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52nd Annual Scientific Meeting

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Letter from the President

Dear Colleagues,

I began to write this letter with a bit of trepidation, for fear of a loss of words and news; however, during preparatory notations, the list of accomplishments for the HMAA grew and grew as did my degree of pride, not personal, because after all personal pride is not a virtue, but for the HMAA!

Since our last conference, the pandemic has continued to rear its ugly head, with many organizations "battening down the hatches" and suspending much of their normal work. The members of the HMAA Board, especially the executive committee members have been hard at work preparing a vibrant program for our membership. In particular, there is a website development ongoing that will engage all members with information. I apologize for the delay, but we are confident the website capabilities will be well worth the wait. Paid Members will have the capability to find colleagues by name, specialty, geographic location, even medical school attended! Also, we will have discussion forums with chronologic entries which enable anyone to share opinion or simply keep up to date, interacting with the group more than simply once a year. (Anyone remember the patient chart, progress note section?!)

In August, 6 Board Members and 4 Presidents of our society were privileged to present lectures at the Magyar Orvos-Egeszsegugyi Vilagtalalkozo, Hungarian Physician World Meeting held at the Hungarian Academy of Sciences in Budapest. Hungarian physicians were also present from Singapore to Johannesburg!

Not to be outdone, many then attended the 15th Balatonfured Conference exceptionally planned and carried out by the Hungary Chapter of the HMAA, under the direction of Drs. Akos Koller, Adam Tarnoki and David Tarnoki. I encourage all members to participate at some point in their career to share your own experiences and teach, as is our responsibility. Appreciate not only the lectures, but the other concomitant programs such as small group poster presentations, discussions with attending physicians and simply interacting and sharing the "wisdom" these young students are hungry for.

Although this year's Sarasota scientific program might have fewer attendees due to travel bans, the Scientific Committee Chair, Dr. Stadler, has prepared a robust program. We look forward to having some extended lectures by a few colleagues and in particular to having more time for erudite and exchange of idea discussions, sharing clinical cases similar to the apparent rarer grand rounds or tumor board styles. We cannot imagine how Dr. Kinga Huzella and the social committee are preparing programs, for an uncertain number of attendees! We even plan to be able to provide live video streaming of the conference to those who cannot attend in person.

Please share your appreciation with members of the Board for their tireless work. Without naming other individuals, I must extend congratulations to our tireless Secretary, Dr Geza Acs, who keeps the machine running. Welcome to our Conference, thank you for your continued support and wishing everyone good health and Jo Munkat!

Ivan Harangozo, MD
President of HMAA

Letter from the President-Elect

Dear HMAA members and friends and first-timers,

I could not wait to be back in Sarasota. Even the pandemic could not prevent us to get together because we want to be here. I was not even sure if the hotel still would still be standing due to the major flooding last year and threats of demolition would be scheduled soon. Just like the first time I came in 1995, I want to see those smiling faces again. We are hungry to learn from each other not only about science but personal and professional challenges during this difficult period.

We are only getting tested because we know we can handle it. We are getting tested for our problem-solving skills not just for our treatment and diagnostic skills. We are facing challenges like we have never seen before. But we are here and together. Good to be back. We are working diligently to have a functioning website soon with many upgrades and we appreciate the patience of our membership.

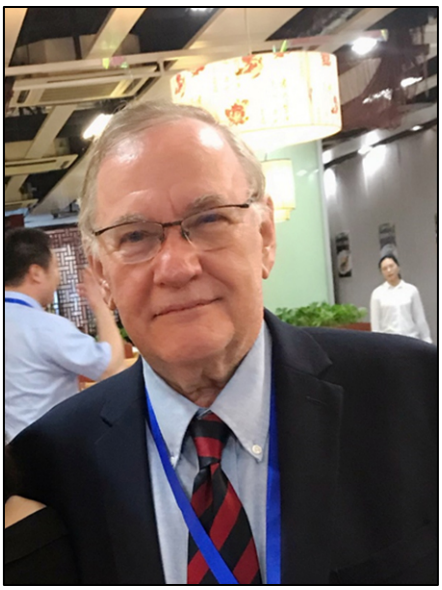
We had to temporarily suspend our student exchange program due to Covid in March of 2020. I am happy to announce that we reopened our Houston program on August 1st, 2021. We have four exchange students currently in the program and they will be with us and presenting at our meeting. The Buffalo program remains closed for now.

I would like to thank the HMAA Board and all the HMAA members for their hard work and tireless efforts to make our Annual Meeting continue to be a great success. Unfortunately, due to the travel restrictions, our Hungarian members are not able join us for the 2021 Annual Meeting but with their virtual talks they will be presenting their work and participating.

Welcome to the 52nd annual meeting of the Hungarian Medical Association of America!

Zsolt Garami, MD
President-Elect of HMAA

HMAA Hungary Chapter Report 2021



ORGANISATION

The board members of HMAA HC remained unchanged. The Hungarian Chapter (HC) launched its own website: www.hmaa-hc.hu, in Hungarian language. The HC page on HMAA website is still not updated (https://hmaa.org/chapters/hungary).

HMAA FURED2021 CONGRESS, BALATONFURED

The HMAA Hungary Chapter organized its 15th Hungarian (14th Balatonfured) multidisciplinary meeting in the State Hospital of Cardiology in Balatonfured on 27 – 28 August, 2021 in an in-person format, following the Congress of the World Meeting of Hungarian Medical Professionals in Budapest (Magyar Orvos-Egeszsegugyi Vilagtalalkozo, MOVT, https://magyarorvostalalkozo.hu/). Due to the Coronavirus pandemic, all participants had to wear a face mask during the congress.

A total of 145 medical students, residents, and PhD students participated in the HMAA Balatonfured Congress from all over the four Hungarian medical universities (Semmelweis University, Universities of Debrecen, Pecs and Szeged) registered and 75 attendees gave oral or poster presentations. This year, 35 invited guests also attended the meeting.

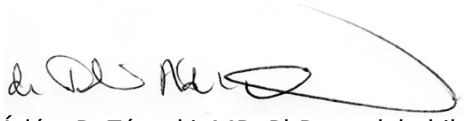
Similar to the previous years, the main aim of the congress was to create a forum for the young scientists in any medical field to present their own work for the audience in English or in Hungarian. The most important social programs were the waffle party and the dinner in Borcsa restaurant, where Prof. Dr. Ildiko Horvath, the State Secretary for Health also attended. The meeting was supported by Prof. Dr. Gabor Veress this year again who provided the venue for free. Drs. Adam and David Tarnoki, on behalf of the chief organizing committee would like to acknowledge the help of Prof. Akos Koller, Dr. Laszlo Csathy, and the student representatives and board members who contributed to the organization and helped to make the two days a memorable event. Over 75 abstracts were submitted, of which oral and e-poster presentations were selected based on the evaluation of the reviewers. The congress Program Committee would like to thank all the abstract reviewers for their time spent grading the abstracts received for HMAA Füred2021 congress.

It was an honor that HMAA President Dr. Ivan Harangozo was also present in the meeting. This year the highlighted lectures and topics were organized with the multidisciplinary sessions. These included: “Pandemic in Hungary” by Prof. Dr. Akos Koller and Prof. Dr. Attila Szabo (vice rector of Semmelweis University), “Traumatic Brain Injury: cerebral autoregulation and neuromonitoring” by Prof. Dr. Laszlo L. Mechtler. Also, a special Highlighted session, entitled ‘Language and Medical law” was organized and chaired by Eva Edes. Among the several special workshops, Dr. Richard Schwab discussed the new findings regarding Microbiome and Health (MIND Clinic) and Johanna Takacs introduced the mystery of statistics to the students. Numerous other well attended workshops were organized in various topics.

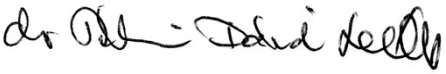
As always, Awards were given to the best performances. The Ivan Krisztinicz Award winner (best English lecture award) offered by Hungarian Medical Association of America Inc. was to Mr. Marton Simon Czikkely (Eotvos Lorand Research Network, Biological Research Centre, Szeged, Hungary) with his presentation titled “Next Frontier in Bacterial Genome Design - increasing the efficiency and extending the host range of recombineering based genome engineering”. The winner of the Istvan Mechtler Award (best Hungarian lecture award) offered by Laszlo L. Mechtler MD and Stephen Mechtler, MD was Ms. Tünde Tóth (Department of Anatomy, MTA-PTE PACAP Research Team, Centre for Neuroscience, University of Pecs), the title of her presentation was “Investigation of

pituitary adenylate-cyclase activating polypeptide in Parkinsonian patients). The full program, the pictures of the congress, list of winners, publications and more information are available at www.hmaa-hc.hu website. For more information on the HMAA/hungarian chapter, please visit www.hmaa-hc.hu.

Respectfully,



Ádám D. Tárnoki, MD, PhD, med. habil.



Dávid L. Tárnoki, MD, PhD, med. habil.

Ákos Koller, MD, PhD, DSc.
President, Hungary Chapter of HMAA

CURRENT DEVELOPMENTS IN BIOMEDICAL AND CLINICAL SCIENCES

Abstracts of the 52nd Annual Scientific Meeting of the Hungarian Medical Association of America

Sarasota, FL, October 24 – 29, 2021

PHYLLODES TUMORS OF THE BREAST

Acs, G.

Women's Pathology Consultants, Ruffolo Hooper & Associates and Department of Pathology and Cell Biology, University of South Florida Morsani College of Medicine, Tampa, FL

Geza Acs, MD, PhD

Medical Director, Women's Pathology Consultants, Ruffolo Hooper & Associates, Tampa, FL and Professor of Pathology and Cell Biology, University of South Florida Morsani College of Medicine, Tampa, FL

Secretary, HMAA

Dr. Geza Acs served as member of the Board of Directors in 2006-2008 and he is the Secretary of the HMAA since 2008. He received his MD and PhD from the University of Debrecen School of Medicine. He served as Postdoctoral Fellow at the National Cancer Institute in Bethesda, MD and trained in Anatomic Pathology and Surgical Pathology at the Hospital of the University of Pennsylvania in Philadelphia, PA. Dr. Acs served as Assistant Professor of Pathology and Laboratory Medicine at the University of Pennsylvania Perelman School of Medicine and subsequently as Associate Member at the Moffitt Cancer Center and Associate Professor of Oncologic Sciences and Pathology and Cell Biology at the University of South Florida Morsani College of Medicine, Tampa, FL. Dr. Acs is currently Medical Director of Breast and Gynecologic Pathology at Women's Pathology Consultants, Ruffolo Hooper & Associates and Professor of Pathology and cell Biology at the University of South Florida Morsani College of Medicine in Tampa, FL. His research interests focus on the mechanisms of lymphatic tumor metastasis, and histologic and molecular prognostic/predictive factors in breast cancer.

Aim: Phyllodes tumors constitute an uncommon but complex group of mammary fibroepithelial lesions. Accurate and reproducible grading of these tumors has long been challenging, owing to the need to assess multiple stratified histological parameters, which may be weighted differently by individual pathologists.

Methods: Based on a review of the literature and the author's personal experience, this presentation consolidates the current understanding of the pathobiology and clinical behavior of phyllodes tumors and includes proposals for a rational approach to their classification and management.

Results: Distinction of benign phyllodes tumors from cellular fibroadenomas is fraught with difficulty, due to overlapping microscopic features. Similarly, separation of the malignant phyllodes tumor from spindle cell metaplastic carcinoma and primary breast sarcoma can be problematic. Phyllodes tumors are treated by surgical excision. However, there is no consensus on the definition of an appropriate surgical margin to ensure completeness of excision and reduction of recurrence risk.

Conclusions: Interpretive subjectivity, overlapping histological diagnostic criteria, suboptimal correlation between histological classification and clinical behavior and the lack of robust molecular predictors of outcome make further investigation of the pathogenesis of these fascinating tumors a matter of active research.

COVID-19 AND NFALD: WHEN TWO PANDEMICS COLLIDE

Baffy, G.

Brigham and Women's Hospital and VA Boston Healthcare System, Harvard Medical School, Boston MA

Gyorgy Baffy, MD, PhD

Associate Professor of Medicine, Harvard Medical School and Chief of Gastroenterology at the VA Boston Healthcare System, Boston, MA

Past-President and Member of the Advisory Council, HMAA

Dr. Gyorgy Baffy served as President of HMAA (2012-2014). He received his MD from the University Debrecen and his PhD as an NIH Fogarty Fellow at the University of Pennsylvania. He trained in gastroenterology at the University of Michigan and the Brigham and Women's Hospital. He is currently an Associate Professor of Medicine at Harvard Medical School and Chief of Gastroenterology at the VA Boston Healthcare System. His current research interests are in nonalcoholic fatty liver disease and hepatocellular carcinoma. He published over 80 scientific articles and book chapters. In 2014, he received a Fulbright US Scholar Award to teach at the University of Debrecen. He is a Fellow of the American Gastroenterological Association, the American Association for the Study of Liver Diseases, the American College of Gastroenterology and the American College of Physicians. He is the recipient of the Hetényi Medal and the Pro Optimo in Gastroenterologia award of the Hungarian Gastroenterological Association.

On 12/31/2019, the World Health Organization (WHO) was informed of pneumonia cases of unknown origin in Wuhan City, China. On 2/11/2020, the International Committee on Taxonomy of Viruses (ICTV) named the causative virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On 3/11/2020, the WHO declared COVID-19 as a global pandemic. By 8/15/2021, a total of 208M cases and 4.37M deaths have been registered. To the credit of human ingenuity and determination, a total of 2.4B people received at least one COVID-19 vaccination by the same time. The COVID-19 vaccine market size is projected to reach $75B by the end of 2021.

In 1980, the term nonalcoholic steatohepatitis (NASH) was coined. In 1986, nonalcoholic fatty liver disease (NAFLD) was mentioned for the first time to describe the spectrum of disease. In 2020, an international consensus panel recommended the term metabolic dysfunction-associated fatty liver disease (MAFLD), based on hepatic steatosis associated with obesity, diabetes and other metabolic derangements. It is estimated that there are up to 2B people affected by NAFLD, which has widely different outcomes from benign steatosis to cirrhosis and primary liver cancer. There is currently no licensed pharmaceutical therapy for NAFLD, while the potential market is estimated $40B.

Both diseases are immensely prevalent with highly heterogeneous outcomes. For many, having either disease has no major impact on their personal health and may not have a visible phenotype. Both diseases are associated with significant (and mostly voluntary) lifestyle choices. COVID-19 may require wearing a mask, practicing social distancing and submitting to vaccination. NAFLD may require physical exercise, dieting and weight management. However, there are major differences as COVID-19 is an infectious disease, while NAFLD is a noncommunicative disorder. They have a different time course and their prevention and containment demand different approaches. There are also significant interactions between these medical conditions. Patients with NAFLD, in particular those with advanced stages, infected with SARS-CoV-2 may have an increased risk of severe COVID-19. This is likely due to markedly higher liver expression of proteins that allow viral entry and altered anti-viral responses. Moreover, the liver inflammatory response may contribute to the cytokine storm so characteristic of severe COVID-19. On the other hand, public health measures in response to the COVID-19 pandemic resulted in diminished physical activity, limiting the impact of lifestyle interventions as the primary treatment of NAFLD. More research is needed to fully recognize the interplay of the two pandemics.

SUBLINICAL PORTAL HYPERTENSION IN NAFLD: DETECTION AND CLINICAL SIGNIFICANCE

Baffy, G.

Brigham and Women's Hospital and VA Boston Healthcare System, Harvard Medical School, Boston MA

Gyorgy Baffy, MD, PhD

Associate Professor of Medicine, Harvard Medical School and Chief of Gastroenterology at the VA Boston Healthcare System, Boston, MA

Past-President and Member of the Advisory Council, HMAA

Dr. Gyorgy Baffy served as President of HMAA (2012-2014). He received his MD from the University Debrecen and his PhD as an NIH Fogarty Fellow at the University of Pennsylvania. He trained in gastroenterology at the University of Michigan and the Brigham and Women's Hospital. He is currently an Associate Professor of Medicine at Harvard Medical School and Chief of Gastroenterology at the VA Boston Healthcare System. His current research interests are in nonalcoholic fatty liver disease and hepatocellular carcinoma. He published over 80 scientific articles and book chapters. In 2014, he received a Fulbright US Scholar Award to teach at the University of Debrecen. He is a Fellow of the American Gastroenterological Association, the American Association for the Study of Liver Diseases, the American College of Gastroenterology and the American College of Physicians. He is the recipient of the Hetényi Medal and the Pro Optimo in Gastroenterologia award of the Hungarian Gastroenterological Association.

Recent advances in the detection, magnitude and pathobiology of early portal hypertension in nonalcoholic fatty liver disease (NAFLD), primarily observed in the presence of nonalcoholic steatohepatitis (NASH), prompt us to revisit certain disease paradigms. This talk will focus on 3 aspects of the relationship between NAFLD and portal hypertension that remain controversial and incompletely understood.

First, hepatic venous pressure gradient (HVPG), which is currently the gold standard for the measurement of portal pressure, has been reported to underestimate portal pressure in NASH-cirrhosis and inaccuracy is more likely in the non-cirrhotic liver, due to a buffering effect of inter-sinusoidal channels and presumably due to contribution from presinusoidal components not detected by the retrograde approach. Thus, there is a need for new and preferably noninvasive methods of portal pressure measurement.

Second, while clinically significant portal hypertension (CSPH, defined by HVPG ≥ 10 mmHg) retains is prognostic significance in NASH, portal hypertension is a continuum that starts with even mildly or moderately increased portal pressure, which worsens and promotes disease progression with gradually increased risk for adverse clinical outcomes. Subclinical portal hypertension (HVPG, 6-9.5 mm Hg) in NAFLD has been repeatedly detected in the absence of cirrhosis or even significant fibrosis. The impact of these findings on pathophysiology and disease outcomes remains unclear and requires further research.

Third, there has been significant progress in the understanding of mechanocrine signaling pathways in various liver cells, which offers molecular basis for the adverse effects of early (i.e., non-CSPH) portal hypertension and suggest a bidirectional relationship between portal pressure and fibrosis. These findings may guide efforts to improve risk assessment and identify novel therapeutic targets in NAFLD.

"WHEN THE ANEURYSM ISN'T AORTIC…"

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Department of Emergency Medicine, University Hospital Kerry, Kerry, Ireland

Alexander Benyovszky, MD

Resident in Internal Medicine, Einstein Medical Center Montgomery, East Norriton, PA

Dr. Benyovszky is a graduate of the University of Pecs Medical School. He currently is a first year resident in Internal Medicine at Einstein Medical Center Montgomery in East Norriton, PA. Prior to his residency, he worked for many years as an Emergency Medicine Registrar in University Hospital Kerry, Ireland.

Case Report: A 70F was brought by ambulance to Kerry emergency department with sudden severe low back pain and collapse. The pain seemed to radiate out from her abdomen. On arrival, she was noted to be hypotensive but otherwise vitally stable. Her background was notable for autoimmune liver disease with portal hypertension and multiple previous bandings for esophageal varices. On assessment, patient was in considerable abdominal distress despite pre-hospital morphine. She was notably pale and jaundiced. There were no signs of vomiting or hematemesis. Her abdomen was soft, distended, diffusely tender with sluggish bowel sounds. Vital signs were BP 69/40; T 35; HR 85; RR 17; SPO2 97%. Bedside testing showed a hemoglobin of 9.0, and Lactate 4.4. The immediate differentials were a ruptured aortic aneurysm vs occult variceal bleed. Bilateral venous access, IV fluids, tranexamic acid, additional analgesia, and antiemetics were instituted, with a transient improvement in BP. Point of care ultrasound noted perihepatic and perisplenic free-fluid, but a normal abdominal aorta. Her abdominal CT scan identified a ruptured 20 mm splenic artery aneurysm with active bleeding into the left retroperitoneal space. Another 36 mm splenic aneurysm was also detected. The massive transfusion protocol was initiated and patient was successfully taken to OR for emergency laparotomy and splenectomy. She was in hospital for 16 days before being discharged home.

Conclusion: Up to 20% of patients with liver cirrhosis and portal hypertension develop splenic artery aneurysms. This diagnosis must be actively considered, particularly in older female patients whose clinical presentation strongly suggests a ruptured aortic aneurysm yet point of care ultrasound finds a normal aorta. Early diagnosis and swift management can save these lives.

LATE METASTASES OF MALIGNANT MELANOMA

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Beata Bodo, MS

Medical Student, Department of Dermatology and Allergology, University of Szeged, Szeged, Hungary

Beata Bodo is a medical student at the Department of Dermatology and Allergology, University of Szeged, Szeged, Hungary.

Aim: Malignant melanoma is considered as one of the most aggressive solid cancers due to its high potential of forming metastases. Metastases usually are reported within the first months or few years, however there are certain cases when lethal metastases appear later - even ten years after the initial diagnosis. Therefore, we are aiming to collect these late (> 10 years) metastatic cases and to examine the clinicopathology of the peculiar late melanoma dissemination.

Methods: In this retrospective analysis from 1990 we collected the disseminated stage IV melanoma patients. From them the late metastatic cases were selected, then detailed clinical data analysis and retrospective histopathological examination were made.

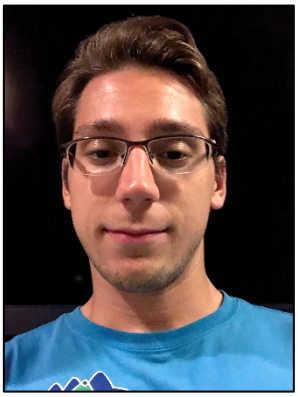
Results: From the last three decade, more than 300 disseminated cases were selected, from them 10 late metastatic patients were collected and their detailed case reports were performed.

Conclusion: Late melanoma metastases are rare, but not unusual findings. Our data highlighted the role of the (life) long lasting dermato-oncological surveillance for our melanoma patients since of the latent minimal residual disease capable of reactivation even decades after the initial diagnosis of melanoma.

HIGHLIGHT THE IMPORTANCE OF THE TREATMENT OF DEPRESSION

Bodrog, P.

Department of Public Health, University of Massachussetts Amherts, Amherts, MA



Patrick Bodrog

Pre-Med Student, University of Massachussetts Amherts, Amherts, MA

Patrick Bodrog is an Honors College Pre-Med student and undergrad researcher of neurodegenerative disorders. He is an experienced technician in Mental Health, currently treating depression and anxiety as a Certified Transcranial Magnetic Stimulation (TMS) Technician and Emergency Medical Technician. He is an intern at South Boston TMS Psychiatric Clinic and volunteers at a neighboring Substance Abuse Clinic. He is tutoring at the Honors College of the University of Massachusetts UMASS Amherst.

Aim and Methods: This presentation includes a review of the current impact untreated depression can have on health, as well as a review of the current standards for depression treatment. The Sequence Treatment Alternatives to Relieve Depression (STAR*D) study is examined to determine the efficacy of current standards to treat depression. The mechanism of action for NeuroStar TMS as well as a review of 6 FDA approved neurostar TMS studies, including 2 multisite, randomized controlled trials, to determine NeuroStar TMS treatment efficacy.Methods: This is non-chemical and noninvasive method was developed in Boston to treat Depression then widely approved in the U.S. by FDA.

Results: Current treatments for depression have 30% success for remission for first line treatment with decreasing remission rates for subsequent attempts. The discontinuation of the current treatment ranged from 8.6% to 42.4% based on the number of treatment attempts. Compared to a sham treatment, the NeuroStar TMS treatment scored 2 points higher on the Hamilton depression 24-item Scale (HDRS24). The HDRS difference between the sham and NeuroStar TMS was significantly different at both the 4 week and six week intervals. Patients receiving active NeuroStar TMS therapy were four times more likely to achieve remission compared to patients receiving sham treatment (P = 0.0173; odds ratio = 4.05). Compared to the next choice of treatment, the NeuroStar TMS treatment had significantly higher response (P<0.0001) response and significantly higher (p<0.0001) remission rates after six weeks of treatment.

Conclusion: In summary, NeuroStar TMS is an effective, proven approach for patients with major depression when initial treatments have failed and for patients that would like to reduce their use of antidepressant medication and their accompanying side effects.

EFFECTS OF MEMBRANE CERAMIDES ON THE MEMBRANE LOCALIZATION AND GATING OF K_V1.3 ION CHANNEL

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Department of Biophysics and Cell Biology, University of Debrecen, Debrecen, Hungary

Bence C. Szabo, MD

PhD Student, Department of Biophysics and Cell Biology, University of Debrecen, Debrecen, Hungary

Dr. C. Szabo Bence is a 25 year, freshly graduated medical doctor. Currently he is starting his PhD in the Department of Biophysics and Cell Biology in Debrecen, Hungary. He has been part of the membrane-biophysics research group for 4 years now. He has been also working as a paramedic officer in the National Ambulance Service since January 2021

Aims: The gating of K_V1.3 voltage-gated potassium channel and its distribution between membrane microdomains (such as lipid rafts, ceramide platforms, and bulk membrane regions) strongly depend on the lipid composition of the cell membrane. As we demonstrated in our previous work, the membrane level of the essential lipid raft constituent cholesterol influences both of these functionally relevant parameters of the channel. On the other hand, the effects of C16-ceramide (Cer) and C16-glycosylceramide (GlcCer), two other membrane lipids contributing to the formation of membrane microdomains, have not been examined yet on the gating and membrane localization of K_V1.3 in spite of the pathological significance of these lipids in various diseases such as neurodegenerative and lipid storage disorders.

Methods: In this study, we examined the effects of loading the cell membrane with Cer or GlcCer on the localization and gating of K_V1.3 applying confocal microscopy and two-electrode voltage-clamp fluorometry (TEVCF). For microscopic imaging, we transfected CHO cells with K_v1.3-FLAG encoding plasmids, while membrane microdomains were labeled with GFP-GPI transfection and anti-ceramide antibodies for the visualization of lipid rafts and ceramide platforms, respectively. During quantitative image processing Pearson correlation coefficients were determined between K_V1.3, raft and ceramide platform markers in control samples and those treated with Cer or GlcCer to quantify their colocalization. TEVCF measurements were performed on K_V1.3 expressed in *Xenopus laevis* oocytes. With this technique besides measuring ionic current thereby monitoring the pore domain (PD), we are also able to characterize the movement of the voltage-sensor domain (VSD) of the channel during the gating process after labeling a cysteine residue introduced into this domain with TAMRA-MTS. By determining steady-state activation (G-V curves) and fluorescence-voltage relationship (F-V curves) we are able to identify the intramolecular target of ceramides.

Results: Increasing Cer level of the cell membrane significantly decreased the strongly positive Pearson coefficient between markers of K_V1.3 and lipid rafts, while increased that between the channels and ceramide platforms, suggesting a relocalization of K_V1.3 from lipid rafts to ceramide platforms. In contrast, treatment with GlcCer significantly increased the colocalization of the channel with lipid rafts without modifying that with ceramide platforms referring to enhanced lipid raft localization of K_V1.3. Distinctive effects of Cer and GlcCer loadings were further corroborated by TEVCF measurements. While both treatments shifted the G-V curves towards more positive membrane potential values, only Cer induced similar changes in the F-V curve and GlcCer exerted no significant effects on VSD movements. These results suggest that Cer modulates K_V1.3 function through affecting the VSD, whereas GlcCer targets directly the PD of the channel.

Conclusion: The intrinsic membrane components Cer and GlcCer affect the function of K_V1.3 channel in a distinct manner possibly through modifying its preferential localization in various types of membrane microdomains, which could play a substantial role in the pathomechanism of diseases characterized by increased ceramide levels.

Support: UNKP-21-3-I-DE-233, UNKP-21-4-II-DE-138, UNKP-21-4-II-DE-137, OTKA K132906, OTKA FK138386, OTKA FK137796 and SNN139532

NEXT FRONTIER IN BACTERIALGENOME DESIGN – INCREASING THE EFFICIENCY AND EXTENDING THE HOST RANGE OF RECOMBINEERING BASED GENOME ENGINEERING

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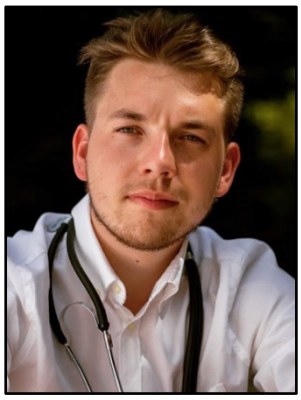
[1]Department of Genetics, Harvard Medical School, Boston, MA and [2]Institute of Biochemistry, Biological Research Center, Eotvos Lorand Research Network, Szeged, Hungary



Marton Simon Czikkely, MS

Medical Student, University of Szeged, Szeged, Hungary

Marton Czikkely is a 5th year MD student at the University of Szeged and conduct research in the Csaba Pal Lab for more than 4 years. His projects focus on genome engineering and the understanding of the evolution of antibiotic resistance. In the 2021 Conference of the HMAA Hungary Chapter in Balatonfured he was the awardee of the Ivan Krisztinicz award which he is as proud of as the Stephen W. Kuffler Scholarship in 2019. After graduating he plans to continue conducting research to be able to aid clinical practice with new preclinical results to combat antibiotic resistance

Aim: A decades-old bacterial engineering technique called recombineering allows scientists to scarlessly edit the bacterial genome. This valuable and versatile approach has remained woefully underused because it has been limited mainly to *Escherichia coli*. Single stranded DNS annealing proteins (SSAPs) play a key role in this process, through the aid of the annealing of the desired sequence to the replication fork. Our goal therefore was to improve the efficiency and broaden the host.

Methods: First, using our new method, based on selective enrichment we found two new SSAP variants (CspRecT, PapRecT) with possible high activity. After that, these SSAPs were inserted to the pORTMAGE plasmid system. Thus, we were able to examine the efficiency of the directed mutagenesis of a given locus in diverse set Gram-negative bacterial species using a LacZ and antibiotic selective assay.

Results: CspRecT doubled thus reached the theoretical maximum efficiency of single locus editing in E. coli. It also increased by ten-fold the efficiency of multiple locus editing in this species. PapRecT made possible to effectively edit the genome of P. aeruginosa, a pathogen that is a frequent cause of deadly nosocomial infections.

Conclusion: Our new screening method enables the identification of highly active SSAP variants. Thus, we can improve the efficiency of recombineering based genome engineering in a given bacterial species. Our work is a huge methodological progress in the field of genome engineering and will aid several fields including antibiotic resistance, biotechnology and evolutionary biology.

RETROGRADE POLIDOCANOL ENDOVENOUS MICROFOAM ABLATION OF SUPERFICIAL VENOUS INSUFFICIENCY IMPROVES HEALING OF CHRONIC VENOUS LEG ULCERS

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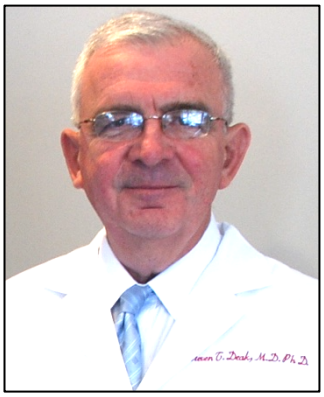

Steven T. Deak, MD, PhD.

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Dr. Steven Deak is a vascular and general surgeon who practices at the Deak Vein NJ Clinic with an emphasis on the treatment of venous diseases. He has been in private practice for over 35 years specializing in vascular and general surgery. Dr. Deak is certified by the American Board of Surgery in the specialty of General Surgery. He is certified by the American Board of Phlebology. He is also certified as having Added Qualifications in General Vascular Surgery. He is a fellow of the American College of Surgeons. He is a member of the Society of Vascular Surgery, the American Venous Forum, the American College of Phlebology, the Hungarian Medical Association of American and the International Society for Vascular Surgery. Dr. Deak has a Ph.D. degree in Pharmacology from the University of Kentucky. He is a member of the American Venous Forum and the American College of Phlebology. He is interested in the biology of the lymphatic and venous circulation and new techniques for the treatment of varicose veins.

Aim: To evaluate outcomes among patients with chronic venous leg ulcers treated with retrograde ultrasound-guided polidocanol endovenous microfoam 1% (PEM) or endovenous laser ablation (EVLA).

Methods: A retrospective chart review from a single vein center between October 2013 and June 2019. Procedures were performed on 1070 patients with CEAP class 2-6 and symptomatic superficial venous reflux of the great saphenous vein (GSV) or anterior accessory saphenous vein (AASV). PEM was used for 550 procedures and followed for 43 +/- 13 months and EVLA was used for 520 procedures and followed for 57 +/- 18 months.

Results: Following complete treatment, elimination of reflux was documented in 93.5% (514/550) and 92.8% (482/520) of the PEM and EVLA procedures, respectively. In C6 patients treated with PEM, 69% (11/16) of ulcers healed in less than one month, compared to 5% (1/21) of patients treated with EVLA. In C4 patients with lesions, resolution of spontaneous bleeding was 100% in both groups. There were no neurological or cardiac adverse events (NCAEs) in the PEM group. Minor complications included asymptomatic DVT (0.5%), 1 common femoral vein thrombus extension, and superficial venous thrombosis (4%) in the PEM group and asymptomatic DVT (0.8%) and 2 EHITs in the EVLA group.

Conclusion: PEM is comparable in safety and efficacy to EVLA for the treatment of saphenous reflux and improves healing of chronic venous leg ulcers after one month. Closure rates for saphenous vein reflux in both groups were maintained 36 months post treatment. PEM was an effective intervention for most patients with C6 disease.

ROBOT INVASION IN THE OPERATING ROOM

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Dr. Garami obtained his medical degree from the University of Debrecen. He has a clinical background in Radiology and is EU board certified in that specialty. He has also received further specialization in intracranial ultrasound in Europe and the United States. In recent years, Dr. Garami has become a nationally and internationally recognized leader in transcranial Doppler (TCD). He is the Medical Director of the Vascular Ultrasound Lab, Houston DeBakey Heart & Vascular Center, Houston Methodist Hospital. Dr. Garami's research focuses on understanding and treating intracranial flow disturbances that cause stroke. He has numerous publications on the monitoring of the cerebral vasculature during vascular procedures such as coronary artery bypass grafting, and carotid artery surgery. His current studies aim to reveal critical patterns of distal intracranial embolization in LVAD patients, TAVR and CAS/CEA cases.

Transcranial Doppler (TCD) is one of the least understood, rarely utilized, yet potentially most valuable tools available for monitoring brain circulation. Since the introduction of TCD by Aaslid in 1982, the most important advancement has been the addition of power M-mode Doppler (PMD) to the single-channel TCD screen in 2000. PMD detects not only the presence of flow but also its depth, direction, and resistance ("DDR"). TCD is the "stethoscope for the brain", is non-invasive, safe, and cost-effective(cheapest) in evaluating cerebrovascular circulation. TCD shows the direction of blood flow and velocity of the brain vessels.

TCD weaknesses are the trained sonographer can perform a standard exam following previously determine protocol. The second weakness is the captured signal interpretation which is not thought in school and only experienced reading physician understand know the values of the data in detailed waveform information of these images. Robotic TCD opened up an opportunity for "green" medical staff, nurses without any TCD training or experience to learn and use the robotic TCD system in few hours.

TCD can also detect embolization (some other foreign particle present in the blood cell stream) and is very sensitive, detecting particles down to 40 microns diameter. Emboli detected on TCD are referred to as HITS (high-intensity transient signals) and the TCD machine provides both a visual and auditory signal of their presence. Emboli traveling up the carotid system pass from deep in the brain, either toward the probe generating unique sound and image. Without large vessel occlusion, these emboli might leave the brain without any symptoms generated as they did not cause permanent brain infarct or damage. Indeed, TCD sensitivity has led to the negative opinion of many non-users: "I do not want to know about this, It has no clinical manifestations. The obvious retort is "explain to me the good emboli which are going up into the brain. Do you what is going on in your brain? "

We have to clear confusion when using TCD and monitoring procedures we hope to prevent harmful embolization to the brain by changing our clinical approaches. We are eager to learn during new surgical and cardiac procedures where most of the embolization and stroke risk occurs. Nevertheless, we believe that any emboli passing into the circulation can potentially be hazardous. "No good" cerebral emboli during surgery. Multiple protection filters were developed to clean the blood flow from these materials. TCD helps to test these and even early in development to decide which could be more effective to use. I believe TCD has the true impact to flow alterations or emboli regression improve outcomes of those procedures. As TCD is the only tool that can provide real-time information about embolization during manipulation of these procedures.

But not just in the operating room but outside in recovery rooms, ICUs, and even every patients' floor this technology gives us valuable medical information.

Hemodynamic and improved emboli counting is the key difference compared to the other "static" radiological images (CT, MRI, DSA, etc) when the patient lays down in most unphysiological body positions.

THE RIGHT TO REPAIR: WHEN IT REALLY MATTERS

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Dr. Halasz is a recently graduated, aspiring emergency medicine physician with a special interest in social emergency medicine and bedside ultrasound.

Aim: It is common practice across industries to restrict product repairs by third-party companies, and to limit access to necessary manuals, tools or software to prevent conducting repairs yourself. In doing so, industries ranging from electronics to farming to ensure ongoing revenue even after the initial sale, and monopolize the market for providing necessary service. The issue becomes even more pressing when the product in question is medical equipment, especially in the midst of a pandemic. Our goal is to raise awareness about the right to repair movement, an issue which has been simmering in the background for years, but has received extra attention during the COVID-19 pandemic, and to encourage our colleagues to keep the right to repair movement's momentum going.

Methods: We outline current events related to the right to repair movement, highlighting the healthcare implications of limitations on servicing and repair, and emphasizing recent legislation as it pertains to the issue.

Discussion: We discuss the Critical Medical Infrastructure Right-to-Repair Act of 2020, and delve into the July 2021 executive order signed by President Biden urging the Federal Trade Commission (FTC) to establish Right to Repair regulations. We also examine the predictions that implementing right to repair laws may move healthcare in a more affordable, sustainable direction and highlight the importance of working together with biomedical engineers in hospitals and lawmakers for the sake of our patients.

ERAS - ENHANCED RECOVERY AFTER SURGERY CONCEPTS

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Dr. Harangozo is a graduate of chemical engineering at Manhattan College. Subsequently, he earned his MD at the State University of New York at Buffalo. After an internship in surgery, he completed an Anesthesiology residency program at the same institution. Currently, he is Medical Director of American Anesthesiology, Northern Virginia and is the Medical Director of Anesthesiology at Novant Health-Haymarket Medical Center, located in Haymarket, Virginia. Dr. Harangozo joined the HMAA in 1986 as a medical student and he was elected to the Board in 1995. He has served the HMAA as Treasurer for many years before becoming President of the HMAA in 2020.

Aim: Elucidate current methods and practices directed by the surgical care team to enhance recovery after surgery.

Methods: A review of ERAS protocols; Pre-habilitation, multimodal analgesia including medications and regional anesthesia, in addition to fluid and temperature management.

Results: Through ERAS protocols, improved outcomes are realized; primarily decreased length of stay and decreased opioid use.

Conclusion: Pre-operative preparation for surgery, via the care team, maximizes the potential for good surgical outcome. Pre-habilitation, peri-operative interventions and protocols maximize quality.

WEIGHT LOSS SURGERY FOR THE GERIATRIC PATIENT

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Dr. Edward Hatchigian is Medical Director of the Weight Loss Surgery Program at Beth Israel Deaconess Medical Center in Boston as well as consultant to the Bariatric Surgery Program at the VA Boston Healthcare System.

Aim: The aim of this paper is to address the growing elderly population because of "baby boomers" who are impacted by the global epidemic of obesity. There is no cure for obesity but the most effective treatment has shown to be weight loss surgery (WLS). The average age of a patient undergoing WLS is 40-45 years with 85% of WLS in the 18-54 age group and those 65 and over making up 1% (70 and over less than 1%). Obesity impacts the elderly and weight reduction would definitely benefit in reducing co-morbid conditions such as type 2 diabetes, obstructive sleep apnea, back and lower extremity joint pain. The risks may be higher and long-term results not as favorable in the elderly, obese patient, but they may still benefit from WLS. This paper will show that WLS can be a relatively safe option for obese elderly patients to have a better quality of life in their golden years.

Methods: Of the 3 procedures currently performed the sleeve gastrectomy has become the most popular especially with patients over 65, as it is less aggressive with less morbidity than the Roux-en-Y gastric bypass. The lap band has fallen out-of-favor and now makes up less than 1% of WLS procedures. Review of patients that had weight loss surgery over 65 were looked at in terms of demographic and clinical characteristics including mean length of hospital stay, post-operative complications, percent excess weight loss and resolution of comorbid conditions.

Results: When compared to younger age group complications were only slightly higher in the older group that was related to comorbidities and not the surgical procedure. There was no significant change in length of hospital stay. Average excess weight loss may not have been as great as with the younger patients that could be attributable to lesser physical activity capabilities of the older group, but the elderly group did show improvement and even resolution of obesity-related comorbidities. Patients over 70 have significant more health risk and will need thorough preoperative evaluation to determine if they will be safe candidates for WLS.

Conclusion: WLS programs that set maximum age of 65 should seriously consider that WLS offers an acceptable outcome in the elderly patient that are **carefully screened** and the sleeve gastrectomy can be a safe and effective tool to offer beneficial outcomes to improve overall quality of health of the older patient.

PERIPHERAL NEURONOPATHY ASSOCIATED WITH EBOLA VIRUS INFECTION IN RHESUS MACAQUES: A POSSIBLE CAUSE OF NEUROLOGICAL SIGNS AND SYMPTOMS IN HUMAN EBOLA PATIENTS

Liu, D.X., Perry, D.L., Cooper, T.K., Huzella, L.M., Hart, R.J., Hishak, A.M.W., Bernbaum, J.G., Hensley, L.E. and Bennett, R.S.

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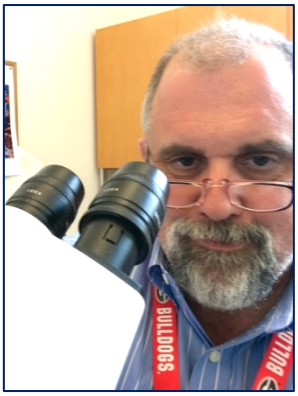

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Dr. Huzella is a biocontainment research pathologist at the Integrated Research Facility, Division of Clinical Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Frederick, MD. He provides pathology support in all levels of biocontainment, with subsequent gross, clinical, and histopathologic examinations of a wide range of species and organ systems. His specialty is veterinary pathology for high risk pathogens in biocontainment.

Aim: This study aimed to examine the peripheral nervous system to aid in understanding of the pathogenesis underlying development of profound neurological signs and symptoms in EVD patients.

Methods: Ebola virus/H.sapiens-tc/COD/1995/Kikwit-9 510 621 (GenBank: MG572235.1) was obtained from the Biodefense and Emerging Infections Research Resource Repository (BEI), National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH) (catalog number NR-50 306). The virus was originally isolated from the blood sample from a fatal human patient in 1995 and passaged 3 times (Centers for Disease Control and Prevention number 807 223, University of Texas Medical Branch number WRC000121, and BEI number NR-596). The virus stock was diluted to a target dose of 1000 plaque forming units (PFU)/mL prior to inoculation without additional passaging at the Integrated Research Facility (IRF), NIAID. Twelve (6 males and 6 females) 5- to 6-year-old rhesus macaques (Macaca mulatta) were inoculated intramuscularly (IM) with a target dose of 1000 PFU EBOV-Kikwit/animal into the left lateral triceps muscle. Two (1 male and 1 female) age-matched rhesus macaques served as uninfected controls and were inoculated IM with 1 mL of phosphate-buffered saline/animal at the same anatomic site. All macaques were observed for the development of clinical signs of EBOV infection and humanely euthanatized when predetermined experimental endpoints were reached. All macaques used in this research project were cared for and used humanely according to the following policies: the US Public Health Service Policy on Humane Care and Use of Animals (2000); the Guide for the Care and Use of Laboratory Animals (1996); and the US Government Principles for Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (1985). All NIAID-IRF animal facilities and programs are accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International. This study was performed in the Biosafety Level 4 Laboratory at the NIH/NIAID, Division of Clinical Research/IRF at Fort Detrick, Maryland.

Results: All 12 macaques that received a target dose of 1000 PFU of EBOV-Kikwit IM succumbed to EBOV disease. Eleven were euthanized and 1 was found dead shortly before the necropsy between 5 and 8 days post exposure (dpe). Preestablished euthanasia criteria allowed morbidity to serve as a surrogate for lethality. Typical clinical signs including fever, weakness, and decreased appetite developed as early as dpe 3 and increased in severity with time post exposure. Two (16.7%) macaques developed watery diarrhea at dpe 6 and 7, but the other 10 macaques showed constipation that varied in severity but was characterized by reduced to no stool at the late stages of disease. All macaques developed maculopapular skin rash that progressed from the face, arms, and thorax to a diffuse distribution terminally.

Conclusions: This study demonstrated that EBOV can cause systemic peripheral neuronopathy that likely contributes to the profound neurological signs seen in acute EVD patients.

THE HUMORAL IMMUNE RESPONSE TO SARS-COV-2 INFECTION AND/OR IMMUNIZATION IN IMMUNOCOMPROMISED VERSUS IMMUNOCOMPETENT INDIVIDUALS

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Aim: Immune responses to SARS-CoV-2 are variable, especially in patients with inborn errors of immunity (IEI). Generally, the quality of the viral antibody response predicts COVID-19 severity and survival. It is unclear how this observation applies to patients with IEI. Hence, we assessed this phenomenon in a unique IEI cohort at a tertiary care center.

Methods: We reviewed the charts of patients with IEI, and history of SARS-CoV-2 infection and/or immunization. We tested antibody responses to SARS-CoV-2 receptor binding domain (RBD) by ELISA and to several other relevant antigens by a photonic ring resonance assay.

Results: We collected demographic and clinical data on 40 patients (median age 39 years, range 3-85) with IEI, and prior COVID-19 infection and/or vaccination. Only 6 patients were infected but not immunized, one was immunized and infected, and the rest were immunized but not infected. Thirteen patients (32%) with no antibody response had agammaglobulinemia or CTLA4 deficiency. Twenty-seven patients (68%) had detectable IgG or IgM to the S1 protein RBD. Antigen-binding profiles of six of these patients resembled primary antibody responses with dominant binding to the S2 epitope of SARS-Cov-2. Twenty-one patients (52%) had a secondary antibody response similar to healthy controls. Two patients received monoclonal antibodies. All infected patients did well with no long-term complications.

Conclusion: We identified IEI patients with primary antibody responses and skewed SARS-CoV-2 antigen-binding profiles. Their risk for severe COVID-19 is yet to be determined. As patients with agammaglobulinemia did well during infection, the protective effect of T cell response should also be considered.

PULMONARY PATHOLOGY IN COVID-19 INFECTION

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Dr. Khoor received his medical degree from Semmelweis University, Budapest, Hungary. After postgraduate training in Hungary, he conducted research on surfactant proteins and other aspects of lung development at Vanderbilt University, Nashville, Tennessee. This was followed by residency in pathology at Vanderbilt University and a fellowship in pulmonary pathology at Mayo Clinic in Rochester, Minnesota. From 1997 to 2000, he was Assistant Professor of Pathology at H. Lee Moffitt Cancer & Research Institute, Tampa, Florida. In 2000, he joined the Department of Laboratory Medicine and Pathology at Mayo Clinic in Jacksonville, Florida, where he served as Chair of the department from 2006 to 2018. Currently, Dr. Khoor is Consultant and Associate Professor of Laboratory Medicine and Pathology and Medical Director of the Biospecimen Accessioning and Processing/Pathology Research Core. Dr. Khoor's research interests include various areas of pulmonary pathology. He has authored more than 70 peer reviewed publications and more than 20 book chapters. He is on the editorial boards of the Archives of Pathology & Laboratory Medicine, Human Pathology, and Pathology & Oncology Research. He is also the Immediate Past President of the Hungarian Medical Association of America.

Aim: Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The infection started in Wuhan, China, in December 2019 and became a global pandemic as recognized by the WHO in March 2020. As of August 27th, 2021, there have been 214,468,601 confirmed cases and 4,470,969 confirmed deaths associated with the virus worldwide.

Methods: This is a traditional review using relevant information from the medical literature and the author's own experience.

Results: COVID-19 frequently affects the lungs and, in severe cases, may progress to acute respiratory distress syndrome (ARDS) and death. The most common histological finding in patients who succumb to the disease is diffuse alveolar damage (DAD). In a study of 68 autopsies by Borczuk et al, DAD was seen in 87%, large vessel thrombi in 42%, and platelet or fibrin microthrombi in 84% of the cases. In a study by Li et al, DAD showed predominantly acute, organizing, and fibrotic patterns in 32%, 25% and 43% of the cases, respectively. Interestingly, Konopka et al did not find significant differences between COVID-19-related DAD and DAD due to other causes. Recent publications, including those by Aesif et al and Bharat et al, as well as our own experience suggest that lung transplantation can save the lives of patients with non-resolving post-COVID-19 interstitial lung disease (ILD). Explanted lungs in these cases usually show fibrotic DAD.

Conclusion: COVID-19 infection may lead to severe consequences, including ARDS due to acute and/or organizing DAD and post-COVID-19 ILD due to fibrotic DAD. Vaccination plays an important role in preventing these complications.

PATHOLOGY OF VAPING ASSOCIATED LUNG INJURY

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Aim: In the summer of 2019, an acute, mysterious, and deadly respiratory illness related to vaping emerged in the US. The CDC coined the term E-cigarette or vaping product use-associated lung injury (EVALI). Cases increased dramatically and peaked in late September 2019.

Methods: This is a traditional review using relevant information from the medical literature and the author's own experience.

Results: The events will be discussed in chronological order:

July 2019: Eight teenagers in Wisconsin are hospitalized with the first known cases of a mysterious lung injury.

August 26, 2019: The media reports the first confirmed death linked to EVALI in Illinois.

August 30, 2019: The cannabis website Leafly reports on the apparent link between the sudden vaping illnesses and a recent development in the illicit tetrahydrocannabinol (THC, the main psychoactive compound in cannabis) vaping industry: the use of vitamin E acetate as a cheap cutting agent.

October 2, 2019: A Mayo Clinic study on the "Pathology of Vaping-Associated Lung Injury" is published. The main histologic finding is bronchiolocentric acute lung injury.

October 4, 2019: Interviews about e-cigarette use were completed with 86 patients in Illinois and Wisconsin. Use of THC-containing e-cigarette products, the majority of which were prefilled cartridges obtained from informal sources, was reported by 87% of patients.

November 15, 2019: Analyses of THC-containing product samples by FDA and state public health laboratories have identified potentially harmful constituents in these products, such as vitamin E acetate.

December 20, 2019: Vitamin E acetate was identified in BAL fluid obtained from 48 of 51 EVALI patients (94%).

Conclusion: Most of the EVALI cases in 2019 were likely related to vaping vitamin E acetate. However, it remains possible that other forms of pulmonary illness related to vaping of other chemical compounds will be identified.

HYPERTENSION AND AGING ELICIT ALZHEIMER-TYPE COGNITIVE DYSFUNCTION AND EXPRESSION OF HIPPOCAMPAL GENES INVOLVED IN ß-AMYLOID GENERATION

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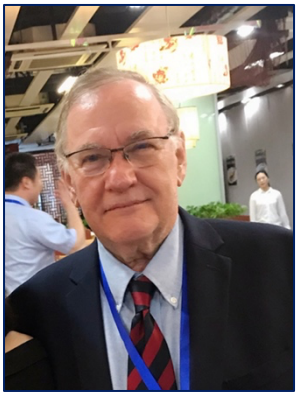

Akos Koller, MD, PhD

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Dr. Akos Koller has started his research work in Hungary after finishing the Semmelweis Medical School in 1969-1975. Then, he started to work on coronary and brain microcirculation with Prof AGB Kovach. He moved from Hungary to the USA in 1982, where he was doing research at the Cerebrovascular Res Center at University of Pennsylvania, with Martin Reivich and Britton Chance on pial microcirculation, regarding the role of adenosine, NADH level/metabolism and spreading depression. Then in Tucson, Arizona where he learned from Paul C Johnson all topics of classical in vivo microcirculation and engaged in microcirculatory network studies to understand important complexity of microcirculation. In 1987, he moved to New York Medical College, Valhalla, NY and with the help Gabor Kaley he became an independent scientist.

He has received several NIH, AHA and Hungarian Research grants which supported his studies on the function of microvessels of various tissues, the newly discovered vasomotor role of endothelium in vivo and the effect of hemodynamic forces in acute and chronic condition on the remodeling of microvascular function in vitro. He was one of the first who discovered in 1989 the role of wall shear stress in eliciting substantial dilation of arterioles, venules and affecting the vasomotion of lymphatic microvessels. Later he investigated the modulation of the function of endothelium by age, gender, exercise and various diseased conditions. He then in 2011 discovered that increases in flow elicit constrictions in cerebral arteries contributing thereby to the autoregulation of cerebral blood flow and clarified the underlying molecular signaling. In addition to basic research, he contributed to clinical research and papers, recently contributed to an ESC guideline on Myocardial Revascularization. In addition, he has trained many young scientists. With his international research network, he provided a network among microcirculatory communities of United States, Europe and Asia.

Total IF: 922.4, Citations: 9969, Hirsch index: 62.

Aim: Epidemiological data suggest that Alzheimer-type cognitive dysfunction (AD) frequently develops in older people with untreated hypertension. Yet the underlying mechanism are still not yet clarified. The a study aimed in mice model to characterize the effects of hypertension in older age on cognitive function and expression of genes involved in β-amyloid generation, both of which are associated with hippocampus.

Methods: Hypertension was induced in 3 month (young) and 24 months (old) C57BL/6 mice by 4-weeks infusion of angiotensin II. Then changes in hippocampal mRNA expression of genes involved in amyloid precursor protein (APP)-dependent signaling, APP cleavage, Aβ processing and Aβ-degradation, synaptic function, dysregulation of microtubule-associated τ protein, and apolipoprotein-E signaling were assessed.

Results: There were spatial memory impairments in the Y-maze and impaired performance in the novel object recognition assay in aged hypertensive mice. Expression of genes involved in the early onset form of AD, such as APP, β- and γ-secretases, or genes involved in tauopathy were not affected. Whereas hypertension in aging was associated with changes in hippocampal expression of APP binding proteins, e.g., [Mint3/amyloid β A4 precursor protein-binding family A member 3 (APBA3), Fe65/amyloid β A4 precursor protein-binding family B member 1 (APBB1)], amyloid β (A4) precursor-like protein 1 (APLP1), muscarinic M1 receptor, and serum amyloid P component, all of which may have a role in the pathogenesis of late-onset AD (DOI: 10.1152/ajpheart.00288.2013).

Conclusion: The present mice model study confirmed that in old age untreated hypertension elicit cognitive dysfunction (similar to those in traumatic brain injury, frequently occurring in sport activities), which correlates with altered gene expressions in the hippocampus, providing basis for further mechanistic studies.

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CASE SERIES OF OXYGENATION WITH HUMIDIFIED RAPID-INSUFFLATION VENTILATORY EXCHANGE DURING RIGID BRONCHOSCOPY

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A proud Semmelweis medical graduate of 2016, born and raised in Nyiregyhaza, Hungary who is currently doing her 2nd year of internal medicine residency at Mayo Clinic Florida. Her mentor at Semmelweis University is Prof. Dr. Veronika Muller who is one of the reasons Anna continues to do research and is planning to go into Pulmonary medicine and Critical Care fellowship. She continued her research in Pulmonary medicine at Mayo Clinic, Florida with the guidance of Dr. Sebastian Fernandez-Bussy learning more about chronic cough, COPD, smoking, Interventional Pulmonology. In her free time, she likes to run on the beach, practice yoga and gives personalized recommendations of the best places to visit in Hungary.

Define: The rate of smoking cessation counseling in Community Internal Medicine clinic (CIM) at Mayo Clinic Florida is 20.3%. We aim to improve this rate to 40.6% by the end of May 2021 without negatively impacting provider workflow.

Measure: The baseline sample size was 355, representing the number of active smokers seen in CIM clinic in 2020. For the improvement measure the numeric baseline was 20.3%, the percentage of cases received smoking cessation counseling documented appropriately.

Analyze: Based on discussion and survey results, we devised a cause and effect diagram to identify the barriers to smoking cessation counseling. Four main factors identified: 1. Workplace: Providers are often managing more imminent concerns. Opportunities to provide smoking cessation counseling are limited to preventive visits. 2. Provider: affecting the provider's decision or ability to offer counseling. Reasons include forgetfulness, time constraints or sensitivity of topic. 3. Patient: may decline, defer or downplay answering. 4. Technology: Our current electronic medical record system (EMR) does not remind about smoking cessation counseling. Shortcuts for documentation on counseling are lacking.

Improve: Interventions to increase the rate of smoking cessation counseling at CIM Clinic in Florida included: educated residents and attendings about proper smoking cessation and its coding in EMR at didactics and meetings; continuing reminder of staff at daily clinic huddles for smoking cessation counseling; smart phrase created in EMR to be used as a shortcut in progress notes about smoking cessation counseling. Following these interventions, in May 2021 the smoking cessation counseling went up to 37.5% on a sample size of 24 active smokers visiting at the CIM clinic in Florida.

Control: The following lessons were learned: 1. Interventions must not significantly interrupt workflow or increase burden of work. 2. Surveying providers to assess how they provide smoking cessation counseling targets well for intervention. 3. Adequate communication is essential to enacting quality improvement interventions and must include multiple modes of dissemination with repetition.

Relevance: It is our responsibility to provide patients with quality care in a progressively growing virtual era too. This includes ensuring that more active smokers are counseled for smoking cessation even at a virtual visit. Increasing the numbers of counseling can help us decrease the risk of these patients of developing severe, life-altering or life-shortening diseases.

"HYPODERMIC EXTREMITY CHECK", VACCINATION METHOD AND MEMORIES AT JENKINTOWN PEDIATRICS

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Eniko Kovats-Ongradi, MD

Retired Pediatrician, Jenkintown Pediatrics, PA, Jenkintown, PA

Dr. Eniko Kovats-Ongradi is a retired pediatrician in Jenkintown, PA.

Aim: The presentation covers the current vaccine preventable childhood diseases and vaccines. It follows history and technology of vaccine development from Dr. Jenner's smallpox vaccine (1796) till mRNA vaccines in 2021. The presentation emphasizes the importance of trust, patience, empathy and education in pediatric care. It explains the humanistic aspect of pediatric medicine, how to administer vaccination without fear and pain. It presents art, poem, painting, humor, old traditional ceremony and folk custom in Hungary, called "Balazsolas", which is a practice to drive away the evil which causes diphtheria.

Methods: I learned the "Hypodermic Extremity Check" method to administer painless needles to children. My own practical experiences in pediatric primary care via interactions with children, parents, family members

Results: Good communication, education, trust and patience resulted in above average vaccination percentage.

Conclusion: Endemics and pandemics are happening throughout human history, like influenza 1918, poliomyelitis 1950s, Covid-19 presently. Scientist fought and won over many previously dreadful childhood diseases. The fight is still on. I am pleased to have a medical profession to be part of this fight against diseases and to distribute many vaccines. Benjamin Franklin said "One ounce of prevention worth one pound of cure".

IN VITRO MODEL INVESTIGATING MAMMALIAN TYMPANIC MEMBRANE REGENERATION IN ADULT MICE

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Winner of the 2021 Ivan Krisztinicz MD Memorial Student Award

Dr. Lippai graduated in 2021 at the University of Pecs, Medical School (Faculty of General Medicine). He enrolled in Students Research Program from 2019 working in basic research in the field of otorhinolaryngology. He gave TDK and HMAA HC Balatonfured Congress winner presentations in 2020 and 2021. He is an active member of the HMAA Hungary Chapter from 2018. He started his PhD studies in September 2021.

Aim: Acute tympanic membrane perforation primarily occurs due to an injury or infection. Distinctly, the spontaneous closure rate is nearly 80% and largely influenced by numerous factors. Three months following an injury, the status is now chronic, for which non-surgical treatment considerations are significantly limited. Thus, to expedite recovery, we investigated the effect of thymosin-beta 4 (TB4), a 43 aa secreted peptide to aid tympanic membrane regeneration in adult mice in vitro.

Methods: Following euthanasia, the parietal-squamal skull area containing the auditory bulla was isolated from C57BL/6 adult mice (n=47). Next, the tympanic membrane was dissected while utilizing the Carl Zeiss dissection microscope (2004015801). The fibrous and bony appendages (excluding the malleus) were carefully purged, and the remaining tissue was placed on collagen gel extracellular matrixes. To enhance potential attachment, explants were incubated for three days and treated via 300 l of DMEM growing medium with 30, 50 and 60ng of TB4 in PBS or PBS alone, respectively. Cell migration was photo detected daily for a span of ten days. The accumulated distance regarding cell migration was measured using ImageJ software. Statistical analyses were performed via SSP (22.0 version) program. To determine normality, we implemented the Kolmogorov Smirnov probe. Multiple comparisons were performed using a one-way analysis of variance ANOVA. Differences among groups were considered significant for $P<0.05$.

Results: Our experiments revealed no significant differences in cell migration at days 6 and 7 among the groups. At days 8 and 9 however, we detected a significant increase in epithelial cell migration in the TB4 treated explants ($P=0,026$). We also discovered 10ng/100ul TB4 concentration may be the most optimal to enhance mammalian tympanic cell migration in vitro.

Conclusion: Our experiments demonstrate TB4 stimulates the migration of mouse tympanic membrane cells in vitro. We conclude, additional, detailed immunhistochemical investigations are mandatory to identify the target cell types, including epidermal stem cells to enhance clinical utilization of the molecule in the near future.

THE IMPACT OF EDUCATING NURSES ON THE REDUCTION OF RESTRAINTS IN THE EMERGENCY DEPARTMENT

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Klara Mark, DBH, LCPC

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Klara Mark worked as an Emergency Psychiatric Evaluator for two hospitals for a total of 12 years, the University of Maryland CRMC and Calvert Memorial Hospital. During the years working as an Emergency Psychiatric Evaluator, she has gained valuable practical knowledge of diagnosing and managing psychiatric patients and dual diagnosis patients presenting to the Emergency Department as well as the medical floors. She is very passionate about helping psychiatric patients have a better quality of life, which is why she has chosen to research how to improve their quality of life by conducting research on the following topic that she is about to present to you.

Aim: 1. Implementation of an educational program discussing the basic symptoms of common psychiatric illnesses causing patients to go into crises, and the behavioral interventions to implement in these situations, would increase nurses' knowledge of such issues, as evidenced by an increase in knowledge scores from pre to post psycho-educational workshop. 2. Educating nurses on how to manage psychiatric patients in crisis would lead to reduction in the use of restraints in the ED as evidenced by medical record data reflecting the number of restraints utilized pre-workshop, during the workshop, and post-workshop.

Methods: Nurses were recruited by posting flyers around the ED and talking to the nurses about the workshop. Emails were also sent out by the nursing educator. However, participation in the workshop was not sufficient, only 9 nurses participated. A plan B had to be implemented, which involved implementing a mini-workshop series throughout the rest of the month. At the time of the workshop and the mini-workshop series a pre-and post-test was administered to measure knowledge gained. For aim number 2, the impact data was collected by the nurse educator as part of her responsibilities, and she shared it with me.

Results: Since I had two different psycho-educational interventions implemented, the workshop and the mini workshop series, with different lengths, a preliminary analysis was performed via independent samples t-tests. My goal was to compare the knowledge gained by the nurses participating in the workshop to the nurses participating in the mini-workshop series. The findings show that there is no statistically significant knowledge gained by the nurses participating in the workshop, versus the nurses participating in the mini-workshop series. An independent samples t-test was performed to test aim one. The findings showed a statistically significant difference in knowledge scores from pre- to post intervention. The medical record data showed that for aim two 8 patients were restrained the month before the implementation of the workshop/mini-workshop series, 4 during it, and 7 the month after. This is an initial 50% decrease, however an overall 12.5% decrease for the month after the implementation of the workshop/mini workshop series.

Conclusion: The goal of the workshops was to increase the knowledge of the nurses on the basic symptoms of common psychiatric illnesses as well as to give them some tools to implement when patients go in crisis. However, the purpose of the psycho-educational workshop was to ultimately decrease the implementation of restraints in the ED. Even though there was statistically significant knowledge increase shown, it did not make a major impact on the restraint usage for the month after implementation of the workshops. It did however decrease the restraint usage by 50% during the implementation of the workshops.

HIGH-DYMENSIONAL BIOLOGY OF REGENERATIVE MACROPHAGES

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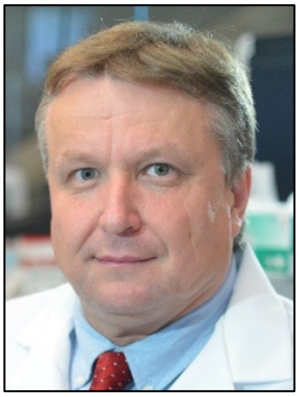

Laszlo Nagy, MD, PhD

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Dr. Nagy is a Professor of Medicine in the Division of Endocrinology, Diabetes and Metabolism, at the Department of Medicine and Professor of Biological Chemistry at the Department of Biological Chemistry in the Johns Hopkins University School of Medicine. He is the Associate Director of the Johns Hopkins Center for Metabolic Origins of Disease, a program that spans Johns Hopkins Medicine campuses in St. Petersburg, Florida, and Baltimore, Maryland. He also is co-director of the Johns Hopkins All Children's Institute for Fundamental Biomedical Research. He has training as both a physician and a molecular and cellular biologist. Dr. Nagy's research focuses on identifying and understanding how cells' identity develops and how their differentiation contributes to human diseases. He seeks to understand how the extra- and intracellular lipid environment contributes to cellular development and differentiation and what impact that has on components of the immune system in particular on macrophages. In this context, Dr. Nagy also studies what causes cells to use certain pieces of genetic information and not others and what causes that process to sometimes result in diseases such as chronic inflammation, tissue degeneration or cancer.

Understanding the mechanisms of tissue and organ regeneration in adult animals and humans is of great interest from a basic biology as well as a medical, therapeutical point of view. It is increasingly clear that the relatively limited ability to regenerate tissues and organs in mammals as opposed to lower vertebrates is the consequence of evolutionary trade-offs and changes during development and aging. Thus, the coordinated interaction of the immune system, particularly the innate part of it, and the injured, degenerated parenchymal tissues such as skeletal muscle, liver, lung, or kidney shape physiological and also pathological processes. In this presentation we provide an overview of how morphologically and functionally complete (*ad integrum*) regeneration is achieved using skeletal muscle as a model. We will review recent advances including our own work about the differentiation, activation, and subtype specification of circulating monocyte to resolution or repair-type macrophages during the process we term regenerative inflammation, resulting in complete restoration of skeletal muscle in murine models of toxin-induced injury.

MEDICAL CYBERNETICS FOR CONTINOUS RISK ASSESSMENT AND VALUE OF INFORMATION ANALYSIS OF TREATMENTS

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Dr. Ori is a practicing internist and hospitalist with previous training in Cybernetics - an applied science using mathematical and control engineering tools to study biological systems for maximum control by creating cyber-physical interactive systems.

Individualized precision methods are needed for continuous non-invasive monitoring of state variables (SV's) of risk indicators not just for early detection of subclinical derangements but also to monitor progress of effect of lifestyle modification and medical therapies throughout lifespan.

For purposes of "precision medicine" we propose here a cloud based Cyber-Physical System (CPS), a mobile technology to integrate sensory data from various mobile devices of a user into individualized dynamic mathematical models of physiological processes to draw life-course trajectories in four domains with major implications for morbidity/ mortality: 1. Cardiometabolic, 2. Cardiorespiratory, 3. Cardio vegetative, and 4. Cardiovascular functioning. The following state variables (SV's) are assessed and predicted daily: Ad1. insulin resistance measuring Rw ratio, lean mass, fat mass, fat vs carbohydrate oxidation ratio, respiratory quotient, de novo lipogenesis, and adaptive thermogenesis; Ad 2. maximum oxygen uptake, exercise capacity, heart rate reserve; Ad3. heart rate variability; and Ad 4. blood pressure, total arterial compliance. The sensor data are picked up from wearable sensors of the fitness industry such as Garmin and from our patented bioimpedance Body-Composition Hydration-Analyzer Photo-plethysmography equipped stand-up scale. All measurement methods can be calibrated to widely available standard office-based measurements.

We were able to prove the feasibility of our modelling concept of the insulin resistance by finding strong correlation $\rho = -0.6745$, $P=0.000024$ between changes of Rw-ratio and insulin resistance HOMA-IR in 12 clinical studies with 39 clinical study arms. Based on these results we found that CPS is a suitable concept to indirectly measure and predict the otherwise very difficult- or impossible-to-measure slow change of SV's of the metabolism capture them for the first time noninvasively in the user's natural environment. Serial fat and weight measurements and energy calculations can help unmask changes of insulin resistance in response to user's diet and exercise habits.

We envision the possibility that the SV's can be plugged into already published risk calculation formulas derived from analysis of cumulative incidence in competing risks and analysis of competing regression. The derived metrics allow for assessing individually calculated risk of "end-point", quality-adjusted life-year (QALY), incremental cost-effectiveness ratio (ICER) and information analysis (VOI) of therapies. Having the effectiveness and cost-saving data could be essential for payers and policy makers to consider incentives or other major structural changes to health care delivery. The continuously provided value metrics especially if showing positive results could incentivize users and facilitate the creation of a sustainable business cycle for social entrepreneurship framework by informing all financial stakeholders in a community program.

The feedback of individualized metrics using tools of the digital health era may amount to channeling focus also to patient-centered individualized care and to accelerating nutrition research.

In conclusion a CPS with machine learning using principles of optimal control theory supervised by physician can provide a truly individualized strategy for estimation, continuous monitoring, and prediction of physiological state variables for self-therapy, guided therapies, and mobile health interventions or cyber-therapy. CPS facilitated interventions allow for improving health, fitness, resilience and the chance of survival of an acute illness.

EFFECT OF SLEEP DEPRIVATION ON THE NEUROVASCULAR CONNECTION

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Reka Palatka has a medical degree and currently she is a PhD student at the University of Debrecen. As a 5th-year medical student she joined the research team at the Department of Neurology and wrote her thesis about the effects of sleep deprivation on the neurovascular connection. After graduation she joined a PhD program at the Doctoral School of Allergology and Immunology and her research topic is the clinical and immunological connection between Hidradenitis Suppurativa and Crohn's Disease. As of 1st October 2021, she is a resident at the Department of Dermatology, and she is planning to specialize as a dermatologist.

Aim: Sleep deprivation is known to have an impact on the cardiovascular system; the elevated risk of arrhythmia and coronary disease are linked to an increased sympathetic tone that occurs after sleep deprivation. In our study we examined the effect of 24-hour sleep deprivation on neuronal activation and cerebrovascular response, the two main components of the neurovascular connection.

Methods: Fourteen healthy volunteers (mean age: 29) were included in our study. Examinations were first conducted in a well-rested state after 8 hours of night sleep (control period) and were repeated the next day after 24-hour sleep deprivation. We detected the cortical activation of the occipital lobe with Visual Evoked Potential (VEP) and registered the amplitude and latency of the P100 wave. With Transcranial Doppler (TCD) we measured the changes in flow velocity in the posterior cerebral artery (PCA) triggered by visual stimulation (vibrating chess pattern). In the medial cerebral artery (MCA) we measured the increase in flow velocity (cerebrovascular reserve capacity, CRC) triggered by breath-holding (hypocapnia). Results from before and after sleep deprivation were compared with paired t-test. Changes in flow velocity triggered by visual stimulation in PCA were compared using repeated measures analysis of variance.

Results: No difference in VEP P100 amplitudes were found however, the latency of P100 wave was significantly higher after sleep deprivation (111,3±5,4 ms) than in the control period (106,6 ms±3,3 ms; $p<0,01$). In the PCA the increase in relative systolic flow velocity triggered by visual stimulation was significantly lower ($p<0,05$) after sleep deprivation. The relative maximal systolic velocity change was also significantly lower after sleep deprivation compared to the control period (118,9±5,4 % vs. 122,1±4,6 %, $p<0,05$). No significant difference was found in the resting pulsatility index and in the CRC before and after sleep deprivation.

Conclusion: After sleep deprivation the velocity response in the PCA triggered by visual stimulation was decreased compared to the well-rested state which shows that the neurovascular connection was negatively impacted by sleep deprivation. Background of this phenomenon could be disturbance in the activation of neurons or regulation of vasodilatation. Since sleep deprivation did not affect neither resting pulsatility nor vasoreactivity, we could not prove that sleep deprivation has a direct negative impact on the cerebral vascular tone or on vasodilatation.

PHARMACOLOGICAL CHARACTERIZATION OF A NOVEL K^+ CHANNEL INHIBITOR PEPTIDE

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Dr. Panyi graduated as a medical doctor from the University of Debrecen in 1991 and started his basic research career right after finishing medical school. He was trained to be an ion channel biophysicist and pharmacologist. He currently moves towards ion channels and cancer and the role of ion channels in the differentiation and proliferation of various cells.

Aim: Antigen-dependent activation of T lymphocytes requires the generation of a Ca^{2+} signal and the maintenance of a negative membrane potential by K^+ channels to provide the necessary driving force for sustained Ca^{2+} entry. Depending on the T cell type inhibition of Kv1.3 K^+ channels by scorpion toxins may lead to a complete block of proliferation of the cells. This provides the basis for therapeutic application of high affinity Kv1.3 inhibitors in the management of autoimmune disease where the inhibition of effector memory T cell activation and proliferation is required. Our aim was to isolate and characterize the biochemical and pharmacological features of novel Kv1.3 inhibitors from scorpions.

Methods: Scorpion venom was collected and subjected to several steps of purification (ion exchange chromatography, size exclusion chromatography, HPLC). The amino acid sequence of the peptides was determined using Edman degradation according to standard procedures. The pharmacological features of the peptides were analyzed using single cell (patch-clamp) electrophysiology. The ion channels were expressed in HEK-293 or COS-7 cells, the pharmacology of Kv1.3 was studied in Human Peripheral Blood Lymphocytes.

Results: Proteomic analysis of soluble venom of the Colombian scorpion *C. margaritatus* revealed that it contains mainly peptides with molecular weights ranging between 2.5-8 kDa. A novel short peptide consisting of 27 amino acids with MW of 2820 Da was identified having nanomolar potency to block voltage gated K^+ channels. This peptide was named Cm28, it inhibited voltage-gated potassium channels Kv1.2 and Kv1.3 with K_d value of 0.96 and 1.3 nM, respectively. Based on the biophysical parameters of ion channel gating and the kinetics of block we conclude that Cm28 is not a gating modifier, rather a pore blocker. We have studied the selectivity of the novel peptide against 5 other subtypes of Kv channels (Kv1.1, Kv1.5, Kv11.1, KCa1.1, KCa3.1), 2 subtypes of Nav channels (Nav1.5 and Nav1.4) and the proton channel hHv1. Cm28 did not affect the activity of any channel at a concentration of 150nM (100x of K_d value for Kv1.3) except ~27% blockage of Kv1.1 current. In biological functional assay, we demonstrated that the Cm28 strongly inhibited the expression of the activation markers interleukin-2 receptor □□(CD25) and CD40 ligand in anti-CD3-activated $CD4^+$ T_{EM} lymphocytes. Sequence analysis identified that Cm28 has less than 40% similarity with other known □-KTx from scorpions and lacks the typical functional dyad (lysine-tyrosine) required to block Kv channels.

Conclusion: Our conclusion is that the Cm28 peptide belongs to a new subfamily of □-KTx toxins with high potency of inhibiting Kv1.2 and Kv1.3. The unique primary structure of Cm28 will enable us to generate a novel group of selective Kv1.3 inhibitors using peptide-engineering.

THE ROLE OF EXTRACELLULAR MATRIX MOLECULES IN THE INVASIVENESS OF GLIAL TUMORS

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Melinda Rostas is a medical student at the Department of Oncology, University of Debrecen, Debrecen, Hungary.

Aim: Malignant gliomas are the most common primary central nervous system tumors of which about 10% are diffuse-growing oligodendrogliomas. Oligodendrogliomas are classified by the WHO as grade II and grade III tumors. Extensive peritumoral infiltration of tumor cells is a characteristic trait, partly due to the extracellular matrix (ECM) of the tumor. The levels of different ECM molecules in intracranial tumors have been studied in several cases, but in oligodendrogliomas no panel-like expression analysis has been performed. The aim of our study is to determine the quantitative changes of ECM components in grade II and grade III oligodendroglioma samples.

Methods: In our study, we examined whether the expression pattern of molecules involved in invasion correlated with the grade of oligodendrogliomas, and whether there was a difference in patients within the same histological group and grade but with different prognoses. We created subgroups with poor and better prognoses within the same grade. Different aspects were considered in the prognostic grouping. The mRNA and protein levels of ECM components in tumor samples were measured. mRNA expression was measured by qRT-PCR, protein level was measured by fluorescent immunohistochemical reactions.

Results: Significant differences were found between ECM components in the samples of both patients with different grades and patients with the same grade but different prognosis. The mRNA expression of BCAN, CSPG5, HAS2, IDH1, and VCAN genes was determined to be significantly different between grade II and III tumors. Additionally, the levels of CSPG5 and NCAN molecules were determined to be significantly different in grade II samples, while BCAN and EGFR differed in grade III samples from patients with poor and better prognoses. These results were confirmed by immunofluorescence reactions.

Conclusion: In conclusion, it was determined that ECM components exhibit different expression levels in tumors with different grades and prognoses. Based on the expression pattern, it is possible to identify more aggressive tumors, thus the invasion spectrum can be used as a prognostic marker.

EFFECTS OF TOFACITINIB THERAPY ON ARGININE AND METHIONINE METABOLISM IN ASSOCIATION WITH INFLAMMATION AND ENDOTHELIAL FUNCTION IN RHEUMATOID ARTHRITIS

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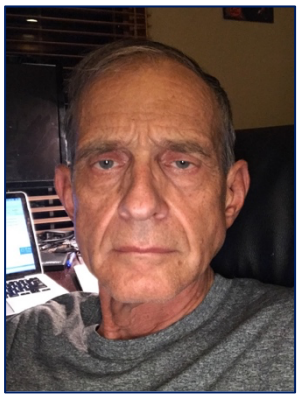

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Dr. Seres is a Cardiac Anesthesiologists at the Department of Anesthesiology, University of Colorado. This study represents a cooperation between the cardiac anesthesia and liver transplant team.

Aim: Rheumatoid arthritis (RA) has been associated with increased cardiovascular (CV) risk and metabolic changes. Janus kinase (JAK) inhibitors, as new therapeutic options in RA, may increase lipid levels, however, we have little information available how these compounds influence vascular pathophysiology, metabolites of the arginine pathways or the methionine-homocysteine cycle in RA patients during long term treatment. Arginine metabolism is essential in NO production and normal endothelial function. Endothelial function is altered by decreased NOS activity and NO production or by increased arginase activity causing vascular muscle cell proliferation. Besides the endothelial function arginine metabolism by NOS and arginase may indicate either enhanced inflammation with increased NOS activity or tissue proliferation and regeneration with increased arginase activity. The goal of this study was to correlate the arginine and methionine metabolism with inflammation and endothelial function.

Methods: Thirty RA patients with active disease were treated with either 5 mg bid or 10 mg bid tofacitinib for 12 months. We determined DAS28, CRP, IgM rheumatoid factor (RF) and anti-cyclic citrullinated peptide (CCP) levels. We assessed brachial artery flow-mediated vasodilation (FMD), carotid intima-media thickness (IMT) and pulse-wave velocity (PWV) by ultrasound at baseline and after 6 and 12 months. We also determined plasma L-arginine, L-citrulline, L-ornithine, inducible nitric oxide synthase (iNOS), asymmetric (ADMA) and symmetric dimethylarginine (SDMA), L-N-monomethyl-arginine (L-NMMA), cysteine, homocysteine, and methionine levels at baseline and after 6 and 12 months.

Results: Twenty-six patients (13 on each arm) completed the study. One-year tofacitinib treatment did not change FMD and PWV in the full cohort. IMT increased despite of treatment. Tofacitinib at 10 mg bid significantly increased L-arginine, L-ornithine, iNOS and methionine levels after 12 months. In addition, tofacitinib at 10 mg bid transiently increased L-citrulline and L-NMMA plasma levels at 6 month and significantly decreased homocysteine level at 12 months. No change in IMT was observed in the 10 mg bid subset. At the same time ADMA and SDMA levels did not change in our study. Multivariate analysis indicated variable correlations of L-arginine, L-citrulline, ADMA, L-NMMA, homocysteine and methionine with DAS28, CRP, ESR and RF but not with anti-CCP after one-year treatment. With respect to vascular pathophysiology, only PWV and methionine after 12 months correlated with each other.

Conclusion: One-year tofacitinib treatment suppressed systemic inflammation in RA. Tofacitinib especially at 10 mg bid may exert CV protective effects in RA, indicated by the not changing FMD, IMT and PWV values as well as by the decreasing homocysteine level. The NOS and arginase activity remained balanced during the treatment period suggesting normal endothelial function and suppressed inflammation.

ASSISTED REPRODUCTIVE TECHNOLOGIES 2021: BRAVE NEW WORLD IN IVF

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In vitro fertilization (IVF) was first developed originally for use in the animal husbandry industry and then adopted to use in humans. Louise Brown was the first baby born in 1978 at the Bourne Hall clinic in England. Dr. Edwards was awarded the Nobel Prize in 2010. There have now been over 8 million babies resulting in the “miracle generation” who otherwise would never have been born.

The first indication for the use of IVF was for women with damaged, missing or blocked fallopian tubes. The technology has expanded now to include patients with endometriosis, pelvic infections, unexplained infertility, recurrent miscarriages, diminished ovarian reserve, advanced maternal age, ovulation disorders, previous sterilization, fibroids, low sperm counts, and genetic disorders (single gene, chromosomal).

The advances in IVF have raced forward at breakneck speed. Embryo culture was initially performed with simple buffered solutions. Today, understanding the micronutrient requirements of early embryos, complex sequential media have been developed. Laboratory air quality with advanced filtration and incubators have dramatically improved embryo growth. As a result, embryos that were transferred day 2 to 3 after fertilization (4-8 cell stage of development) are now routinely transferred 5-7 days at the blastocyst stage (>100 cells). Traditional fertilization of oocytes requires thousands of healthy sperm. Now with the advent of intracytoplasmic sperm injection (ICSI), a single sperm may be injected into the oocyte, bypassing the need to digest the zona pellucida (oocyte outer shell). This has revolutionized the treatment options for couples faced with low sperm counts. Surgical sperm retrieval techniques allow the “needle in the haystack” to be found. Sperm, embryos and now oocytes and may be stored in liquid nitrogen for decades. Third party reproduction, surrogates and gestational carriers all offer additional opportunities.

Preimplantation genetic testing for aneuploidy PGT-a (chromosomal abnormalities) and preimplantation genetic diagnosis (PGD) for gene mutations can be performed on embryos. The human genome project has identified the addresses of countless genetic disorders (Tay Sachs, Sickle Cell, Cystic fibrosis, etc). These are performed prior to embryo transfer to prevent the transmission of a genetic disease/abnormality thereby optimizing a healthy outcome.

The future is here. Assessment of embryo protein, metabolic, and genes critical for embryo development is possible. Gene therapy has been used to edit out mutations using CRISPR. Uterine transplantation, stem cell maturation, in vitro gametogenesis, EVATOR microhuman biology, SHEEF’s (synthetic human entities with embryo like features), ectogenesis and 4D printing are all part of science fact…not fiction.

THE EPILEPTIC BABOON BRAIN: FROM DNA TO THE IMAGING OF NETWORKS

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Dr. Szabo was born Tarrytown, New York, and after living in different states, moved to Vienna Austria, where he completed most of his schooling, including medical school. He returned to the United States for his residency training in Neurology and Fellowship in Epilepsy, both completed at the Cleveland Clinic Foundation. From there, with his Colombian wife, Luz, and two young sons, Miklos and Daniel, he moved to San Antonio, Texas, in 1996. He joined UT Health San Antonio, and helped build the South Texas Comprehensive Epilepsy Program, which he currently directs. Over the past 15 years, his research was focused on the characterization of the baboon as a natural model of photosensitive, genetic generalized epilepsy (GGE). He has collaborated closely with the Texas Biomed in San Antonio, Texas, which houses one of the largest baboon colonies in the world, and definitely the largest and oldest captive baboon pedigree. His work ranged from phenotyping a large portion of the pedigree with scalp EEG to characterizing the electroclinical syndrome and underlying pathophysiology with functional and structural neuroimaging, intracranial EEG, and brain pathology. The baboon also provides an excellent model for studying sudden unexpected death in epilepsy, SUDEP, which is the focus his animal and human research currently.

The epileptic baboon represents a model for genetic generalized epilepsy (GGE) in humans, most closely resembling juvenile myoclonic epilepsy in humans. Recent research identified a genetic marker for the epilepsy, RBFOX1, which has been implicated in human genetic epilepsy syndromes, including GGEs. One of its main functions is the regulation of splicing multiple epilepsy candidate genes, including FLNA, SLC1A3, DCX, GABRB3, GAD2, KCNQ2, SCN8A, SLC12A5, SV2B, SYN1, fulfilling the role of a susceptibility gene. While no genome-wide protein-altering variants were identified, gene set enrichment analyses (GSEA) revealed significant positive enrichment for genes involved in the extracellular matrix structure (ECM; FDR = 0.0072) and collagen formation (FDR = 0.017), which was reflected in a major protein-protein interaction (PPI) network cluster. Recent neuroimaging studies in two epileptic baboons highlighted potential anti-seizure effects of standard low-frequency (20-30 Hz) and the novel high-frequency, microburst, vagal nerve stimulation (VNS) therapy. Both modes of stimulation demonstrated activations in the brainstem involving the right substantia nigra (SN) and globus pallidum (GP), but more robustly with the high-frequency VNS. High-frequency VNS Therapy also suppressed interictal epileptic discharges (IEDs) in one baboon, with widespread cortical deactivations of brain regions that were activated by IEDs. This study demonstrated anti-seizure cortical and subcortical targets of VNS Therapy.

MECHANICAL CIRCULATORY SUPPORT IN CHILDREN – OUR EXPERIENCE OVER THE LAST 10 YEARS FROM GOKVI

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Mihaly Daniel Szonyi is a medical student at the Gottstegen Gyorgy National Institute of Cardiology, Budapest, Hungary.

Aim: Mechanical Circulatory Support has progressed a tremendous amount over the last two decades. In case of an unsuccesful conservative therapy in acute or chronic circulatory failure, MCS is a great bridge therapy in children. A successful transplant program is unimaginable without MCS. Compared to adults, MCS therapy in children has it's specific difficulties and challenges. Our goal was to assess and look back on 10 years of pediatric mechanical circulatory support in the Gottsegen György Gottsegen National Institute of Cardiology's Children's Center. We took a look at the indications, the complications and outcomes of the supported children.

Methods: Our research was retrospective, we mainly utilised the MedSol infromatics system. Based on international literature, we took a look at the following characteristics of the therapy: what kind of devices were implanted, the length of the therapy, the side effects, the outcomes, the number of transplanted patients, and the number of deceased children.

Results: Of the 32 children observed, 7 were excluded due to them only being on ECMO therapy, which would have distorted the results. Of the remaining 25 patients, 40% were male, while 60% were female. The mean age was 10,45 years (+/- 5,8 SD). The indications were as follows: 72% was due to myocarditis/ primary myocardial disease, 24% were due to congenital heart diseases, 4% of the therapies were administered due to other causes. There were 15 intermediate-term, extracorporeal, continuos flow VADs, 6 long-term extracorporeal pulsatile flow VADs and 6 long-term intracorporeal continuos flow VADs implanted. 32% of the children received a HTx. And 36% were decease. We found significant differences in overall survival rate, in relation to the type of the therapy.

Conclusion: Mechanical Circulatory Support is an essential tool for HF's treatment, even in children, and it's also necessary for a successful transplantational program. Hopefully with more available devices, improved technology, better anticoagulant protocolls and better side effect profiles, the use of MCS's in children will increase, and the therapy will be more effective.

FUNCTIONAL MRI IN CLINICAL PRACTICE – ANALYSIS OF THE EFFECTSOF THE OPTIMIZED CENSORING TOOLBOX

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Hedvig Tarjan is a 6th year medical student from Semmelweis University, graduating in November 2021. Throughout her academic years she took greater interest in the fields of Cardiology, Neurology and Radiology. Later on as she got acquainted with the Medical Imaging Centre at the Semmelweis University it became clear to her that she wanted to pursue a career in Radiology. She found the modality of fMRI exceptionally intriguing and so started to entrench herself more in the subject. In the future, she intends to familiarize herself better with Interventional Radiology and hopefully enroll in a training that can provide her with such qualification.

Aim: Functional Magnetic Resonance Imaging is an important tool of pre-surgical workup of tumors and/or epileptogenic lesions near to or within eloquent brain areas. Profound methodical considerations are crucial in order to draw well-founded conclusions from the detected signs; therefore, the prudent paradigm selection, data collection and statistical analysis are all essential. Analysis of the effects of the Optimized Censoring Toolbox using our own fMRI data. We wanted to know, how paradigm-dependent the OptCens processing is, how competent it is in the identification of potential false-negative and false-positive voxels and whether the divergence of the corrected activity-maps depends on the number of identified scattered data.

Methods: We analyzed the fMRI data of 34 patients from the preoperative language mapping program of the Semmelweis University MRI Research Center after applying exclusion criteria. Picture naming, Synonym task, Speech comprehension and Auditory decision were the four tasks used for the language mapping. We used high resolution 3D-TFE T1-weighted sequence for the anatomical imaging, which was then co-registered with T2*-weighted EPI sequence functional images, followed by data pre-processing. The data was then analyzed with general linear model (GLM) and used as the input for the OptCens Toolbox.

Results: The four different paradigms used activated the various language networks to a different extent; the Picture naming task resulted in the largest activity-map. There wasn't any significant difference in the number of scattered values between the paradigms. The algorithms used by the OptCens appeared to be stable on a group level, the application of the toolbox did not cause any drastic change on the activity-maps. On an individual level however, the differences became more pronounced. As the number of scattered values increased the effect of OptCens processing became stronger as well, which was attributable rather to the elimination of false-positive than the correction of false-negative voxels.

Conclusion: In conclusion the OptCens Toolbox appears to be a promising tool in the fine correction of fMRI activity-maps in group analyses, in identification of false-positive and false-negative activities, however whether it is suitable for preoperative planning on an individual level needs further investigations.

INTRODUCTION OF MEDICAL EXERCISE SPECIALIST TRAINING IN HUNGARY

Vernes, R.
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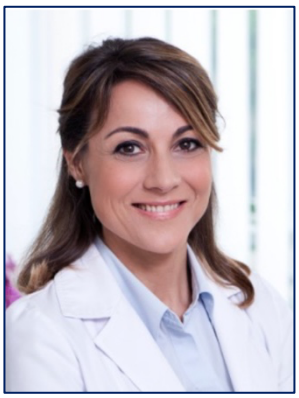

Reka Vernes, MD

Family Medicine Physician, Family Medicine Practice, Budapest, Hungary

Dr. Reka Vernes is a Family Medicine physician practicing in Budapest, Hungary.

Aim: In the last decades we see a dramatic increase in the number of patients with chronic, non-communicable disease (NKDs). The Covid pandemic draw the attention to the fact, that people with chronic conditions are much more susceptible for the infection and serious complications from the disease. One of the key elements of treating NKDs is exercise therapy. Fitness centers and gyms now have to be prepared to work with clients with heath challenges and special needs like pregnant woman and aging population. The American Council of Exercise developed the Medical Exercise Specialist training to educate fitness professionals to work with health-challenged clients.

Methods: The base of the training is an eBook and instructors adjust the study material to local conditions and treatment protocols with supplemental material and webinars. It is necessary to develop a new nomenclature and communication platform to work between the exercise specialist and other members of the healthcare team.

Results and Discussion: Such training keeps up with the increasing demand for trained personnel who can work securely and effectively with clients with health challenges and working within the health care community. Scope of practice and role of MES needs to be established and adapt to the local regulations and feasibilities.

RESTENOSIS RATES IN PATIENTS WITH IPSILATERAL CAROTID ENDARTERECTOMY AND CONTRALATERAL CAROTID ARTERY STENTING

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Boldizsar Voko is a sixth-year medical student at the Semmelweis University in Budapest. He was lucky enough to got into the HMAA's Houston Clinical Program. He had his fourth-year surgical internship at the Charité University in Berlin. During his last two years at medical school, he did his clinical research in the field of vascular interventional radiology. For his presentation at the XXXV. National Conference of Students' Scientific Associations Conference (OTDK) he won the first prize in the radiology section. His professional interests are minimally invasive surgery and medical imaging during surgery. After his graduation in November he is going to start a urology residency in Budapest.

Aim: We aimed to evaluate the long-term outcome of carotid endarterectomy (CEA) and carotid artery stenting (CAS) in patients who underwent both procedures on different sides.

Methods: In this single-center retrospective study (2001–2019), 117 patients (men, N=78; median age at CEA, 64.4 [interquartile range {IQR}, 57.8–72.2] years; median age at CAS, 68.8 [IQR, 61.0–76.0] years) with ≥50% internal carotid artery stenosis who had CEA on one side and CAS on the other side were included. The risk of restenosis was estimated by treatment adjusted for patient and lesion characteristics.

Results: Neurological symptoms were significantly more common (41.9% vs 16.2%, P<0.001) and patients had a significantly shorter mean duration of smoking (30.2 [standard deviation {SD}, 22.2] years vs 31.8 [SD, 23.4] years, P<0.001), hypertension (10.1 [SD, 9.8] years vs 13.4 [SD, 9.1] years, P<0.001), hyperlipidemia (3.6 [SD, 6.6] years vs 5.0 [SD, 7.3] years, P=0.001), and diabetes mellitus (3.9 [SD, 6.9] years vs 5.7 [SD, 8.9] years, P<0.001) before CEA compared to those before CAS. While the prevalence of heavily calcified stenoses on the operated side (25.6% vs 6.8%, P<0.001), the incidence of predominantly echogenic/echogenic plaques (53.0% vs 70.1%, P=0.011) and suprabulbar lesions (1.7% vs 22.2%, P<0.001) on the stented side was significantly higher. Restenosis rates were 10.4% at 1 year, 22.3% at 5 years, and 33.7% at the end of the follow-up (at 11 years) for CEA, while these were 11.4%, 14.7%, and 17.2%, respectively, for CAS. Cox regression analysis revealed a significantly higher risk of restenosis (hazard ratio [HR], 1.80; 95% confidence interval [CI], 1.05–3.10; P=0.030) for CEA compared to that for CAS. After adjusting for relevant confounding factors (smoking, hypertension, diabetes mellitus, calcification severity, plaque echogenicity, and lesion location), the estimate effect size materially did not change, although it did not remain statistically significant (HR, 1.85; 95% CI, 0.95–3.60; P=0.070).

Conclusion: Intra-patient comparison of CEA and CAS in terms of restenosis tilts the balance toward CAS.

STATUS EPILEPTICUS

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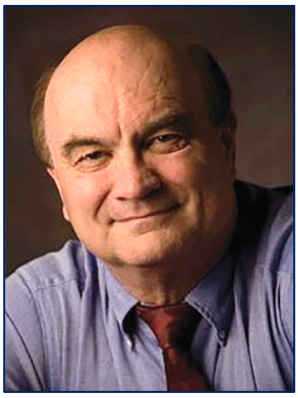

Gabor Zoltay, MD

Neurologist, Nathan Littauer Hospital, Gloversville, NY

Dr. Gabor Zoltay graduated from medical school at the University of Pecs. He finished his residency program in one of the biggest neuroscience centers in the Mid-West. After finishing a 2-year epilepsy fellowship, he started to work in New York State.

Aim: Status epilepticus (SE) is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms, which lead to abnormally, prolonged seizures. It is a condition, which can have long-term consequences, including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures. It is a neurological emergency.

Methods: It is a retrospectively analyzed observational study of 50 patient in 3 year, between 2017-2020). Patient who had either convulsive or nonconvulsive status epileptics were included. A total of 80 episodes in 50 patients were considered as definite status epilepticus.

Results: We identified 50 patients with median age of 69 years (range 20 -80) years). The most frequent etiology was remote (32%), followed by acute (31%), or mixture of acute and remote factors (10%). Semiology was generalized convulsive in 44%, focal motor in 27%, and nonconvulsive in 30%. Only few patients did not have relevant comorbidities. Median latency between SE onset and the first treatment was 16 hours. 16 (32%) of the patients were treated within a few hours after onset. Treatment in elderly is essentially the same as in younger adults with benzodiazepines, (lorazepam, diazepam, clonazepam) and longer acting antiseizure drugs (phenytoin, fosphenytoin, valproate, levetiracetam, brivaracetam and lacosamide). 24 (49%) were refractory (defined as an ongoing SE after application of benzodiazepine and intravenous anticonvulsant). Neurologic outcomes were poor 41% of patients, and 20 % died. The mean duration fo SE was 6-days vs 2 days in the group with and without MRI alteration, respectively.

Conclusion: All current interventions for SE involve antiseizure drugs that were developed for treatment chronic epilepsy. Treatments should be developed that are more specific for various etiologies and involve drugs that work on the underlying cause of the SE.

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