seoul in 2025. The program committee has started its work. It is a generous venue and and a vibrant city. The Korean Neurological Society is putting much effort into this important congress, and it will provide

see **PRESIDENT’S COLUMN** page 6



Meeting with the Korean Committee in Seoul.



The WFN president high above Seoul.

PALLIATIVE CARE

continued from page 1

several neurological disease entities different concepts are needed.

For acute strokes, several guidelines and and recommendations exist (example: Braun et al. 2016), however little information exists on the palliative situations in stroke survivors, who have a high risk of recurrence as well as a high morbidity within five years. Stroke often leaves patients with impairment and disability (Wijeratne et al. 2023).

Following the hospital phase, often pain, sensory disturbances , sleep pathology, weakness, and sarcopenia appear. Loss of independence, existential worries, and often stigma with disability follow. Mental symptoms such as depression, apathy, also anxiety, agitation, and delirious states may occur (Cowey et al. 2021). (See Table 1.) Depending on the strategic localization of stroke, also neuro-cognitive sequelae of various nuances can be observed (examples: Anton’s syndrome, Capgras syndrome, among others).

The ability of communication can be compromised by several factors. (See Table 2.)

Suicidal tendencies in stroke patients are rarely mentioned and have been described in mainly small studies (Paolucci and Ngeh 2015), (Paolucci and Ngeh 2015) and in few general reviews. (Vyas et al. 2021).

Particular attention should be paid to the fact that increasing frailty impairs the compensation of the entire organ system and leads to a global decline in performance “Seneca effect”. (Bardi 2017). Stroke is one cause of the collapse of complex, poorly compensated biological systems in older and often multimorbid and frail patients.

It is worth noting that data from nursing home patients on chronic stroke treatment, therapies, and rehabilitation are largely lacking (Cowman et al. 2010), and this is a gap between acute stroke treatment and the long term follow-up.

The next session was given by Prof.

Table 1

MENTAL CHANGES IN PATIENTS WITH STROKE
During acute treatment: Mental changes Anxiety 12%-18% Delirium 8%-19% Agitation
After hospital discharge: Depression Neuropsychological changes Existential needs Hopelessness Loss of meaning Hopelessness
From: <i>Int J Stroke</i> . 2021 Aug; 16(6): 632-639. Published online 2021 May 17. do: 10.1177/17474930211016603 (Mod)

Gilian Mead (UK) and highlighted the role of the family in the course of the disease and in decision-making processes (Visvanathan et al. 2020). Ethical principles such as autonomy, doing good, doing no harm, and justice are the principles, as well as basic principles of palliative care in neurological diseases (Kluger et al. 2023).

An important aspect is the patient’s mental capacity, which determines the decision-making process: the ability to understand information, to critically analyze its content in terms of discussion or reflection, and finally to make decisions. The role of the family in patients who cannot express an opinion is important and requires many considerations. The literature has not yet addressed this issue in sufficient detail. Concepts for information about the disease, symptoms, and measures such as “tailored talks” with detailed and understandable templates for patients and relatives are useful. The concept of shared decision making involves the doctor, patient, and family (or partner) making further decisions together (Armstrong 2017) (Prick et al. 2022). Important aspects are unrealistic expectations about prognosis, outcome, and prognostication, both on the part of the patient/ family and the clinician.

The effects of severe strokes on the further quality of life are often underestimated. This might cause an enormous impact on future lifestyle. (Fig.1)

In addition, cultural differences must be taken into account, and the effects caused by the stroke must be considered. Immediately after the stroke, there are important challenges for the family, which often needs support.

Prof. DJ Oliver (UK) spoke about the meaning of “end of life” and expected death. In contrast to many other neurological conditions, the changes occur suddenly, often without warning, and are accompanied by major changes in lifestyle. For the family, the catastrophic changes are compounded by uncertainty about future developments, such as the possibility of regression of the neurological deficit. The sometimes-unjustified hope of improvement through neuro-rehabilitation needs to be explained and discussed, and the expectation needs to be realistic.

In all cases, appropriate symptomatic



Table 2

FACTORS THAT FREQUENTLY IMPAIR COMMUNICATION.
<ul style="list-style-type: none">• Fatigue and loss of tenacity: depression, apathy, irritability• Impairment of expression: facial expressions speech, tonality, prosody• Loss of body image: neglect, disfiguration• Loss of function, such as motor and coordination• Social aspects: communication, isolation, incontinence,• Stigma
From: Neurological Ddisorders With a Significant Psychiatric Disturbance, Grisold, W. and Grisold, S., Lecture: World Congress of Psychiatry (WPA) , September 2023, Vienna.

treatment is important. Particularly in acute cases, there are unstable and complex situations that require complex decisions. Mental and psychosocial aspects also need to be considered.

However, preferences and priorities for desired future treatment require intact mental capacity.

In the joint discussion, the importance of the patient and family coming to terms with the stroke was discussed. There are undoubtedly more recommendations for the acute stroke phase than for the chronic phase, with the factor of permanent or increasing disability also having to be considered. Studies of nursing home patients show that there is a strong need to consider special measures for institutionalized patients with a history of stroke.

A further focus of investigation and research should be dedicated to stroke survivors who are prone to recurrence in the following five years, have a high comorbidity, and a high mortality rate. Especially for patients with disabilities and institutionalized patients, the aspects of palliative care need to be considered. •

Wolfgang Grisold is president of the WFN.

References

Armstrong, M. J. 2017. Shared decision-making in stroke: an evolving approach to improved patient care. *Stroke Vasc Neurol* 2 (2):84-87.

Bardi, Ugo. 2017. The Seneca Effect: Why Growth is Slow but Collapse is Rapid. Book: Springer; *The Frontiers Collection* DOI <https://doi.org/10.1007/978-3-319-57207-9>.

Braun, L. T., K. L. Grady, J. S. Kutner, E. Adler, N. Berlinger, R. Boss, J. Butler, S. Enguidanos, S. Frieber, T. J. Gardner, P. Higgins, R. Holloway, M. Konig, D. Meier, M. B. Morrissey, T. E. Quest, D. L. Wiegand, B. Coombs-Lee, G. Fitchett, C. Gupta, W. H. Roach, Jr., and Committee American Heart Association Advocacy Coordinating. 2016. Palliative Care and Cardiovascular Disease and Stroke: A Policy Statement From the American Heart Association/American Stroke Association. *Circulation* 134 (11):e198-225.

Cowey, E., M. Schichtel, J. D. Cheyne, L. Tweedie, R. Lehman, R. Melifonwu, and G. E. Mead. 2021. Palliative care after stroke: A review. *Int J Stroke* 16 (6):632-639.

Cowman, S., M. Royston, A. Hickey, F. Horgan, H. McGee, and D. O'Neill. 2010. Stroke and nursing home care: a national survey of nursing homes. *BMC Geriatr* 10:4.

Jansen, L. A. 2022. Medical Beneficence, Nonmaleficence, and Patients' Well-Being. *J Clin Ethics* 33 (1):23-28.

Kluger, B. M., P. Hudson, L. C. Hanson, R. Buzgova, C. J. Creutzfeldt, R. Gursahani, M. Sumrall, C. White, D. J. Oliver, S. Z.

Pantilat, and J. Miyasaki. 2023. Palliative care to support the needs of adults with neurological disease. *Lancet Neurol* 22 (7):619-631.

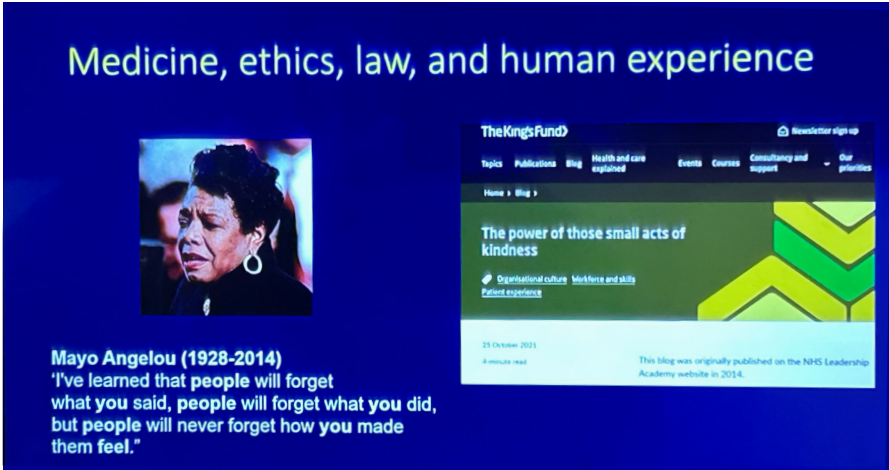
Paolucci, S., and J. Ngeh. 2015. Suicide in stroke survivors: frequency and risk factors. *Neurology* 84 (17):1724-5.

Prick, J. C. M., S. M. van Schaik, I. A. Deijle, R. Dahmen, Pjam Brouwers, P. H. E. Hilkens, M. M. Garvelink, N. Engels, J. W. Ankersmid, S. H. J. Keus, R. The, A. Takahashi, C. F. van Uden-Kraan, P. J. van der Wees, R. M. Van den Berg-Vos, and Vbhc Stroke group Santeon. 2022. Development of a patient decision aid for discharge planning of hospitalized patients with stroke. *BMC Neurol* 22 (1):245.

Steigleder, T., R. Kollmar, and C. Ostgathe. 2019. Palliative Care for Stroke Patients and Their Families: Barriers for Implementation. *Front Neurol* 10:164.

Visvanathan, A., G. E. Mead, M. Dennis, W. N. Whiteley, F. N. Doubal, and J. Lawton. 2020. The considerations, experiences and support needs of family members making treatment decisions for patients admitted with major stroke: a qualitative study. *BMC Med Inform Decis Mak* 20 (1):98.

Wijeratne, T., D. W. Dodick, S. L. Lewis, and W. Grisold. 2023. World Brain Day 2023 “Brain health and disability; Leave no one behind a World Federation of Neurology (six regions) and World Federation of Neurorehabilitation Collaboration. *J Neurol Sci* 451:120733



Slide shown by Prof. Mead at the WSO session in Toronto (reproduced with permission). Prof. Mead quoted Maya Angelou.

26th World Congress of Neurology Plenary Speakers

Plenary speakers shared their latest research on topics such as diabetic neuropathies, Parkinson's disease, ALS, and global health care equity.

The 26th World Congress of Neurology was held Oct. 15-19 in Montreal. This combined in-person and virtual meeting was attended by over 3,500 neurologists from 129 countries. The highlight of the meeting was a series of plenary lectures given by world experts in a variety of subjects, ranging from a rare disease to neuroepidemiology. They brought their insights into a plethora of important neurological problems, from rare diseases to the World Health Organization's plan to address neurological diseases across the globe. Summaries and salient messages are presented below. All of the subjects covered important issues that concern neurologists and that can potentially affect billions of people around the world.

—Guy Rouleau, vice president of the WFN



Hosted in Montreal, the 2023 World Congress of Neurology united experts to address key neurology challenges. Plenary speakers shared their latest research on topics such as diabetic neuropathies, Parkinson's disease, ALS, and global health care equity.

Dr. Tarun Dua from the World Health Organization emphasized the urgency in tackling neurological disorders, shaping a collaborative atmosphere.

The congress served as a hub for diverse perspectives and initiatives. Explore the discussions in each plenary lecture by reading the full press releases linked with each lecture.

The Global Importance of Diabetic Neuropathies

Eva Feldman, MD, PhD, James W. Albers Distinguished University Professor, and Russell N. DeJong, Professor of Neurology, University of Michigan

Type 2 diabetes has reached epidemic proportions, and complications like ulcers and amputations not only impact quality of life but also strain health care systems worldwide. During her plenary lecture, Dr. Eva Feldman cast a light on diabetic peripheral neuropathy (DPN), a major complication of diabetes and a leading cause of global disability. Discover the latest insights into the global burden of DPN and learn about the urgent need for new treatment approaches, education, and lifestyle changes to combat this worldwide challenge.

[Read the full press release.](#)

The WHO, IGAP, and Brain Health

Tarun Dua, MD, Head, Brain Health Unit, World Health Organization, Switzerland

Neurological conditions are the second-leading cause of death and the leading cause of disability worldwide. The World Health Organization's new Intersectoral Global Action Plan provides a critical blueprint for combating neurological conditions and calls for urgent action from governments and health care organizations around the world. Dr. Tarun Dua discussed this landmark coordinated effort to tackle the challenges posed by neurological disorders, including the five key objectives for addressing these conditions worldwide and 10 global targets to be achieved by 2031.

[Read the full press release.](#)

The Epidemiology and Burden of Neurological Disorders

Valery Feigin, MD, PhD, Professor of Neurology and Epidemiology, National Institute for Stroke and Applied Neurosciences, Auckland University of Technology, New Zealand

Low- and middle-income countries currently experience a disproportionate degree of the global burden of neurological disorders. Dr. Valery Feigin revealed groundbreaking findings from the latest Global Burden of Disease (GBD) study. Learn about the top 10 neurological conditions causing 90% of global disability and see how this data can aid neurologists and global health

organizations in reducing health care disparities in low- and middle-income countries.

[Read the full press release.](#)

Status of Disease-Modifying Therapy in Parkinson's Disease

Anthony Lang, MD, Professor of Neurology, Jack Clark Chair for Parkinson's Disease Research and Lily Safra Chair in Movement Disorders, University of Toronto, Canada

Parkinson's disease is one of the fastest-growing neurological diseases on the planet. But what if researchers could detect signs of the disease years before symptoms start to show? During his plenary lecture, Dr. Anthony Lang presented a groundbreaking new model for identifying and studying Parkinson's disease. This approach will help researchers investigate biological aspects of the disease that may be detectable many years before symptoms begin to show.

[Read the full press release.](#)

Clinical Trial Progress in ALS

Merit Cudkowicz, MD, Chair, Massachusetts General Hospital Department of Neurology; Director, Sean M. Healey & AMG Center for ALS, Massachusetts General Hospital; Julieanne Dorn Professor of Neurology, Harvard Medical School

One of the central challenges of amyotrophic lateral sclerosis (ALS) research is finding ways to slow the progression of this relentlessly degenerative disease. Several late-stage clinical trials in ALS have had positive results. In addition, recently, two promising experimental drugs were advanced to phase 3 clinical trials as part of the innovative HEALEY ALS Platform Trial. Dr. Merit Cudkowicz's lecture highlighted the drugs currently being tested in the HEALEY ALS Platform Trial as well as several other recently approved ALS medications, the promise of gene therapies, and a proposed new biomarker that is aiding in the development of treatments and research.

[Read the full press release.](#)

The Rett Syndrome: From Clinics to Genetics

Huda Zoghbi, MD, Professor of Molecular and Human Genetics, Baylor College of Medicine

Rett Syndrome is a delayed-onset childhood disorder that causes a broad range of severe neurological disabilities, including loss of the ability to speak and socialize, and the development of tremors, ataxia, seizures, autonomic dysfunction, and stereotypic hand-wringing movements. In her lecture, Dr. Huda Zoghbi, MD, discussed what her lab has learned about Rett pathogenesis and the significance of MeCP2 protein levels in maintaining healthy brain function. She outlined how an insufficient amount of this protein contributes to Rett syndrome, while an excess (resulting from gene duplication) leads to another severe neurological condition.

[Read the full press release.](#)

Transformations in the Treatment of Stroke

Liping Liu, MD, PhD, Director, Neurointensive Care Unit (NICU), Neurology and Stroke Center, Beijing Tiantan Hospital, Capital Medical University, China

Stroke is a leading cause of disability worldwide. However, giving certain treatments—called reperfusion therapies—soon after the start of a stroke can dramatically improve patient outcomes and minimize long-term brain damage. Dr. Liping Liu highlighted recent advancements in stroke treatment and strategies for addressing the global burden of stroke. She presented recent research on the effectiveness of reperfusion therapies for ischemic stroke and advocated for increasing awareness and training in these types of therapies for the global neurology community.

[Read the full press release.](#)

President of African Academy of Neurology Calls for Urgent, Unified Action to Address Lack of Trained Neurologists



THE WFN COMMITTEES AND SPECIALTY GROUPS

Publication Committee and the History of Neurosciences Specialty Group

Author reviews the history of the Neurosciences Specialty Group and reviews the function of the WFN Publications Committee.

BY CHANDRASHEKHAR MESHAM

This column, intended to explain the work of the WFN committees and specialty groups in World Neurology, was started by Prof. Wolfgang Grisold during his tenure as Secretary General in 2020. I plan to take it forward. The WFN committees contribute greatly to the work of the WFN. The chairs are appointed by the trustees, and the committees are composed of members of the regions.

The present composition and membership of all of the WFN committees and specialty groups can be seen on the WFN website.

The committees work on specific issues and are an essential part of the WFN activities.

In the September/October issue of World Neurology, information about the nominating committee was published.

The specialty groups, previously known as Applied Research Groups, focus on specific aspects of neurology.

The idea of this column is to introduce one committee and one specialty group in each of the subsequent issues of World Neurology.

The WFN Publications Committee

The WFN Publications Committee is chaired by Dr. John England. Dr. England is the Richard M. Paddison professor and chair of the Department of Neurology at the Louisiana State University Health Sciences Center School of Medicine in New Orleans. He is also the editor-in-chief of the *Journal of the Neurological Sciences*. The Publications Committee



JOHN ENGLAND



PETER KOEHLER

provides oversight for the *Journal of the Neurological Sciences*, *eNeurologicalSci*, and *World Neurology*.

The *Journal of the Neurological Sciences* (JNS) is the flagship journal of the WFN. JNS publishes original scientific articles, review articles, guidelines, letters, and special issues in the field of clinical and basic neuroscience. Over the last several years, JNS has shown a steady and substantial rise in platform usages, cite scores, and impact factor. Special issues are popular and well cited. Recently, a special issue on tropical neurology was published, and special issues on environmental neurology and recent advances in stroke are in progress.

eNeurologicalSci (eNS) is the new online companion journal for the JNS. Dr. Walter Struhal from Austria is the editor-in-chief. *eNeurologicalSci* has a globally represented editorial board and has demonstrated a steady and significant rise in cite score over the past two years. It publishes original scientific articles and novel case reports.

World Neurology is the popular longstanding newsletter for the WFN. The editor is Dr. Steven Lewis from



CHANDRASHEKHARA MESHAM

the U.S., and the co-editor is Dr. Walter Struhal from Austria. *World Neurology* publishes news items, updates, and opinions in neurology from around the world. *World Neurology* serves an important

function in communicating important updates from the WFN to neurologists. It is published every two months and is sent to 25,000 neurologists worldwide with two email blasts for each issue and online access.

Each of the three publications are accessible via the [WFN website](#) or via their respective websites.

History of Neurosciences Specialty Group

This specialty group has studied the history of the neurosciences for many decades. The mission is to study the history of the neurosciences and bring together neurologists with an interest in the subject and inform them about what is going on in the field.

In 1992, Frank Clifford Rose, who had become the WFN secretary-treasurer-general in 1989, started a journal, *Journal of the History of the Neurosciences*. It was associated with this WFN specialty group that, at the time, already existed for more than 10 years. This research group was founded by Dr. Macdonald Critchley, and its first official meeting was in 1980. A few years after starting

the journal, the International Society of the Neurosciences (ISHN) was added as a second group associated with the Journal, to which the subtitle was added Basic and Clinical Perspectives. It became a platform not only for neurologists interested in the field, but also for other neuroscientists with an interest in the history of their subject.

The specialty group is currently chaired by Peter J. Koehler, faculty of health, medicine and life sciences, Maastricht University, The Netherlands.

The group has 26 members and Egle Sakalauskaitė-Juodeikiene (University of Vilnius, Lithuania) and Edward J. Fine (University of Buffalo, New York) contribute significantly. The specialty group, in cooperation with the ISHN, started a monthly virtual seminar in 2020. These monthly meetings are open for specialty group and ISHN members, as well as all persons interested in the history of the neurosciences. They are usually held on the third Wednesday of each month, except northern summer. Information can be found at [ISHN-monthly-programs.pdf \(ucla.edu\)](#) or [ISHN Monthly Zoom Meeting | Neurohistory.nl](#).

Since 2010, the specialty group has published bimonthly articles in *World Neurology*. Some of the recent titles include “Todd, Faraday, and the Electrical Activity of the Brain,” “Named Lectures at the World Federation of Neurology,” and “Deep Brain Stimulation for Psychiatric Indications Preceded Movement Disorders: A Historical Sketch.” •

PRESIDENT'S COLUMN

continued from page 3

strong input for neurology in the region. For September 2024, we are planning a virtual educational update meeting: **World Federation of Neurology Digital Update 2024** (WNU2024) Sept. 26-27. Eminent speakers will provide an update on the most frequent diseases, and the meeting will offer online teaching courses on these topics.

It will be a useful update instrument between the WCN congresses. Updates, education, and CME will be the strategy. The meeting will be virtual only.

WFN educational days will be continued, with the AFAN WFN educational day on neuropathies on Feb. 17, 2024, followed by a joint headache day with AFAN and GPAC/IHS. Another educational day with the AOAN is

planned. This format has been successful, attracting many attendees, not only from the regions, but worldwide. Recordings of the meeting can be seen in the [WFN e-learning hub](#).

We need to encourage and increase our efforts for CME and continuous professional development (CPD) worldwide. This is an essential part of professional practice in neurology, and needs constant update and development. Worldwide, many countries have established CME programs, belonging to the portfolio of practicing neurologists and are often linked with recertification. Usually the time of participation in a meeting or an activity is converted into a system of credits. This works well for individual countries but, for many reasons, in most circumstances cannot be exchanged or compared.

For large international congresses such

as the WCN, the [UEMS EACCME](#) system is used, which has a detailed and strict separation of industry and other possible influences on the scientific program. This system is acknowledged by most European countries, and it also has an agreement with the American Medical Association and the Canadian Royal College of Physicians.

The WFN has a Standards and Evaluation Committee (chaired by Prof. Laszlo Vecsey) in place that receives applications for meetings and events which fulfil the criteria of the WFN. This committee endorses international meetings according to the requirements of the WFN. The endorsed meeting is allowed to use the WFN logo for its event.

This was a short update on important WFN activities. Please follow us on our website and social media as well as the new WFN service page in JNS for more information. •



BOOK REVIEW

Stroke: A History of Ideas

A book review of the history of cerebrovascular disorders.

Jan van Gijn. Cambridge University Press, 2023.

BY JAN STAM

Jan van Gijn hardly needs an introduction. He is well known for his clinical research of cerebrovascular disorders. He chaired the Utrecht team that made many contributions to our knowledge of different types of stroke, notably transient ischemic attacks and aneurysmal subarachnoid hemorrhage. Many participants of stroke conferences will remember his well-designed presentations, often illustrated with paintings by Dutch masters.

In September 2023, a Dutch national newspaper featured a long interview with Van Gijn. The occasion was his recently published book: *Stroke. A History of Ideas*. After his retirement, Van Gijn continued to study cerebrovascular diseases, but now mainly in the role of an historian of science, a career switch that resulted in this impressive monograph.

In the foreword, the author mentions some pitfalls for amateurs who write about the history of their own profession. One is consulting secondary, translated, and often unreliable sources. A second is known as *presentism*, the fallacy to reconstruct history, looking back from the vantage point of today's knowledge, as a rational process that leads in a straight line, through a sequence of major discoveries to the present. Van Gijn has avoided these pitfalls by thorough preparation. He studied Latin and enrolled as a student of history and philosophy of science.

The story begins with descriptions of apoplexy by Galen and other authors of Greco-Roman antiquity, followed by a brief overview of medieval thinking, which mainly recycled or paraphrased antique ideas, embedded in the then-dominant religious worldviews. The modern era starts about halfway in the 16th century with what is often called the medical renaissance.

During the 16th century, the ancient dogmas slowly made way for personal observations (*"auto-opsia"*) and insights, with the anatomist Andreas Vesalius (1514-1564) as one of the iconic innovators. Theories about the role of the ventricles as the site or origin of a neural signaling substance (such as Descartes' *esprits animaux*) or mental activity became obsolete, and the function of the circulatory system was slowly revealed. The era covered in the book ends in 1975, with a picture of the first CT scan showing a large pixelated image of a cerebral hemorrhage.

Numerous clinical case histories, often translated from Latin by the author,

increasingly large series of published autopsies, and finally the first prospective studies and trials, show how the ideas about stroke gradually changed. One of the first clinical observations was by Conrad Wolffhart (*Lycosthenes*; 1518-1561). He recovered from his own apoplexy and was able to give a careful description: "I not only lost my voice, but also all sensation and movement of the right side, from head to heel (except sight and hearing)". During his long recovery, he could communicate with his friends by pointing with his left index finger to the letters which were written on a slate in alphabetical order. He finally recovered almost completely, a miracle for which he thanked "God almighty in the first place, and thereafter Dr. Gratoloro". Van Gijn added a beautiful etching of Lycosthenes from the Rijksmuseum, Amsterdam, one of the many historical images that accompany the text.

As more causes of acute cerebral disorders were identified, the concept of apoplexy became diluted and could refer to about any kind of sudden cerebral dysfunction, by whatever cause, or spontaneously. Around 1800, more than 20 variants were distinguished, including nervous, traumatic, lymphatic, and abdominal apoplexy, orderly summarized in a table in a French treatise published in 1811. Autopsy findings often did not help, due to endless confusion about the nature and causes of brain softening (*"ramollissement,"* Chapter 6) and of infection and inflammation, which lasted until the mid-19th century. Chapter 7 describes the clarification of thrombosis and embolism as causes of brain softening, based upon the work of Rudolf Virchow (1821-1902) and others. The developing insights in the role of atherosclerotic changes of the carotid arteries are described in Chapter 8, including the discussion about the contribution of obstructed blood flow versus artery-to-artery embolism. The last four chapters discuss lacunae, transient ischemic attacks, subarachnoid hemorrhage, and sinus thrombosis. The increasingly important contributions of technological innovations, such as microscopy and the use of X-rays to the understanding the different kinds of stroke are given its due place in the final chapters.

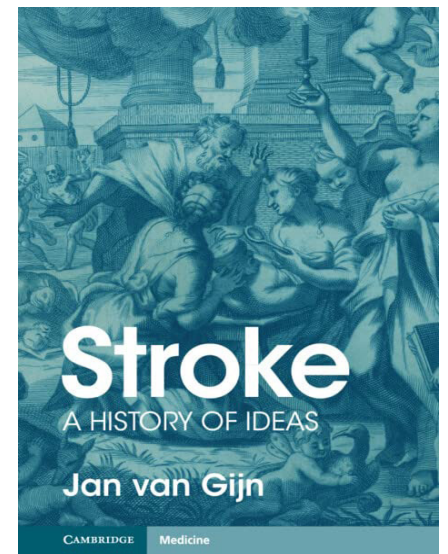
As we approach the year 1975, prevention and treatment, both surgical and medical slowly enter the scene. A background theme discernible throughout the book is Van Gijn's bibliophilia. Beautiful illustrations, often copied from

his own library, enliven the text, with interesting footnotes about illustrators and graphic techniques.

Additional historical context is presented in 43 boxes with short, highly readable, and often witty biographies of some prominent figures, such as Vesalius, Variolo, Wepfer, Willis, Virchow, Boerhaave, Charcot, Gowers, and Miller Fisher. Lesser-known physicians who contributed to the knowledge of stroke are also honored, such as Charles le Pois (1563-1633), who, perhaps not coincidentally, received the smallest box. Interesting asides enrich these brief portraits and show how these scholars were often active outside their medical practices or the autopsy theatre. Both Virchow and Egas Moniz (1874-1955) for instance were prominent national politicians. The first had severe disagreements with the Prussian Chancellor von Bismarck, apparently a risky position since he barely escaped a duel. Egas Moniz, known for introducing frontal leukotomy (honored with the Nobel prize in 1949) and for pioneering cerebral angiography, was imprisoned for republican activism when he studied medicine and later became a member of parliament, ambassador, and minister of foreign affairs.

Box 2.3 is dedicated to the Swiss physician and scholar Johann Jakob Wepfer (1620-1695). He was a vigorous proponent of post-mortem dissection, including of his own body after his death. In 1658, he was the first to carefully describe cases of apoplexy without apparent cause, which showed a hemorrhage in the brain at autopsy. He proposed that a rupture of an artery was the cause of the hemorrhage, agreeing with William Harvey's (1578-1657) theory of the circulation that was published 30 years before but still controversial. Wepfer acknowledged the senate of Schaffhausen for the permission to do post-mortem examinations and denounced those who, "led by whatever religion, maliciously proclaim that any corpse must be buried intact, while they themselves are destined to become food for the worms."

Wepfer's name is linked to the yearly award by the European Stroke Conference for outstanding researchers. Jan van Gijn was honored with the Wepfer award in 2010 for his many contributions to the clinical science of cerebrovascular disorders. In the laudation, Peter Sandercock called him a "renaissance man" because of his multifaceted interests and knowledge. The publication of this book confirms



that reputation. If a chapter with recent developments were ever added, Van Gijn would have to dedicate a box to himself. This must be one of the good reasons for the author to end the story in 1975.

The subtitle — a history of ideas — is explained in the final paragraph of the last chapter, on cerebral sinus thrombosis. After discussing the various concepts covered by the term *pseudotumor cerebri*, Van Gijn observes: "... names of diseases do not refer to entities that exist by themselves. They only stand for ideas."

Obviously, the book is much more than a history of mere ideas. To paraphrase Immanuel Kant: ideas without observations are empty, observations without ideas are blind. Ideas about stroke have been proposed, rejected, corrected, and developed through clinical observations, autopsies, technological innovations, microscopic and radiological research, and experiments.

This book provides a splendid insight into that process. It will be a standard reference about the history of stroke for many years to come, both for historians of medical science and for doctors interested in the history of neurology. •

Jan Stam is emeritus professor of Neurology, Amsterdam University Medical Centre, the Netherlands.

DEPARTMENT VISIT

My Experience in the Asian WFN Department Visit Programs

Author visited Postgraduate Institute of Medical Education & Research (PGIMER) in Chandigarh, India.

BY DR. DUC NGUYEN

2023 was a special year for me, a Vietnamese neurology resident, as I was honored to join the first Asian Department Visit Program by the World Federation of Neurology (WFN) and the Indian Academy of Neurology (IAN). This program allows young neurologists from low- to middle-income Asian countries to visit the Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh, India, and learn from its neurology department. Thanks to the arrangement of WFN and IAN, I achieved all the objectives of the program and more.

During my time at Nehru Hospital, I had the opportunity to deepen my expertise in neuro-ophthalmology, a specialty for which the hospital's neurology department is renowned. The faculty and residents at PGIMER shared their extensive knowledge and invaluable experience with me, enhancing my clinical acumen to diagnose and manage conditions, such as idiopathic intracranial hypertension (IIH), IgG4-related diseases, and ischemic optic neuropathy. For instance, I now place greater emphasis on measuring cerebrospinal fluid (CSF) pressure in patients who exhibit headache and disc edema, which are indicative of IIH.

Another area that I gained an understanding was the approach to the patients suspected of vasculitis as a cause of stroke in young individuals and as a differential diagnosis for demyelinating diseases. This has heightened my awareness significantly of angitis, marking an essential first step in the diagnostic process that could ultimately help prevent further deterioration.

I was impressed by the efficiency of using information technology in outpatient settings. It streamlined patient

management by saving time, ensuring thoroughness, and providing a concise summary of the patient's extensive history. In addition, my clinical skills, knowledge, and critical thinking have been enriched, particularly in formulating a working diagnosis list. I have also acquired valuable insights into maintaining an efficient medical and educational system within a dynamic environment.

As Prof. Aastha from PGIMER said, "The experience is more important than the knowledge." The Department Visit Program enabled me to immerse myself in an international academic environment, gain insight from diverse clinical contexts, network with new colleagues, and promote collaboration between countries. These experiences empower me to expand my knowledge and skills, foster my professionalism, and consequently help me advance the neurology specialty in my country. Hence, I strongly recommend this scholarship to young neurologists, especially trainees like me. I wish WFN, IAN, and PGIMER continued success with the future Asian Department Visit Programs.

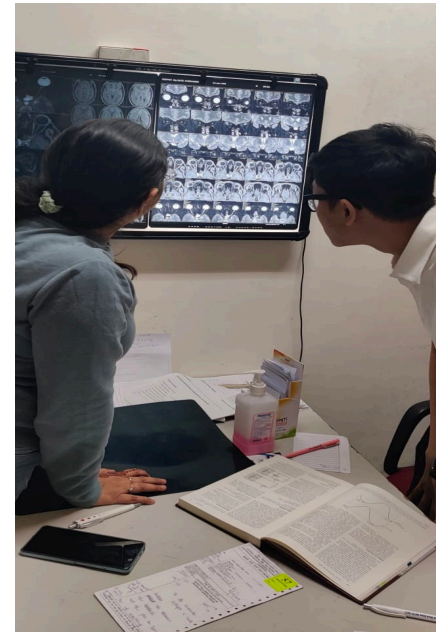
Acknowledgment

I am grateful to the World Federation of Neurology, Indian Academy of Neurology, and Post-graduate Institution of Medical for organizing such a valuable Department Visit Program for developing countries. I thank Prof. Vivek Lal and Prof. Aastha Takkar Kapila for their thoughtful and considerate arrangement for my stay. I also appreciate the hospitality and kindness of all the faculty members and residents of the Neurology Department from Nehru Hospital. •

Dr. Duc Nguyen is a neurology resident at the University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam.



I learned to use a handheld fundus camera and discussed a case of idiopathic intracranial hypertension in the neuro-ophthalmology clinic.



The EEG laboratory was where I visited to learn every afternoon.



Dr. Tanya Banerjee (right) and me in the outpatient setting.



Professor Vivek Lal on my last day at PGIMER.

Leveraging Technology in Resource Poor Settings: Not an Improbable Dream

Identifying problem statements, technology can help provide simple solutions that go a long way in bridging lapses in treatment.

BY DR. BINDU MENON AND DR. MEDHA MENON

Epilepsy, when put simply, is a brain disorder that causes recurrent seizures. This disease can manifest as the typical jerky movements of limbs as well as only sensory complaints recorded as electrical disturbances on electroencephalography (EEG). This wide variation of disease manifestation makes it a condition one must be wary of and have a high index of suspicion. The number of cases of epilepsy touches 50 million globally, 80% of whom reside in middle- to low-income countries like India¹.

It is important to realize why one must be wary of a disease that's prevalent in such high numbers. Surely, its ubiquity implies the presence of a well-structured management plan? However, the enormity of the problem can become the hamartia of the disease.

One must first realize that more than three-quarters of the disease burden resides in regions that are struggling to bridge the treatment gap. In a world where everything is run by money, the catastrophic expenditure on health burdens every family in the lesser privileged sections of economy. This expenditure encompasses costs of medication, hospitalization, and continuation of care. The onus to balance livelihood and health falls on the patient, and when this burden becomes too much, they tend to stop being compliant to treatment — an ignition to the vicious cycle of expense and hospitalization.

Another stark problem one sees



BINDU
MENON



MEDHA
MENON

in the lower income countries is the stigma attached to the disease. The typical flailing of limbs often described as demonic possession in archaic times still brings out a level of unnecessary discomfort in onlookers of a seizure episode. These thoughts are easily curbed through a proper understanding of the disease. In a way, the stigma that hurdles a patient's progress when vanquished empowers the community to provide moral support to the patient and their family.

The root of these problems is often lack of knowledge of the disease and so it is only natural that the solution is proper education and awareness. In this digitally advanced world, we must keep up and take advantage of the speed and extent of the reach of technology. Where once it was physically difficult to reach remote areas, in this day and age the internet and satellite connections help us reach the same areas remotely.

One such advancement is the Epilepsy Help App launched by our Foundation in India² April 2016 — a free mobile app that can be downloaded on Android phones. It is available in English as well as vernacular languages and keeps

record of a patient's personal details, appointments, and reports.

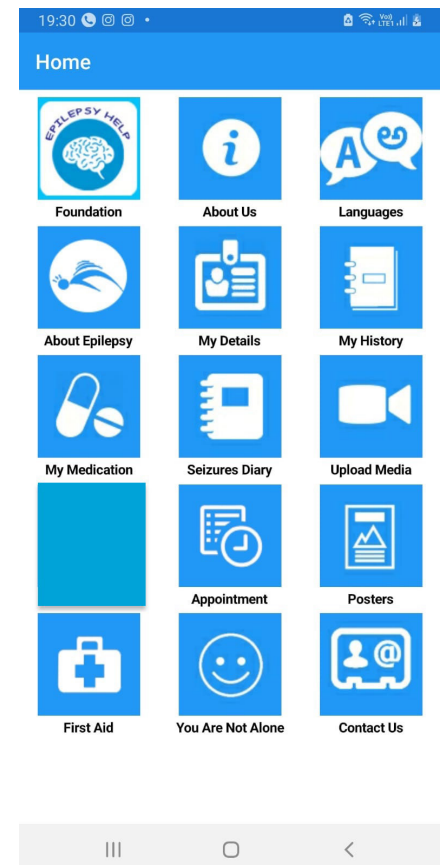
When a patient presents to the emergency department with a seizure, it is of utmost importance that the doctor knows which medication and dosage the patient is on. The app shows the record of patient's medications as well as has alarms for taking them, since a single missed medication can prove to be devastating to their life. Besides this, the patient can maintain a seizure diary within the app. The app has facilities for a bystander to take a video of a patient having a seizure attack, which proves to be of great value to a doctor to discern a diagnosis. On the whole, this app helps keeps track of a patient's disease for their as well as the doctor's benefit.

Among the patient stories we have permission to share was of one college student on three anti-seizure medicines. He often received different injections in the emergency department and was prescribed different cocktails of medicines due to his lack of record keeping. But with this app, he is documenting his prescriptions and scans and has currently been seizure free for eight months. The most useful feature for him, "For me, the drug reminder alarm is a huge help, and it makes sure I have not missed medications like I used to before."

Another story was about the usefulness of keeping a video diary. An office worker who stayed in the dorms away from his family suffered from jerky motions, which were misdiagnosed as a seizure attack. Hence, he was put on wrong medication. But record-keeping of videos at several instances — once in the dorms, another at his home, and one while he was outside with friends who all knew of the app in his phone, helped in reaching the right diagnosis of a nonepileptic attack disorder upon physician review.

Another application is a Tele Awareness³ initiative, which is a toll-free number that can be called to receive information about epilepsy. It is accessible to all, and this number when disseminated in large numbers when in medical camps, helps ensure that the general population is made aware of the disease, its risk factors, management, and the need for treatment compliance. Furthermore, it is in these medical camps that they are made aware that the societal stigma about the disease needs to be abolished.

Stroke is another disabling disease



that affects everybody differently. The life of a patient and their family changes drastically after a stroke which makes rehabilitation a crucial part of the spectrum of stroke care. Rehabilitation is all about getting back to a normal life and living a life as independently as possible. A venture in this direction is the Stroke Help app. This app has various physiotherapy exercises which are specific to the stroke deficits. The exercises are for passive and active limb exercises, handgrip and dexterity, positioning of the body, turning and mobilization, visual training, and balance exercises. This app has been extremely helpful for stroke patients especially during COVID, when medical services were not as accessible, but we did not want to falter in patient care. It is still being used⁴.

A novel project in the country is the Neurology on Wheels program where treatment-inaccessible areas are approached in a bus equipped with medical facilities. It follows the motto, "We Reach, We Teach, We Treat" Upon reaching the remote areas, there is an awareness camp followed by a medical camp with distribution of free medicines. An extension of this is We Care, wherein patients with epilepsy are followed up remotely. This is done with the help of the village head who gathers the patients in



Improving Brain Health in Honduras

Community education programs and the creation of the Neurology Postgraduate Program at the Universidad Nacional Autónoma de Honduras.

BY MARCO TULIO MEDINA, FAAN, FEAN

Neurological disorders are the leading cause of disability and the second leading cause of death both worldwide and in Honduras. Among these neurological disorders are cerebrovascular disease (or “derrames” in Honduran argot), Alzheimer’s disease, Parkinson’s disease, epilepsy, migraine, developmental disorders among others, which substantially affect the brain health of millions of human beings, including that of our fellow citizens

In May 2022, the Assembly of the World Health Organization (WHO) approved the Global Intersectoral Action Plan (IGAP) for Epilepsy and other Neurological Disorders, so that between 2022 and 2031, the countries of the world can improve the approach to brain health through specific actions for prevention, treatment, rehabilitation, and palliative measures.

As highlighted in the recent scientific article led by Mayoba Owolabi and collaborators, global synergistic actions

are required to improve brain health for human development. (The author’s team participated as co-authors and the article was published in 2023 in the British journal *Nature Reviews Neurology*.)

In Honduras, after a process of community intervention, we were able to reduce the frequency of a cerebral parasitosis, neurocysticercosis (incorrectly called “triquina” in Honduras), caused by fecal contamination by tapeworm or *Taenia solium* worms, in Salama, Olancho, through environmental sanitation measures and the educational campaign “the piggy is not to blame,” among others. Access to anti-epileptic drugs was also improved, thereby reducing the treatment gap.

The training of human resources has been another great challenge. The creation of the Neurology Postgraduate Program at the Universidad Nacional Autónoma de Honduras (UNAH), 25 years ago, has trained 37 neurologists and neurologists in our country to date. This postgraduate program had

the support of the World Federation of Neurology (WFN), as well as the late U.S. professor, Ted Munsat, among many other national and international collaborators.

The creation of this postgraduate program had many detractors, who argued that there were not the necessary conditions in Honduras for its development, but despite these critics, the postgraduate course was certified worldwide for its high quality in 2006 by the WFN and named a WHO collaborating center for research and community intervention in epilepsy (HON01), thus supporting the Strategic Plan and action of the Pan American Health Organization (PAHO) between 2011 and 2022.

On Nov. 6, 2023, at UNAH, we had the presence of the Secretary-General of WFN, Prof. Steven Lewis, our mentor from the University of California at Los Angeles, Prof. Antonio V Delgado Escueta, with whom we have jointly published more than 40% of our indexed scientific papers and who has contributed a patent to UNAH, as well as the distinguished academic and dear Costa Rican friend Prof. Franz Chaves-Sell. Along with the university community, we celebrated a quarter of a century of advances in neurology and the foundation of his postgraduate program of excellence in our alma mater. •

Dr. Prof. Marco Tulio Medina is vice chancellor of International Relations at UNAH and past president of the Panamerican Federation of Neurological Societies.



TECHNOLOGY

continued from page 9

one place and sets up a telecommunication link to the doctor who can then follow up with each patient. This ensures compliance and treatment satisfaction especially in a resource-poor setting by curbing expenditure from both ends.

Technology doesn’t need to be used in grandiose gestures to be of use to the people. Identifying problem statements and finding simple solutions goes a long way in bridging lapses in treatment. A resource-poor country does not imply that the whole nation is lacking. Technologically linking the better-off areas to help the lesser privileged sections doesn’t have to be a lofty feat. Once the key to unraveling the tangled ball of problems is in sight, it is only

a matter of like-minded individuals putting smart and economic solutions to improve health care. •

Dr. Bindu Menon is professor and head of the department at Apollo Speciality Hospitals in Nellore, India, secretary general of the Indian Epilepsy Association, and president of Dr. Bindu Menon Foundation. Dr. Medha Menon is resident in internal medicine at the Kasturba Hospital Manipal, India, and treasurer of the Dr. Bindu Menon Foundation.

References:

1. <https://www.who.int/news-room/fact-sheets/detail/epilepsy#:~:text=Key%20facts,%2D%20and%20middle%2Dincome%20countries>
2. <http://drbindumenon.com/epilepsyapp/>
3. <http://drbindumenon.com/teleawareness/>
4. https://play.google.com/store/apps/details?id=appinventor.ai_bindumenon2013.StrokeHelp



WORLD FEDERATION
OF NEUROLOGY

Connect with WFN

<https://wfneurology.org/>



The Global Neuro Research Coalition: A Call for Collaboration

Join the collective network of neurologists, neuroscientists, and allied specialty professionals to create a research environment that tackled problems of global neurology.

BY DR. ORLA HILTON

Founded in 2020, the **Global Neuro Research Coalition** works to advance research in global brain health and improve patient care through an ever-expanding international network of clinicians, allied health care workers, scientists, and policymakers who are passionate about brain health.



ORLA HILTON

COVID-19 was the initial catalyst for the founding of the then-called **Global COVID-19 Neuro Research Coalition**, as the global neurological community began to be confronted with the largely unknown effects of SARS-CoV-2 on the nervous system and the inequalities in the management of patients who developed neurological complications of the virus. We have now expanded our focus and established as the Global Neuro Research Coalition, comprising over 120 members from 38 countries, with skills and translational expertise spanning from basic neuroscience research to clinical neurology and guidelines/policy decision-making.

Our coalition invites and welcomes new members of the global neurological community to join our collective network of neurologists, neuroscientists, and allied specialty professionals to create an inclusive research environment that can better understand and tackle the ever-evolving problems the field of global neurology faces.

Our mission statement: *Advancing brain health research through interdisciplinary*

global collaboration.

The five pillars of the World Health Organization's (WHO) **Intersectoral Global Action Plan (IGAP) on Epilepsy and Other Neurological Disorders** lie at the heart of our mission, as we work to harmonize networks and strategies for future neurological research and to develop clinical guidance by establishing open lines of

communication between international colleagues and institutions, especially in low- and middle-income countries (LMICs).

The building and strengthening of such a coalition remain vital as we investigate and understand the long-term neurological and cognitive sequelae of COVID-19, and look forward to pursuing the translation of current and future neurological research into policies that promote a 'one health' approach.

To date, the coalition has published over 10 papers together. A key example of the power of our consortium to perform global neurological research is the **International Inter-observer Variability Study by Tamborska et al.** (*Journal of the Neurological Sciences*, 2023), undertaken in collaboration with the World Federation of Neurology. This brought together 146 researchers and clinicians from 45 countries, who looked at the diagnostic accuracy for the acute neurological complications of COVID-19 and demonstrated the need for training in the global reporting of neurological syndromes. Other key works of our coalition have addressed



Dr. Tamara Welte (Germany), scientific coordinator; Prof. Benedict Michael (UK), co-director; and Prof. Andrea Winkler (Germany), co-director



the neurological manifestations of acute COVID-19 infections. Examples include the **Consensus Clinical Guidance for Diagnosis and Management of Adult COVID-19 Encephalopathy Patients** by Michael et al. (*The Journal of Neuropsychiatry and Clinical Neurosciences*, 2023), in addition **Neurological Events Reported after COVID-19 Vaccines** by Frontera et al. (*Annals of Neurology*, 2022), and **Evaluation and Treatment Approaches for Neurological Post-Acute Sequelae of COVID-19** by Frontera et al. (*Journal of the Neurological Sciences*, 2023).

In addition, our coalition has also led to the creation of the **Global Brain Health Clinical Exchange Platform** in collaboration with the WHO. This platform hosts monthly free, online sessions, engaging hundreds of participants from over 50 countries to hear the latest from world leaders in neurology and exchange experience on the current challenges and future directions of a wide spectrum of neurological research. Topics have included the neuroepidemiology of

emerging pathogens, management of acute neurological presentations, patient-and-public engagement and long-term care, and the delivery of improvements in health care systems.

The coalition is grateful for the ongoing support of the World Federation of Neurology and our other partner institutions. We endeavor to continue to collaborate and partner in an interdisciplinary way with other medical and allied specialties, especially in LMICs which often carry the heaviest burden of neurological disease. We welcome all new members. If you are interested in becoming part of the coalition, please visit <https://www.liverpool.ac.uk/neurosciences-research-unit/knowledge-exchange/global-neuro-research-coalition/> and/or send an email to covidcns@liverpool.ac.uk. •

Dr. Orla Hilton (UK) is an academic foundation doctor in infectious diseases and clinical researcher for the national COVID-19 Clinical Neuroscience Study based at Infection Neuroscience Lab in Liverpool, UK.

PLENARY SPEAKERS

continued from page 5

Dr. Augustina Charway-Felli, President of the African Academy of Neurology

Africa is faced with critical shortages of neurologists and health care funding, leading to some of the world's highest rates of disability from neurological disorders. Dr. Augustina Charway-Felli presented a strategic plan at the WCN. The proposal underscores regional training to bolster Africa's neurologist count and prioritizes educating primary care providers. Dr. Charway-Felli advocated for a unified approach focusing on training, reducing brain drain, increasing specialized neurologists, and public education. Interregional collaboration and WFN accredited training centers in Dakar, Senegal; Rabat,

Morocco; Cairo, Egypt; and Cape Town, South Africa, are vital components. The plan aims to alleviate the severe neurologist shortage and improve neurological care accessibility in Africa. **Read the full press release.**

Kathy Oliver Champions Global Action for Patient Organizations at the 26th World Congress of Neurology

Kathy Oliver, chair of the International Brain Tumor Alliance

Patient engagement is gaining prominence in healthcare with Kathy Oliver championing this movement. Oliver emphasized the pivotal role of patient organizations in shaping clinical trials, drug development, health care policy, and regulatory issues. Patient engagement enhances

research quality and resource allocation by aligning with patients' priorities. Oliver highlighted five priorities for effective patient collaboration, stressing clear expectations, focusing on patients' perspectives, promoting mutual learning, fostering effective collaboration, and ensuring timely involvement. Central to this approach is the principle "nothing about us, without us," advocating for patient centrality in health care decisions. **Read the full press release.**

Neurologist Reveals the Hidden Neurological Consequences of Historic Pandemics

Hadi Manji, MD, Consultant Neurologist and Honorary Associate Professor at the National Hospital for Neurology, United Kingdom

Although the height of the COVID-19 pandemic may be behind us, millions of people continue to experience disabling complications like long COVID—and researchers still don't understand the full scope of COVID-19's impact on the brain. During the congress, Dr. Hadi Manji shed light on the neurological complications of COVID-19 by exploring similar long-term complications of global pandemics, including the Spanish flu pandemic of 1918, HIV/AIDS, and Zika virus. This enlightening lecture explored what past pandemics can teach us about diagnosing and treating current post-infection complications like HIV-associated neurocognitive disorder (HAND) and long COVID, which impact millions of people worldwide. **Read the full press release.** •

The Online Mendelian Inheritance in Man (OMIM) Database

A useful genetic data repository for clinical neurologists.

FOREWARD BY MARTIN KRENN, DEPARTMENT OF NEUROLOGY, MEDICAL UNIVERSITY, VIENNA, AUSTRIA

A large number of neurological disorders are characterized by a strong genetic component, either in a monogenic or a more complex polygenic sense. This is illustrated by the extensive portion of the human genome actively expressed in the central and peripheral nervous systems. Over the past decade, new genome-wide sequencing technologies have enabled us to identify single-gene etiologies in an increasing number of cases. More recently, these methods have also entered clinical routine diagnostics. As most of these conditions are very rare, the utilization of publicly available genetic databases is of utmost relevance for clinical neurologists to better understand human gene-disease relationships in neurogenetic disorders.

The *Online Mendelian Inheritance in Man* (OMIM) database offers a widely used, comprehensive, and constantly updated compendium of a vast number of monogenic (Mendelian) conditions. It is based on the most recent biomedical literature and thus constitutes a particularly useful resource for clinicians, often referenced in genetic diagnostic reports. It can be expected that the clinical value of such repositories will further increase in the coming years, as new neurogenetic disorders are still being discovered at a rapid pace, and more targeted treatments for patients are being developed.

The Online Mendelian Inheritance in Man

CASSANDRA KNIFFIN ARNOLD AND JOANNA AMBERGER

In 1863, Nikolaus Friedreich described a juvenile-onset form of hereditary ataxia (Friedreich ataxia). Several years later, George Huntington described an adult-onset hereditary chorea (Huntington disease). Nearly 100 years later, these familial genetic neurologic disorders, along with over 1,400 other genetic disorders, were included in Dr. Victor McKusick's seminal textbook *Mendelian Inheritance in Man: Catalogs of Autosomal Dominant, Autosomal Recessive, and X-linked Phenotypes* (MIM). These catalogs were updated and published regularly, and in 1987, MIM was made freely available and searchable online as OMIM™. Today, www.OMIM.org is a continuously updated, freely available compendium containing over 27,000 structured descriptions of human genetic disorders and genes. Currently, OMIM describes over 7,400 disorders caused by pathogenic variants in over 4,800 genes. On average, over 35,000 clinicians and researchers worldwide use OMIM daily to assist in disease gene discovery, clinical diagnosis, and management of genetic diseases, as well to understand the molecular bases of disease and the underlying medical science.

The information in OMIM is based on the peer-reviewed biomedical literature. Priority for inclusion in the database is given to published papers that provide significant insight into the phenotype-genotype relationship, expand our understanding of human biology, or contribute to the characterization of a genetic disorder.

Each OMIM entry (phenotype or gene) has a preferred title, with alternative names if relevant, and is given a unique 6-digit number that remains stable, even if the name changes. These OMIM accession numbers are used widely in publications and databases. OMIM entries are text-based and organized into consistent headings. Gene entries include information on gene structure, expression, function, animal models, and allelic variants, when available. Phenotype (disorder) entries include information on clinical features, inheritance, pathogenesis, genotype-phenotype correlations, and molecular genetics. In addition, each phenotype entry has an accompanying Clinical Synopsis, a concise tabular anatomical listing of the clinical features described in patients with

the disorder. The relationship between phenotypes and genes is summarized in OMIM's tabular Gene Map.

From its inception, MIM has played a foundational role in the nosology and naming of genetic disease.

In general, the naming and classification of disorders (phenotypes) in OMIM reflect that used in the respective medical community or as designated in the published paper(s).

OMIM curators evaluate reports of new phenotypes in the context of those present in the catalog and consider the following questions.

- How many patients have been described in how many reports?
- What shared features actually define the phenotype, and how thorough are the clinical descriptions?
- Does this constellation of features represent a new entity?
- Do the different features of a disorder constitute clinical variability of a single disorder or define separate disorders?
- Have the same or similar features been described under a different name?
- Is the phenotype similar to others in OMIM?
- Can the phenotype be classified with any other disorders?

Answering these questions must also take into account the views and possible disagreements in the genetics community as well as published nosologies. Since the definition of a phenotype (constellation of features) as a genetic entity is an evolving process, the names of a disorder in OMIM may change over time, but an OMIM number remains stable. Disease names should be unique, enhance clinical care and classification, and be easy to communicate. Acronyms and eponyms can both serve in this capacity, although eponyms should be used sparingly. When disease names, designations, and classification schemes are not provided in the papers or are not agreed upon in the medical community, the process of disease naming and classification involves defining recognizable patterns of features and highlighting those that allow one condition to be distinguished from another. For new disorders, the three to five most clinically significant features are selected to create an acronym or initialism that is both informative and memorable. It may seem appealing to name a genetic disorder after a gene; however, this is not recommended for several reasons. Patients present with clinical features,



and not all phenotypes have a recognized molecular basis. Importantly, many people around the world will not be sequenced and their conditions should be catalogued. Additionally, one-third of disease genes cause more than one phenotype, each with its own unique features, prognosis, molecular pathogenesis, and treatment. Phenotypes and genes are distinct concepts, and their names should change appropriately and independently to reflect greater knowledge. The OMIM number unifies clinical names and aliases under a single identifier.

If the same or similar phenotype exists in OMIM but that phenotype is caused by variants in a different gene, the existing name is used and a serial number is added at the end. These genetically heterogeneous phenotypes are then assembled into "Phenotypic Series" and given a unique PS accession number. Grouping similar phenotypes using clinical naming provides unique insights into molecular mechanisms and disease etiology, and offers a broader context for understanding the complexity of similar diseases. Examples of genetically heterogeneous neurologic disorders include Charcot-Marie-Tooth disease (CMT, PS118220), hereditary spastic paraplegia (SPG/HSP, PS303350), spinocerebellar ataxia (SCA, PS164400), and developmental and epileptic encephalopathy (DEE, PS308350). The clinical synopses of members in a Phenotypic Series can be viewed side-by-side on the website; such a view reveals differences that can guide physicians toward the right diagnosis and management or treatment. Each Phenotypic Series sheds light on shared molecular pathology and mechanisms of disease and/or can reveal

new divergent avenues of investigation.

OMIM.org is freely accessible and is intended for use primarily by physicians and other professionals concerned with genetic disorders, by genetics researchers, and by advanced students in science and medicine. The entries have copious directed links to external resources including DNA and protein databases (GenBank, Ensembl, UniProt), clinical resources (genetic testing sites, ClinGen, Orphanet), genetic variant resources, (ClinVar, gnomAD), and animal model databases (Mouse Genome Informatics, OMIA). OMIM supports programmatic access to its content via an API (Application Programming Interface). Also available from OMIM.org is the service MIMmatch. MIMmatch is a way for a user to follow OMIM entries of interest and to find other researchers who may share interest in the same topics. Registered MIMmatch users are able to receive alerts about updates to genes and diseases of interest and/or receive notification of new phenotype-gene relationships added to OMIM. Help in using OMIM.org is available from the website with both written guides and short video tutorials.

For over 55 years, OMIM has chronicled the collected knowledge of the field of medical genetics and remains one of the primary repositories of curated information on both genetic disorders (phenotypes) and genes and the relationships between them. •

Cassandra Kniffin Arnold, MD, is senior medical writer, and Joanna Amberger is program manager at OMIM, Johns Hopkins University in Baltimore, Maryland. Dr. Martin Krenn, PhD, is from the Department of Neurology, Medical University of Vienna in Austria.

Placebo/Nocebo and the Brain

Toward a pharmacology and toxicology of words.

Placebo and recently the term nocebo are often used in situations where uncertain effects, possibly the effect of the mind works, and have been often disregarded as scientific activities. All of us working with patients are implicitly using the concept of placebo, and sometimes the negative prediction, the nocebo.

As members of the health profession, we are part of placebo effect, and investigations have shown that also in regular approved and effective drugs a percentage of placebo effect can be calculated. The awareness of these important effects are important. The perception of placebo effect can in several instances be blocked or denied by cultural practices, and for neurology, it is important to spread and enhance the global perception.

Prof. Benedetti has worked on the placebo effect over many years and has given the placebo effect a rational and scientific background.

We are pleased that Prof. Benedetti has accepted our invitation and given a short summary of his important work.

- Wolfgang Grisold

FABRIZIO BENEDETTI, MD, MAE

Modern medicine and neurology have progressed in parallel with the advancement of biochemistry, anatomy, and physiology. By using the tools of modern medicine and neurology, today the physician and the neurologist can treat and prevent a number of diseases through pharmacology, genetics, and physical interventions, including surgery. In addition to this *materia medica*, the patient's mind, cognitions and emotions play a central part as well in any therapeutic outcome. Placebo effects are at the very heart of these issues and, maybe paradoxically, they can be approached by using the same biochemical, cellular, and physiological tools of the *materia medica*, which represents an epochal transition from general concepts such as suggestibility and power of mind to a true physiology and biology.

Placebo effects remind us of the old tenet that patients must be both cured and cared for, and they teach us that these complex issues can today be investigated by using a physiological and neuroscientific approach. The intricate psychological factors involved can be approached through biochemistry, anatomy, and physiology, thus eliminating the old dichotomy between biology and psychology. This is both a biomedical and a philosophical enterprise that is changing the way we approach and interpret medicine, neurology, and human biology.

In the first case, curing the disease only is not sufficient, and care of the patient is of tantamount importance. In the second case, the philosophical debate about the mind-body interaction can find some important answers.

Although a terminological confusion still persists and the terms placebo effect and response are often used

interchangeably, placebo effect could be considered different from placebo response. In the same way as the drug response is the global response to drug administration, so the placebo response is the whole response to placebo administration, including natural history of disease, regression to the mean, and such like.

Conversely, in the same way as the drug effect is the specific pharmacodynamic effect of a drug, so the placebo effect is the specific effect of placebo administration, that is, the real psychobiological phenomenon deriving from the psychosocial context around the patient. What neuroscientists have learned over the past few years is placebos are not inert substances. Instead, they are constituted of different words and therapeutic rituals as well as of different symbolic elements which, in turn, can influence the patient's brain, thus they are amenable to classic neuroscientific investigation. Therefore, overall, a placebo is the whole ritual of the therapeutic act. Neuroscientists use the placebo effect as a model to understand how the human brain works, and indeed the study of the placebo effect is today a melting pot of concepts and ideas for neuroscience. In fact, there is not a single but many placebo effects, and there is not a single but many mechanisms across different conditions and interventions. The nocebo effect goes in the opposite direction, namely, clinical worsening after negative words that induce negative expectations.

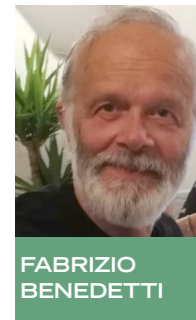
In neurology, the most studied and understood conditions where placebo effects have been investigated in depth are pain and Parkinson's disease. In pain, the opioid system activation by placebos is the most understood, as shown by the blockade of placebo analgesia by the opioid antagonist naloxone and by in vivo brain imaging of endogenous

opioid release. By contrast, the cholecystokinin (CCK)-antagonist, proglumide, enhances placebo analgesia on the basis of the anti-opioid action of CCK, whereas the activation of the CCK type-2 receptors by means of the agonist pentagastrin disrupts placebo analgesia. Therefore, the activation of the CCK

type-2 receptors has the same effect as the opioid receptor blockade, which suggests that the balance between CCKergic and opioidergic systems is crucial in placebo responsiveness in pain. Some brain regions in the cerebral cortex and the brainstem are affected by both a placebo and the opioid agonist remifentanyl, thus indicating a related mechanism in placebo-induced and opioid-induced analgesia. A role of the CB1 cannabinoid receptors has also been found in some types of placebo analgesia that is not mediated by endogenous opioids. The CCK pro-nociceptive system has also been found to mediate the nocebo hyperalgesic effect. For example, expectation of pain increase leads to nocebo hyperalgesia, and this increase can be blocked by the CCK antagonist proglumide. Interestingly, there is compelling experimental evidence that the whole lipidic pathway, e.g. arachidonic acid, endogenous cannabinoid ligands, prostaglandins and thromboxane, is importantly involved in both placebo and nocebo effects, for example in hypoxia-induced headache.

In Parkinson's disease, dopamine receptors are activated in both ventral (nucleus accumbens) and dorsal striatum when a placebo is administered. The release of dopamine corresponds to a change of 200% or more in extracellular dopamine concentration, and it is comparable to the response to amphetamine in subjects with an intact dopamine system. Intraoperative single-neuron recording in Parkinson patients during the implantation of electrodes for deep brain stimulation, shows that the firing rate of the neurons in the subthalamic nucleus and substantia nigra pars reticulata decreases after placebo administration, whereas the firing rate of thalamic neurons in the ventral anterior and anterior ventral lateral thalamus increases, along with the disappearance of bursting activity in the subthalamic nucleus. Importantly, from a clinical point of view, these neuronal changes are accompanied by a reduction in muscle rigidity.

It is clear from this brief description that placebos modulate the same biochemical pathways that are modulated by drugs, such as narcotics and non-steroid anti-inflammatory drugs for pain as well as dopaminergic agents for Parkinson's



FABRIZIO BENEDETTI

disease, thus giving rise to the concept that placebos and drugs share common mechanisms of action. Overall, these findings provide compelling evidence for a true pharmacology and toxicology of words and of social interaction, thus leading to a new physiology of the doctor-patient relationship. Much remains to be done to understand

where, when and how placebos work, that is, in which medical conditions, in which circumstances, and how they affect the brain across different neurological disorders. This challenge is certainly worth undertaking, as it will provide important pieces of information for clinical practice, clinical trials, and a better understanding of the human brain. •

Fabrizio Benedetti, MD, is professor of neurophysiology at the University of Turin Medical School, Turin, Italy, and professor of medicine, physiology, and neuroscience for the Innovative Clinical Training, Trials and Healthcare Initiative (ICTHI), Zermatt, Switzerland. He has been nominated member of The Academy of Europe and of the European Dana Alliance for the Brain. He is author of the book *Placebo Effects* (Oxford University Press, 3rd Edition, 2020), which received the Medical Book Award of the British Medical Association in 2009. In 2012, he received the Seymour Solomon Award of the American Headache Society, in 2015 the William S. Kroger Award of Behavioral Medicine from the American Society of Clinical Hypnosis, in 2023 the Lifetime Achievement Award by the Society for Interdisciplinary Placebo Studies.

For additional information:

Benedetti F, Carlino E, Piedimonte A (2016) Increasing uncertainty in CNS clinical trials: the role of placebo, nocebo, and Hawthorne effects. *Lancet Neurol*, 15: 736-747.

Benedetti F (2020) *Placebo effects. Understanding the other side of medical care*. 3rd Edition, Oxford: Oxford University Press.

Frisaldi E, Zamfira DA, Benedetti F (2021) The subthalamic nucleus and the placebo effect in Parkinson's disease. In Swaab DF, Kreier F, Lucassen PJ, Salehi A, and Buijs RM (Eds). *Handbook of Clinical Neurology: The Human Hypothalamus: Middle and Posterior Region*. San Diego: Elsevier BV, pp 433-446.

Benedetti F, Frisaldi E, Shaibani A (2022) Thirty years of neuroscientific investigation of placebo and nocebo: the interesting, the good, and the bad. *Annu Rev Pharmacol Toxicol*, 62: 323-340.

Frisaldi E, Shaibani A, Benedetti F, Pagnini F (2023) Placebo and nocebo effects and mechanisms associated with pharmacological interventions: an umbrella review. *Br Med J Open*, 13: e077243.