

ARCHIVES OF THE HUNGARIAN MEDICAL ASSOCIATION OF AMERICA



50TH Anniversary Annual Scientific Meeting

PRESIDENT OF THE REPUBLIC OF HUNGARY

Half a century has passed since seven Hungarian doctors came together in Cleveland, Ohio to establish an organization for the promotion of medical excellence. What motivated them was not only love for their vocation, but also love for their motherland and for their new home – the United States. This inner drive, passed on to subsequent generations of Hungarian doctors living in the United States, created a lasting legacy. The result is that this year we are able to celebrate the 50th anniversary of the establishment of the Hungarian Medical Association of America (HMAA): a respected professional community which is still going strong after five decades.

This anthology of medical studies written by members of the Association is an excellent showcase of their talent and experience – both in research and in the practice of medicine. Every one of these articles reflects their outstanding achievements, of which we can all be proud. It is truly heartwarming to know that doctors of Hungarian origin are also making a difference in these parts of the world. We are also grateful for their willingness to share their knowledge with their colleagues in Hungary.

The Association has likewise done a great deal for Hungary. The famous Hungarian writer Sándor Márai once gave a perfect description of the kind of loyalty to the motherland that is shown by the members of the HMAA: “Patriots swagger, sing songs, perorate and swear oaths. But there is only one true patriotism: to acquit oneself well in one’s work, with complete loyalty and unconditional effort – wherever one finds oneself. This is what truly has the power to benefit the motherland. All else is just cheap spectacle and freeloading.”

In this vein, I wish all members of the Association great success in their professional activities, which have brought relief and recovery to so many people in need – and have thereby also enhanced the reputation of Hungarians worldwide.

I wish you a happy anniversary!



János Áder

President of the Republic of Hungary

Letter from the President

Dear Colleagues and Guests,

This year, we are celebrating the 50th anniversary of the Hungarian Medical Association of America (HMAA). It all started in the Fall of 1968, when Gustav Batizy invited six of his friends, including Laszlo Bandy, Rudolf Bogнар, Joseph Erossy, William Kovats, Zoltan Peller and Julius Prehal, to his house to discuss the outlines of the HMAA. The tradition of an Annual Scientific Meeting started with the first President, Gyorgy Vareska (1970 – 1971), a well-known and highly respected pathologist and was firmly established by the second President, Gustav Batizy (1971 – 1973). It was the next President, Laszlo Kaveggia (1973 – 1975), who persuaded his colleagues to move the Annual Scientific Meeting to Sarasota, Florida (some people think that the move had to do something with his condominium there, but it is a great location anyway). As President, Imre Magoss (1975 – 1981) helped the society become a reputable professional organization with English as the official language. During the tenure of Arndt Peter Schimert (1981 – 1985), the bylaws were revamped according to the norms of other scientific societies. Tibor Doby (1985 – 1987) and Elemer Zsigmond (1987 – 1989) continued the work of their predecessors and elevated the level of the Annual Scientific Meeting. After the fall of the iron curtain, the new, democratically elected government frequently consulted the HMAA in healthcare related issues and HMAA President George Alker (1989 – 1991) and President-Elect Irene Levay-Krisztinicz were warmly received by President Árpád Göncz in his offices in the Parliament. The Presidency of Dr. Levay-Krisztinicz (1991 – 1993) was very eventful; she represented the HMAA at several meetings, including the World Association of Hungarians, where she was seated next to Prime Minister, József Antal. Until his untimely death, Dr. Cornelius Navori (1993 -1994) worked diligently on staff development for a proposed hospital in Budapest. During the Presidency of Dr. Alexander Matolcsy (1994 -1997), the Student Exchange Program, the significance of which parallels that of the Annual Scientific Meeting, was born. President Ivan Krisztinicz (1997-1999) had many major accomplishments, including consolidation of the student exchange program, which today carries his name. Under the Presidency of Dr. Peter Petrusz (1999 – 2001), the HMAA, in collaboration with the MET (Magyar Egészségügyi Társaság), participated in multiple lecture series in Hungary. President Peter Forbath (2001 – 2003), actively recruited new leaders and is credited for the revitalization of the Board. Under the Presidency of Dr. Gabriel Haas (2003 – 2005), the HMAA participated in several international projects in collaboration with the MET. President Laszlo Mechtler (2005 – 2008) strongly believed that the HMAA had an obligation to improve healthcare in Hungary and played an important role in the passing of a bill that now prohibits smoking in restaurants and other facilities. During the Presidency of Dr. Tamas Peredy (2008 – 2010), the HMAA website was transformed into a more comprehensive site capable of on-line meeting registration and membership management. President Istvan Somkuti (2010 – 2012) continued to foster the relationship with the MET and the four medical universities in Hungary. As President, Dr. Gyorgy Baffy (2012 – 2014) is credited for bringing many young talents, including medical students and recent graduates, to the Annual Scientific Meeting. President Thomas Krisztinicz (2014 – 2016) signed a renewal of the Memorandum of Understanding between HMAA and the four Hungarian medical universities and oversaw the expansion of the Student Exchange Program. As current President (2016 – present), my focus is to develop a relationship with North American medical students studying in Hungary.

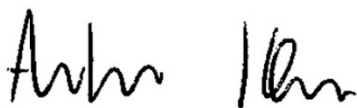


I know that one sentence about each President does not do justice and there are many other people who contributed to the success of our society. If you are interested, I encourage you to read “Fifty Years of the Hungarian Medical Association of America.” It is an outstanding book edited by Drs. Geza Acs and Istvan

Somkuti.

I believe our founding fathers would be proud of the current state of our society. Thanks to Drs. Irene Levay-Krisztinicz, Laszlo Mechtler, Zsolt Garami, and Alexander Matolcsy, the Ivan M. Krisztinicz Student Exchange program is flourishing and has expanded to other sites.

As far as the Annual Meeting is concerned, with the leadership of Secretary Geza Acs, it is well organized. Program Chair Istvan Stadler has received a record number of abstract submissions, and Public Relations Chair Alexander Matolcsy and President-Elect Ivan Harangozo have been able to secure the participation of prominent guests. János Áder, President of Hungary, and Dr. László Szabó, Ambassador of Hungary to the United States, will speak at the Opening Ceremony. Speakers of the scientific program will include Nobel Laureate Dr. Craig Mello. Guests of the Gala at the Sarasota Yacht Club will be addressed by Dr. Miklós Kásler (Minister of Human Resources of Hungary), Dr. Béla Merkely (Rector of Semmelweis University), and László Mátyus (Dean of the Faculty of Medicine, University of Debrecen) and will be entertained by world renowned vascular surgeon-magician Dr. Peter Gloviczki. We will have a great meeting. Please enjoy!

A handwritten signature in black ink, appearing to read 'Andras Koor'.

Andras Koor, MD, PhD
President of HMAA

Welcome to Our 50th Annual Meeting

Greetings All,

By now you all have heard enough of the festivities. Please enjoy them, our 50 years. Since the Board has asked me to write a few words, please indulge me.

It is important to realize where we have been, in order to realize where we are going. I believe it makes sense, since my 23 and 24-year-old sons are actually quoting it! Are we making progress? Who are “we”? Most of us, as physicians have had difficult travails to get “where we are right now”. Is this where we would like to be? I pose the question: What is different? The answer: A sense of belonging - there is something more important than each of us individually. I hope you can appreciate my words. Wherever you read the words I or me, replace with yourself.

The HMAA has been for me a place of solace, an anchor in my life - whether the institution or the members I have met, who have had a kind word to say or a bit of wisdom; what I should do with my career. Thirty years later, I am an average community anesthesiologist - not only making a living as medical director of our practice in 3 hospitals, but fulfilling the responsibility that our predecessors ingrained into us - “primum non nocere”; doing our best to advocate and take care of the patient, without requiring anyone else to tell us to do so!

The HMAA is an organization which has wanted to make a difference in its work. We have expanded to attempt to have influence with improving healthcare in Hungary. Its members took me in as a young student and through their example, directed me to something greater than I myself could have realized. It was a continuation of my concurrent association with the Magyar Cserkész, only a touch more professionally.

I realize and hope you do as well, keeping a sense of community in your professional, as well as personal life, is paramount to success. Realize, the HMAA is here for you as that anchor in your professional and private life; to help you flourish as the individual you were meant to be! Welcome and enjoy not only the conference, but also the comradery of fellow physicians and scientists associated with Hungary.

You don't have to be a professor with 8 pages of publications - We look for “average” clinicians as well, who work to their best ability, taking care of individuals who need our expertise in our respective fields.

With all best wishes,



Ivan Harangozo MD
President-Elect, HMAA



Secretary's Note

Dear Colleagues, Dear Friends,

We celebrate the 50th Anniversary of the Hungarian Medical Association of America and our 50th Annual Scientific Meeting. In the context of human history, 50 years is not such a long time. One might raise the question whether it calls for a celebration. If you only look at the number of years, the answer is maybe not. Yet, I think that this anniversary is worth commemorating for two reasons. For one, an anniversary is always a time and opportunity to explore and reflect on the past, account for the present, and contemplate the future. The other important reason to commemorate this 50th anniversary is that today we are fortunate to have among us those who had laid the foundations, the people who are responsible for creating this great ethnic medical society, and we can express our gratitude to them. They took on a tremendous task and carried it out successfully, and for that, we owe them many thanks. Not only did they bring together the Hungarian physicians and scientists living and working on this continent far away from our motherland, but they also provided the opportunity for continuing close contacts with our colleagues working in the Carpathian Basin, exchanging professional skills and knowledge, meeting with one another on a regular basis and establishing and nurturing life-long friendships. And all of this was achieved in an inclusive, multidisciplinary environment.



The first time we attended the Annual Meeting was in 1999, during my residency, our younger daughter less than 1 year old, at the encouragement of our friend from medical school, Zsolt Garami, who told me “dude you have to come, it’s an awesome meeting!”. So, we drove down from Philadelphia with the kids and (surprise) Zsolt turned out to be right, we had a terrific time enjoying the wide array of high level multidisciplinary lectures on topics I would never ever hear about otherwise (being a pathologist, but I assume it applies to all other medical specialties as well) and the welcoming, friendly atmosphere of the meeting. So, we came back next year, the year after, and never missed a meeting since. The Annual Meeting became part of our yearly calendar, a meeting with friends every year we would not miss. Not even for a hurricane – when the meeting was canceled due to a hurricane in 2007, we still came to Sarasota the next week, only to find that many other members decided to do the same to have an “unofficial meeting”. It is this friendship, the comradery, the desire to spend time with friends what holds the Society together. Seeing one another’s children growing up, spending long evenings together on the beach or by the pool and sharing our experiences with the younger generation and bringing them into our “family” are priceless.

I am confident that our Society not only has a beautiful past we all can be proud of, but also a brilliant future. However, for this bright future to actually come true, it is not enough to simply believe in it, we all have to want it and be willing to diligently work for its realization. Only if we all work together in honest professional and personal relationships, can we preserve and improve the status, reputation, independence and future of Hungarian medicine and science in today’s often challenging and sometimes controversial environment and health care system. Welcome to the 50th Annual Meeting of the HMAA!

Best wishes,

A handwritten signature in blue ink, appearing to read 'Geza Acs'.

Geza Acs, MD, PhD
Secretary of HMAA

From the Editor

Dear Members and Guests,

I have served as your humble editor now for over a decade. I also have had the honor of serving as President of the HMAA between 2010-2012. I hope you all approve of this year's 50th Anniversary Meeting special edition of the Archives. Dr. Acs and I have completed the comprehensive history of our organization and will be available to you all at the meeting.

I first attended the HMAA as a medical student in 1986 at the urgings of Drs. Ivan and Irene Krisztinicz. My lifelong Hungarian scout (cserkész) friends Ivan Harangozo and Tamas Krisztinicz were also attending. The three of us all received awards for our student presentations from the society. Well, as they say the rest is history.

The HMAA meeting held every last week of October has been one of the most anticipated yearly events for myself and my family. The friendships that have been forged over these past 30 years are some of my most treasured. There are few intimate medical venues that have afforded such opportunities as one memorial afternoon where I shared a beer with my next door neighbor at the hotel, Dr. William Ganz. I could have never imagined hearing one-on-one, the recounting of his life's adventures and path to the development of one of the world's most revolutionary medical devices. The opportunity to interact with the students, help advise and mentor them to fulfill their dreams and then see them later in life successful in their chosen careers has been most rewarding. I will always be thankful to the elders of our society that had the foresight to establish the HMAA. I will always have a special place in my heart for our society's doyenne, Anna Sandor. It was she who invited her long time neighbor from Erdély, Ms. Eniko Mara in 2011 to visit her here in Sarasota. She is now my most loving and beautiful wife.

My fervent hope is that this tradition is carried on in the future by the new generation of young physicians. It has been these experiences and memories that have kept me coming back faithfully year after year.

Sincerely,



Istvan Somkuti, MD, PhD
Editor of HMAA Archives



Greeting by the President of the Hungarian Medical Association of the United Kingdom

Dear HMAA Members,

On behalf of the Hungarian Medical Association of the United Kingdom (HMAUK), I'd like to congratulate HMAA for their 50th anniversary of their Annual Conference and send our greetings to all participants of the historic event in Sarasota.

HMAUK, representing doctors living and working in the UK of Hungarian origin with over 450 members, was founded in 2014 based on HMAA's inspiration. As a sister organization across the Atlantic, we share several common goals and objectives in support of our members. Since the beginning, HMAUK enjoyed heartfelt support of HMAA, from strategic advice for our future development, technical support for our on-line presence, to mutual participation at our conferences. Dr Thomas Krisztinicz kindly joined our first Annual Conference in 2016 in Manchester representing HMAA.

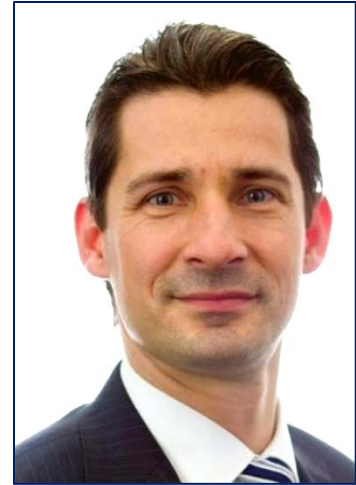
HMAUK was also honored to have joined this year's annual scientific meeting in Balatonfüred in August. We had some great discussions following the presentation of Dr Attila Vegh, HMAUK's president on strategic collaboration with HMAA and perspectives on Hungarian doctors' migration trends in Europe. Dr Gyorgy Rakoczy, HMAUK Vice President will join the conference in Sarasota.

On behalf of Hungarian doctors in the UK, we wish all participants of this historic event fruitful discussions and a fantastic time together. We're looking forward to deepening our collaborations with further joint events in the future and wish HMAA another 50 years of great success.

Best wishes,



Dr. Attila Vegh
HMAUK President





The American Hungarian Federation

Serving the Community since 1906 - Fidelissimus ad Mortem

Hungarian Medical Association of America
HMAA, P.O. Box 421
Amherst, NY 14226-0421

September 12, 2018

Dr. Andras Khor MD, PhD
President

RE: 50th Anniversary of the founding of HMAA

Dear Dr. Khor:

On behalf of the American Hungarian Federation we congratulate the Hungarian Medical Association of America on the 50th anniversary of its founding!

Excellence in medical science is part of the national culture of Hungarians and the recognition of Hungarian contributions to this field enriches and gives credit to our homeland's good name.

What an accomplishment that you were able to work on a voluntary basis for fifty years in disseminating knowledge about clinical medicine and the basic medical sciences, and the related contributions of Hungarians and those of Hungarian ancestry. The networking opportunities that you provided and interactions among those exceptional physicians and scientists that you brought together to share their research have served to substantially improve medical science.

How wonderful also that you were able to provide so many scholarships and exchange programs for medical students from both America and Hungary.

What superb accomplishments. As Americans of Hungarian descent we are proud of your work.

May your contributions continue for at least 50 more years!

Best regards,

Akos L. Nagy
President

Gyula E. Balogh
Co-President

Dr. Imre Nemeth
Vice President

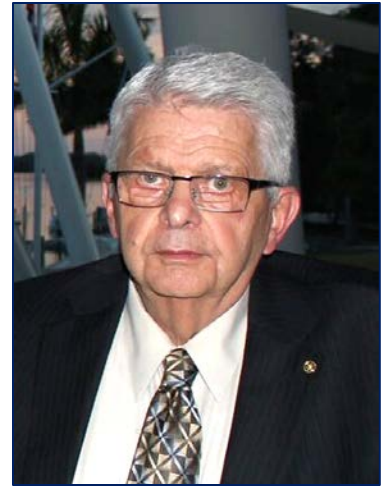
Summary and Evaluation of the 49th Scientific Meeting

Istvan Stadler PhD

The 49th Annual Scientific Meeting of the Hungarian Medical Association of America was held from October 30 through November 3, 2017 at the Sandcastle Resort at Lido Beach, Sarasota Florida. The main title of the 49th Scientific Meeting was: "CURRENT DEVELOPMENTS IN BIOMEDICAL AND CLINICAL SCIENCES".

The scientific sessions were as follows:

1. Latest Developments in Ophthalmology (Monday, Oct 30)
2. Multidisciplinary session: Immunotherapy, Oncology and Neurology (Monday, Oct 30)
3. Young Investigators' Multidisciplinary Session I (Monday, Oct 30)
4. Young Investigators' Multidisciplinary Session II Student Award Recipients (Tuesday, Oct 31)
5. William Ganz MD Memorial Session in Cardiology and Vascular Surgery (Tuesday, Oct 31)
6. Multidisciplinary Session: Internal Medicine, Translational Research, Health Care (Tuesday, Oct 31)
7. Multidisciplinary Session: Internal Medicine, Healthcare Management and Imaging, (Wednesday Nov.1)
8. Healthcare Management Wednesday, Nov. 1)
9. Update in Oncology (Thursday, Nov.2)
10. Special presentation by Distinguished Speaker (Thursday, Nov.2)
11. Multidisciplinary session: Immunology, Internal Medicine, Primary Care and Gynecology (Thursday, Nov.2)
12. John Ertl, MD, Memorial Session



There were 64 submitted abstracts and 60 presentations. This activity has been planned and implemented in accordance with the requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME). The University at Buffalo Jacob School of Medicine and Biomedical Sciences accredited 22.25 AMA PRA Category 1 Credit(s) TM.

There were 32 presenters (50%) from the US, 23 (36%) from Hungary, three (5%) from other countries, (Romania/Transylvania, UAE). There were 14 (22%) young investigators from: 10 from Hungary, two from (Romania/Transylvania), and two from the US.

We had eight world-wide recognized experts accept our invitations to present. His Excellency Dr. Laszlo Szabo, Ambassador of Hungary to the United States was a distinguished, as well as, keynote speaker at our Gala Banquet. The list of the invited speakers is available upon request.

MONDAY, OCTOBER 30:

Latest Developments in Ophthalmology: The diagnosis and treatment of macular degeneration was presented. Two lectures focused on the symptoms of diabetic macular edema and the advantage to using optical coherence tomography /angiography to establish the status of macular edema in diabetic patients.

Multidisciplinary session: Immunotherapy, Oncology and Neurology: In the multidisciplinary session new immune-therapy approaches for lung cancer were presented. Another exciting lecture focused on a living cell's "little memory" and their metabolic control on communication with other tissues in different diseases. The latest developments in colorectal cancer screening was also discussed. There was a lecture on new wearable seizure detecting devices. The future direction of evaluation and developmental markers and their role in genetic generalized epilepsy in juveniles was the topic in the last lecture of this session.

Young Investigators' Multidisciplinary Sessions I and II: The Young Investigators' Multidisciplinary Sessions (Monday, October 30 and Tuesday November 1) included a wide range of basic biomedical science

topics and the diagnostic and clinical applications of their results. The lectures by the HMAA Student Award Winners were included here. The session was well received by the audience.

TUESDAY, OCTOBER 31:

William Ganz MD Memorial Session in Cardiology and Vascular Surgery: Topics of this session included the latest approach for diagnosis and possible treatment of acute and chronic coronary syndrome/heart failure. The outcome and unexpected difficulties in their management of trans-catheter aortic valve replacement were presented. The comparison and the outcome of three diagnostic tests for detection right to left cardiac shunts also were discussed as was the advantage and relevancy of the troponin test in no ST elevation acute coronary syndrome. The measurement of ventricular trabecular mass index by cardiac MRI in Non-Compact Cardiomyopathy (a genetic disorder) as a new diagnostic method was also well received. Applications of pacemaker therapy in Hungary was insightful and the retrograde chemical microfoam ablation of superficial venous insufficiency in 250 patients was equally informative.

Multidisciplinary Session: Internal Medicine, Translational Research, Health Care: This session included a wide range of topics such as the special treatment and outcome of a rare disease paroxysmal nocturnal hemoglobinuria. There were presentations on the role of antioxidants in pathogenesis of diabetes mellitus, the weight management and evaluating the serotonin-boosting diet of veteran taking antidepressant and well as the latest non-human model for Ebola virus replication.

WEDNESDAY, NOVEMBER 1:

Multidisciplinary Session: Internal Medicine, Healthcare Management and Medical Imaging: Eleven lectures on a series of wide ranging topics were presented in this session. Twin studies on the influence of genetic versus environmental factors on heart rate, mean arterial pressure, carotid intima medial thickness were fascinating. Two additional lectures included twin studies: role of epigenetics and microbiome on the onset of diseases, measuring liver stiffness by ultrasound elastography and its genetic control in twins as well as a comparison between management of insulin resistance with new metabolic health monitor applications. There was a provocative lecture on a new method for the treatment of obesity and metabolic syndrome by fecal transplant. The upper limit of the obesity surgery and the risk benefit paradigms were also reviewed.

Healthcare Management: In the Healthcare Management session successful investment in physicians and technology to optimize inpatient documentation (Six Sigma application) as well as how artificial intelligence applications such as "Watson" is impacting healthcare were discussed. There were lectures on imaging studies in primary care, the amortization of radiologic equipment in Hungary and the results of a randomized double blinded trial of a new home care device for vascular therapy, "BEMER".

THURSDAY, NOVEMBER 2:

Update in Oncology: In this session there were seven lectures covering a wide range of oncology topics. Complementary and alternative medicine pediatric oncology approaches between Hungary and the United States were compared. A new tool utilizing a patient's molecular genetic profile for targeted cancer therapy was provocative. The anatomical examination of axillary sentinel lymph node drainage and its role in early breast cancer was insightful. The presentation on the diagnosis, taxonomy and possible treatment of melanocytic neoplasia in the genomic era was informative. There were talks on invasive breast carcinoma with extracellular mucin production, and another on liver directed therapies in metastatic colorectal cancer as well as the effect of red light therapy on chemotherapy induced alopecia in breast cancer.

Multidisciplinary Session: Immunology, Internal Medicine, Primary Care and Gynecology: This session included topics on iron homeostasis and its relationship to erythropoiesis and innate immunity, transforming primary care for transgender patients and fertility and preservation option and pregnancy outcome for transgender individuals.

FRIDAY, NOVEMBER 3:

John Ertl MD Memorial Multidisciplinary Session: Gynecology, Cosmetic and Vascular Surgery and Neurology: Lectures included a case study of uterine dehiscence, updates in cosmetic surgery with body sculpting procedures for both women and men, a case presentation for C1q deficiency leading toward lupus erythematosus, sleep disorder and epilepsy issues, radiation induced optic neuropathy, and the application of Transcranial Doppler during in aorta surgery., There were also presentations on a new technique to treat Thoraco Abdominal-Aortic Aneurysm, wireless thrombotectomy procedures, and acute stroke intervention of the over-90 population.

Each session had questions and answers for the presenters from the audience. The 49th Annual Scientific Meeting was closed with remarks by Ivan Harangozo MD, the Acting President of the HMAA.

Response–feedback from the audience was very favorable, requesting the continuation of this type of meeting. The evaluation score for the meeting was between 4.85-4.95 (score ranging from 5=strongly agree to 1= do not agree) for the different evaluation definitions. 91% stated that No commercial biases (9% said yes). The general score for presenter performance for Knowledge of Subject Matter was 4.97-4.75 and for Ability to Communicate Effectively was 4.90-4.75. Based on audience responses all sessions were clinically relevant. 80% of responders were attracted by educational format while 40% by the accreditation, 63% were attracted by the site, 59% by faculty, and 27% by cost. Also 40 % of responders in the evaluation form stated that they willing to change their patient care approach based on information gained from this meeting. 63% of responder stated that they don't have barriers that would prevent them applying the gained knowledge in their practice in the future. The audience had a chance to gain new information from the lectures, and the friendly atmosphere of the meeting promoted to establish new relationships between interested parties and many discussions continued after the official lecture hours.

Lecture quality and the technical organization and location of the meeting also were outstanding. In conclusion, the feedback clearly emphasizes the fact that this was a very successful meeting and reached the stated goals. I thank everyone for the opportunity to continue to be the HMAA Program Chair. I also express my appreciation and thanks to Program Committee Members including Drs. Andras Khor, Ivan Harangozo, Geza Acs, Gyorgy Baffy, Zsolt Garami, Szilard Kiss, Stephen Mechtler, Istvan Somkuti and Janos Tanyi, for their efforts and collaboration in putting together the scientific program.

Finally, I would like to express my appreciation and many thanks to the people who help us to reach our success beyond the scientific goals: Istvan Somkuti MD, PhD, Editor in Chief for putting together and editing our Archives and gifts for meeting participants, Andrea Varga MD for organizing and managing our excellent and enjoyable social program, Agnes Stadler PhD for helping in administrative and registration work, putting together the Program Booklet for printing, and Gabor Horvath MD for managing the onsite registration process during our meeting.

The Program Chair received numerous topics with wide interest for the upcoming meeting. Proposals will be reviewed by the Program Committee and, based on the review results, will be considered for the upcoming meeting.

Respectfully submitted by



Istvan Stadler, PhD
Scientific Program Director

Membership Committee Chair's Report

Stephen Mechtler, MD

I have the privilege of being the Chair of the Membership Committee for over 15 years, taking over from Dr. Szabolcs Fejer. Why am I proud to be the Chair? It's because it's an important function of the HMAA. Making sure the members receive invoices, collecting the dues, and sending out receipts if needed. It's easier since we have our website, and now members can pay their dues online, and new members can register quite easily.

One may ask why is it important to be a member of the HMAA? One reason is camaraderie. Many of us have been members for over 25 years, we've brought our children to the Sarasota conferences, and now many of these children are members. This has been going on for 50 years. During the year, many of us get together at our homes, wherever that may be: Buffalo, Philadelphia, Washington, Boston or Florida.

Secondly, we have a responsibility to "give back" to our Hungarian colleagues. Our Hungarian Student Exchange Program has been successful for over 10 years. The membership dues are a huge part in supporting this program.

Our numbers are growing every year. However, I do urge everyone to try to recruit a new member to the Association, so we can celebrate another 50 years!



A handwritten signature in black ink that reads "Stephen Mechtler MD". The signature is written in a cursive, flowing style.

Stephen Mechtler, MD
Chair of the Membership Committee

Ivan M. Krisztinicz MD Student Exchange Program Committee Chair's Report

Laszlo Mechtler, MD

The education program of the Hungarian Medical Association of America (HMAA), which was initially called the HMAA fellowship program, was started in 1992. This program was chaired by Dr. Laszlo Mechtler (1992-2002) and allowed Hungarian physicians to spend 3 months in Buffalo, New York. The program was supported by a generous stipend from the HMAA. Every year, 3-4 physicians had the opportunity to spend 1-3 months in Buffalo, New York. Some of the initial fellowship recipients have become very successful in Hungary, such as Laszlo Tamas, MD, PhD, who was part of the program in 1994. Presently, he is the Chairman of Otorhinolaryngology at Semmelweis University. At the annual Board meeting in October 1993, the HMAA made the decision to develop a formal student exchange program, independent of the Fellowship program.



In April 1994, Drs. Alexander Matolcsy, Irene Krisztinicz, Ivan Krisztinicz, Peter Forgach, Laszlo Mechtler and John Feather (SUNYAB representative) met to develop a specific proposal. In December 1994, Drs. Matolcsy and Krisztinicz made several visits to Hungary to appraise the interests of various medical universities. Eventually, a delegation from the State University of New York at Buffalo School of Medicine and Biomedical Sciences, in cooperation with the HMAA, arrived in Budapest on May 22, 1995. Dr. Alexander Matolcsy, Dr. Irene Krisztinicz and Dr. Peter Forgach led the delegation. The representatives from SUNY at Buffalo included Dr. Dennis Nadler, Associate Dean, Dr. John Feather, Primary Care Resource Center and Dr. Martin Mahoney. During their visit, they met with the leadership of the four Hungarian medical schools and visited them (Budapest, Pécs, Szeged and Debrecen).

The first student arrived in Buffalo in December 1995 with the initial chair of the program being Dr. Peter Forgach. During the initial years, there was difficulty in obtaining financial support for the students' 3-month rotations in Buffalo. In 1998, Dr. Ivan Krisztinicz changed the program leadership to having Dr. Krisztinicz chair the program while also being president of the HMAA. Since 2002, due to his untimely passing, the program has been chaired by Drs. Laszlo Mechtler and Irene Krisztinicz. Due to his dedication to the student exchange program, the program was formally named the Ivan M. Krisztinicz Student Exchange Program.

On August 22, 2007, the four Hungarian Medical Universities and Roswell Park Cancer Institute created an agreement, which was signed ceremoniously in Budapest, Hungary. The attendees at that meeting included Dr. Judy Smith, representing Roswell Park Cancer Institute, Drs. Laszlo Mechtler, Tamas Peredy and Eszter Bodnar, representing the HMAA. In addition, the administrative leadership of the four Universities attended. This included, Dr. Tivadar Tulassay, Rector of Semmelweis University, Dr. György Benedek, Dean of the Faculty of Medicine, University of Szeged and Dr. Péter Németh, Dean of the Faculty of Medicine, University of Pécs. Since then, Roswell Park Cancer Institute (RPCI) has been a key player in the success of this program, as a nationally recognized cancer hospital that has embraced the Hungarian medical students over the years. Roswell Park is among the oldest National Cancer Institutes, founded in 1898 in Buffalo, NY, and was the first facility in the world dedicated specifically to cancer research.

One cannot forget that this has been a bilateral exchange program since 1995. Since the beginning of the program, 100 US trained medical students from SUNY Buffalo have gone to Budapest, Hungary. Students spend one month in Hungary with the support of Semmelweis University, rotating in pathology and forensic pathology. This experience for American students has been wholeheartedly positive.

In addition, Dr. Gabriel Haas in Syracuse, New York at the SUNY University initiated a student

exchange program. This was a very successful program for many years. Presently Dr. Alexander Matolcsy in Boston, MA and Dr. Zsolt Garami in Houston, TX are also developing programs. The future appears bright for these organizations and our society.

Every year the student alumni of this program have meetings in Balatonfüred, Hungary. The leaders of the HMAA and hundreds of students attend these meetings, including a number of alumni. This is a wonderful way to monitor the success of this program. The student alumni have also been responsible in coordinating a website that offers information for the new students coming to United States.

Over the years, numerous Hungarian doctors have led the HMAA Hungary Chapter. Dr. Gábor, Horváth, Dr. László Csáthy and the Tárnoki Twins, Dávid and Ádám presently lead it. The Hungary Chapter organizes the student interview process and is also responsible for ensuring that the American students enjoy Hungary both professionally and socially.

Since 1995, over 400 Hungarian medical students from the four universities in Hungary have attended the three-month rotations at various hospitals in Buffalo. The students lodge in an attractive seventh floor apartment overlooking the skyline of Buffalo, NY. Prestigious hospitals, including Roswell Park Cancer Institute, Buffalo General Hospital, Jacobs Vascular Institute, Oshei Children's Hospital and the Dent Neurologic Institute, participate in the exchange program.

The students are welcomed and entertained by several Buffalo Hungarian families and friends supporting the program. This includes Stephen and Katalin Mechtler, Istvan and Agnes Stadler, Laszlo and Katalin Mechtler, Nandi Pinter, Gizella Mechtler and Eva and Istvan Tamoga. Without the sacrifice of these individuals, this program would have never succeeded. They also organize social programs, through which the students gain a sense of belonging.

The logistics of the program is very much dependent on Eva Tamoga, who has been the backbone of this program. Without her organizational skills and dedication, we could not be able to run the program. She is uniquely skilled and has been able to infuse her enthusiasm into this program.

Dr. Irene Krisztinicz and I are proud to be the directors of this altruistic and tremendously successful program. We feel that over four hundred Hungarian 6th year medical students have had an opportunity to expand not only their knowledge, but also their experience by gaining a new perspective in a medical system that is different from their own. Ultimately, this is beneficial in helping the students' careers and subsequently, improving healthcare in Hungary, not to mention the lifelong relationships that are formed. Thus, the HMAA for the past 50 years has nurtured bright Hungarian physicians' careers and futures. I am proud to be part of such a society that has molded so many brilliant young doctors' careers. It is a legacy that any society can and should be very proud of.

"Isten, áldd meg a magyart"



Laszlo Mechtler, MD, FAAN, FASN
Chair of the Student Exchange Program Committee

Fellowship Program Chair's Report

Zsolt Garami, MD

We have recently rejuvenated our fellowship program and opened more locations for participating Hungarian doctors and other health care professionals.

HMAA – Miskolczi Stroke Mini Fellowship Program

Dr. Laszlo Miskolczi has started a Stroke Mini Fellowship for young, Hungarian neurologists for two weeks at Holy Cross Hospital in Fort Lauderdale, FL. The first two fellows participating in this program were Drs. Máté Héja and Ferenc Szőnyegi from Hetényi Géza County Hospital in Szolnok, Hungary. Their reports about their experience will be posted on our website.



HMAA – Houston Fellowship Program

We would like to express our special thanks to Drs. Marcel Pop and Ádám and Dávid Tarnoki for their help in the establishment of a true exchange program between Semmelweis University and Houston Methodist Hospital. Two residents in their research years (Drs. Philip Auyang and Mujeb Zubair) from Houston went to Hungary and three PhD students from the Department of Radiology (Drs. Bianka Forgó, Anita Hernyes and László Szalontai) came to Houston. Of note, in this Erasmus Plus program, not only the students but even teachers are able to exchange classes between the two cities. In addition, a 6th year medical student, Khai Doan Nang, from Semmelweis University won a Scholarship from HAESF and spent 6 months at the Houston Methodist DeBakey Heart & Vascular Center. His research about TAVR and LVAD devices resulted in multiple publications and presentations.

We are also happy to report that our first research fellow from Marosvásárhely (Dr. Tamás Szabó) spent 6 months at the Department of Obstetrics and Gynecology of the Houston Methodist Hospital. The first sport and rehabilitation specialist student (Timea Tóth) from the Department of Sport Medicine of Semmelweis University, also spent 2 months at the Houston Methodist Hospital in November and December 2017.

Under the auspices of the Student Exchange Program the first American (Rebekka Hooks, Stephanie Zority, Samantha DeLuca, Lisa Csedrik, Emoke Csernus) and Hungarian (Réka Rajzák, Viktória Rosta, Nádor Polk, Vencel Juhász and Timea Tarján) students from Semmelweis University have started their surgery or anesthesia rotation in Houston in 2018.

We are happy to announce that several new locations are now willing to accept candidate for short, mini fellowships. The application form is available on the HMAA website and the program is open for applications twice a year with deadlines of April 15 and October 15.

Congratulations to our fellows and students, we wish that in the future they can use the knowledge they obtained during their rotations. Please keep in touch with your hosting organization, the HMAA.

Respectfully submitted,



Zsolt Garami, MD
Chair of the Fellowship Committee

Social Program Committee Chair's Report

Andrea Varga, MD

Dear HMAA Members and Colleagues,

Another exciting week of events has been planned. This year we are celebrating the 50th Anniversary of the HMAA.

The Opening Reception on Sunday will be held in the ballroom of the Sandcastle Resort and we will have the honor to have distinguished guests including HE János Áder, President of Hungary and HE Dr. László Szabó Hungarian Ambassador to the US. A remembrance of the 1956 Hungarian revolution will be held along with a champagne toast, followed by a buffet style dinner in the restaurant and at poolside for all registered participants.

Additional programs include the Wednesday afternoon traditional water polo match accompanied by freshly made lángos and palacsinta.

The Gala Banquet on Thursday will be held at the Sarasota Yacht Club, an elegant venue for our award ceremony and student recognition.

Tickets are available at the registration desk or via the conference smartphone app.

The Halloween themed Kocsma Party on Friday evening in the restaurant of the Sandcastle Resort has always been a fun way to close the conference. Don't forget your costumes and dancing shoes.

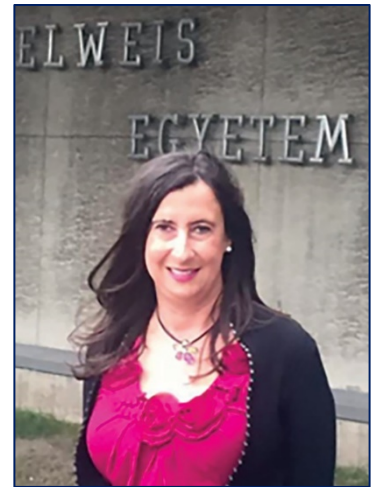
Additional activities include beach run, tennis tournament and a popular kayak tour.

See you in Sarasota!



Andrea E. Varga

Chair of the Social Program Committee



Public Relations Committee Chair's Report

Alexander Matolcsy, MD

This year due to the 50th Anniversary of our Society, the Public Relations Committee with the help of Board Members and members of our Society, as well as non-members who took interest to make our Anniversary meeting a success, has accomplished a lot and I want to express all my gratitude and thanks for all those who contributed to our Committee and Society.

Last year has been very productive for our Committee. In December 2017 I attended a Christmas event at the National Institute of Oncology in Budapest to be awarded by the Institute for making possible a co-operation agreement between Harvard Medical School, Brigham & Women Hospital and the Hungarian National Institute of Oncology in lung transplant surgery. At that event I had the honor and privilege to sit next to Anita Asszony, wife of Hungarian President János Áder and I invited her and the family to Sarasota to attend our 50th Anniversary. Later on, I asked Árpád Gógl, former Minister of Health of Hungary to meet with President János Áder to see if he can attend our meeting. The President informed Dr. Gógl that he will attend our meeting.



In May 2017 I had dinner with Dr. Craig Mello, Nobel Prize winner in medicine from the University of Massachusetts, who I knew from before, and I invited him to our 50th Anniversary. With the help of Dr. Agnes Virga, who knows Dr. Mello well, he has accepted our invitation and he is to deliver a very exciting lecture.

I was recently in Hungary and had the opportunity to meet twice with the Minister of Human Resources of Hungary, Dr. Miklós Kásler who expressed his congratulations for the accomplishments of our Society, and he accepted an invitation to our 50th Anniversary and plans to address our Society at the Gala Dinner. Minister Kásler, who is in charge of the Ministry of Education and the Ministry of Health, called the State Secretary of Health, Dr. Anikó Nagy, and asked her to meet with me. We had a very productive meeting and I am happy to report that she will work with us in the future.

Dr. György Matolcsy, President of the Hungarian National Bank, has accepted our invitation and will attend our meeting. He wants to congratulate us for our 50th Anniversary meeting.

Our Society also invited Márta Mátrai, Deputy Speaker and elected Member of the Hungarian Parliament, and she will attend our conference.

Coming to our meeting is Dr. Béla Merkely, Rector of Semmelweis University. Dr. Merkely has been a great supporter of our Society and had attended multiple conferences in Sarasota. Our Association is thankful for his support.

Dr. Laszlo Mechtler invited Former Governor of New York State George Pataki, who has attended our conference in the past and is of Hungarian origin to attend our 50th Anniversary meeting.

We are also planning to have someone from the Administration of Sarasota Memorial Hospital to attend our opening ceremony, as they have offered in the past to have Hungarian physicians tour the hospital.

Respectfully submitted by

A handwritten signature in black ink that reads "Alexander Matolcsy". The signature is written in a cursive style and is positioned above a horizontal line.

Alexander Matolcsy, MD
Chair of the Public Relations Committee

HMAA New England Chapter Report

Gyorgy Baffy, MD, PhD

The New England Chapter (NEC) was established in 2004, fulfilling the long-time vision of Dr. Alexander Matolcsy, Past-President of HMAA (1994-1997). Rules of operations for the NEC were subsequently incorporated in the HMAA bylaws in 2005. The primary objective of NEC was to create a social and scientific platform locally for current and potential HMAA members. The Boston metropolitan area attracts many physicians of Hungarian origin who are engaged in private practice or academic activities at various universities and other higher educational and research institutions, many of them already HMAA members. It was therefore a natural choice to form the first-ever HMAA chapter in New England.



The first NEC president and secretary, respectively, were Dr. Eva Szigethy and Dr. Eva Bálint, followed by Dr. Ildiko Halasz as president and Dr. Agnes Virga as secretary, who have been leading the chapter since 2005. Since its inception, the NEC has held over 30 events, mostly organized as potluck meetings at the home of members with 15 to 40 participants. With the exception of the less formal summer retreats taking place on Cape Cod, each NEC meeting is organized around a scientific talk given by a renowned expert from the New England area or from elsewhere.

Some of the most memorable NEC seminars featured William Kannel (Boston University), one of the founders of the Framingham Heart Study initiated in 1948; Albert-László Barabási (Northeastern University), best known for his groundbreaking work on scale-free networks; 2006 Nobel Laureate Craig Mello (University of Massachusetts), the discoverer of RNA interference; Ferenc József (Harvard Medical School), the father of image-guided therapy; George Kunos (National Institutes of Health), an internationally recognized expert on the physiology of endocannabinoids; and Tamás Vekerdy (Budapest), founder of the Waldorf school system in Hungary.

The NEC served as a model for the subsequent establishment of the HMAA Hungary Chapter, which was a key step in strengthening the presence of HMAA in Hungary by supporting the student selection process for the Buffalo exchange program and launching the extraordinarily popular HMAA summer conferences in Balatonfüred. Based on the great success of these initiatives, additional chapters will hopefully succeed to further promote the mission of HMAA.

Respectfully submitted by



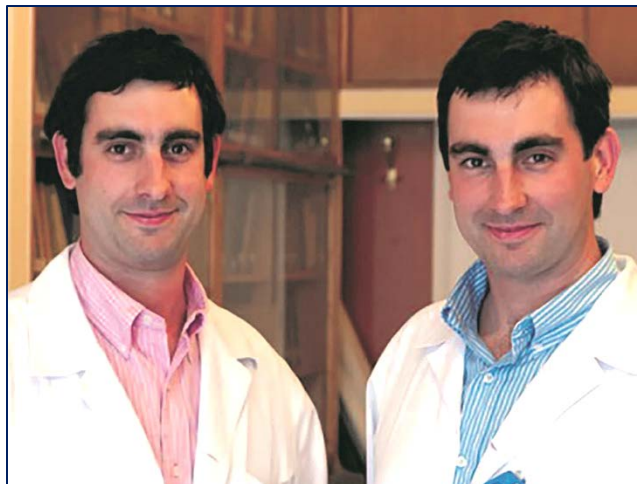
Gyorgy Baffy, MD, PhD

Update on HMAA Hungary Chapter Events 2018

Adam Domonkos Tarnoki MD, PhD and David Laszlo Tarnoki, MD, PhD

BALATONFÜRED MEETING

The HMAA Hungary Chapter organized its 12th Hungarian (11th Balatonfüred) multidisciplinary meeting in the State Hospital of Cardiology in Balatonfüred on August 24-25, 2018. This year, around 150 medical students, residents, PhD students, doctors and professors from all over the four Hungarian medical universities (Semmelweis University, Universities of Debrecen, Pécs and Szeged) attended the meeting again. As in previous years, the main aim of the conference was to create a forum for young scientists on any medical field to present their own work for the audience in English or in Hungarian and meet with famous invited guests. HE János Áder, President of Hungary, had sent a letter greeting the attendees of the Conference.



The meeting was organized in the usual familiar environment thanks to the continuous support of Prof. Dr. Gábor Veress. Special thanks went to those guests who arrived from abroad to Balatonfüred, especially past HMAA Presidents Drs. Peter Forbath and Istvan Somkuti, as well as Dr. George Szollar. Their attendance was highly appreciated and contributed to the high quality of the meeting. The organizing committee would also like to acknowledge the continuous help of Dr. László Csáthy, Bálint Környei, Dorottya Szabó, Dr. Gábor Horváth and all the student representatives and volunteers who contributed to the



Participants on the 2018 Balatonfüred Conference

organization and helped make the two days a memorable event. As in previous years, nearly 100 abstracts were submitted, among which oral and poster presentations were selected from based on the evaluation of the reviewers. The conference Program Committee would like to thank all the abstract reviewers for their time spent grading the dozens of abstracts received for HMAA Füred2018 congress.

The highlighted topics and sessions of this year's conference included Updates in OBGYN; Working in the UK as a doctor, healthcare REmodeling; E-health and artificial intelligence; Update in Respiratory medicine 2018 (Session of the Society of Hungarian Pulmonologists). On Friday, the opening ceremony included the greeting address of Prof. Dr. Gábor Veress, past HMAA President Dr. Peter Forbath, HMAA



Workshop with Drs. Marcel Pop and Peter Forbath



Drs. George Szollar, Istvan Somkuti and Peter Forbath with Zsuzsanna Petyko and Lilla Juhasz

Hungary Chapter President Dr. László Csáthy and Vice-President Dr. Ádám Domonkos Tárnoki. Nearly 100 presentations competed for awards during the two days, and the best presentations were awarded in each session. Every session was chaired by HMAA Board members and invited professors. The abstracts were published in the HMAA Archives journal thanks to Dr. Somkuti. Thanks to the sunny weather, poster sessions, which were organized in the garden, were very popular. Participants also enjoyed the lunch provided by the hospital each day. During lunch, lunch sessions were organized featuring invited speakers. The water polo game was held in the pool of the hospital on Friday afternoon. The referees were Dr. Vilmos Dani and Prof. Dr. László Tamás. Two games were organized, including the game of invited professors against HMAA HC board members. Each player received a gold or silver medal after the game. The dinner was held traditionally in the Borcsa Restaurant where Prof. Dr. Kinga Karlinger was awarded by the HMAA HC to acknowledge her continuous activity in the past decade during the HMAA HC conferences.

The second day also started with multidisciplinary presentations in two main halls and in the Ciba workshop room as well as in the poster presentation area. Participants had the opportunity to choose from many programs during the two days. The exit interview for 2017/2018 HMAA Buffalo exchange students, interactive workshops were very popular. A workshop was organized on the Buffalo exchange program as well, where Buffalo Alumni shared their experiences and answered questions.

This year we tried to strengthen the workshop format of the conference: therefore, almost 20 different types of workshops were organized, such as The importance of identification and determination of biomolecular interactions to answer questions in cell- and molecular biology and in pharmacology; Simulation



Dinner in Borcsa Restaurant

of endovascular techniques on simulator (e.g. stent graft implantation); A worldwide acknowledged Hungarian invention for the detection of clean hands; How to create a good presentation; Importance of oral cavity prevention for the general health status, proper care of teeth and mucous membranes, and prevention of oral tumors; Alternative investment opportunities in a low yield environment - Investment advice for doctors; Surgical basic technical training (knitting technique, instrument management); Medical legal cases - lessons learned from artificial defects? In addition, the students could meet the professors of their field of interest, such as Assisted Reproductive Technologies: the nitty gritty of how it all works with Dr. Istvan Somkuti; Meeting of Medical Students working in the field of surgery with Prof. Dr. József Sándor and Prof. Dr. Gábor Menyhei; Meeting of Medical Students working in the field of cardiology with Dr. Peter Forbath; Meeting of Medical Students working in the field of OBGYN with Prof. emer. Dr. György Bártfai; Meeting of Medical Students working in the field of biochemistry, biophysics and physiology with Prof. Dr. László Mátyus and Prof. Dr. Ferenc Erdődi; Meeting of Medical Students working in the field of pediatrics with Prof. Dr. Tibor Ertl.

The waffle party made the conference also memorable by providing a possibility of tasting different kinds of marmalades offered by the student representatives from the four Hungarian universities. At the end of the second day the best lecture awards were distributed. Zsófia Nozomi Karádi (University of Pécs, Stroke Centre) won the Ivan Krisztinicz Award (best English lecture award) offered by Hungarian Medical Association of America. Máté Szabó (University of Debrecen) won the Istvan Mechtler Award (best Hungarian lecture award) offered by Drs. Laszlo and Stephen Mechtler.

The pictures of the conference, publications and more information are available at the <https://hmaa.org> website. The organizers would like to acknowledge the financial support of the Hungarian Medical Chamber (MOK), PADI and Society of Hungarian Pulmonologists.

BUFFALO EXCHANGE PROGRAM

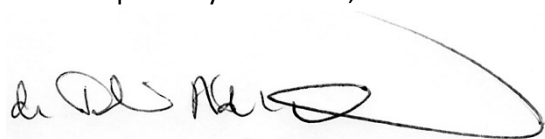
This year 53 Hungarian students applied for the Buffalo exchange program (32 from Semmelweis University, 4 from the University of Szeged, 6 from the University of Debrecen and 10 from the University of Pécs). Twenty-one applications had to be rejected due to the lack of requirements in the application (delayed submission, no HMAA HC membership, etc.). The examining committee included Drs. Marcel Pop, Gábor Horváth, László Csáthy and Ádám Domonkos and Dávid László Tárnoki. The 32 applicants were scored and the first highly ranked 16 students were accepted to participate in the program. The exit interview was organized in Balatonfüred, unfortunately, only 9 alumni participated (the committee included Drs. Csáthy, Pop, Horváth and D.L. Tárnoki).

Thanks to the tireless work of Drs. Alexander Matolcsy and Laszlo Mechtler, the PADI Foundation increased the financial support of the Buffalo exchange students. From this year the PAIGEO (former PADI) support is distributed by the HMAA.

FUTURE PROGRAMS

The HMAA Hungary Chapter will start the organization of the 2019 Balatonfüred meeting. Please check the exact dates on the website. HMAA members, who come to Hungary in the future to give a lecture as part of the HMAA HC lecture series are welcome. For more information please visit <https://hmaa.org/chapters/hungary> for further information regarding the HMAA Hungary Chapter.

Respectfully submitted,



Adam Domonkos Tarnoki, MD, PhD
Vice-President of HMAA HC



David Laszlo Tarnoki, MD, PhD
Secretary of HMAA HC

HMAA FOR MEDICINE, SCIENCE AND CULTURE: FIFTY YEARS OF PROGRESS

**Abstracts of the 50th Anniversary Annual Scientific
Meeting of the Hungarian Medical Association of America
Sarasota, FL, October 28 – November 2, 2018**

MECHANISMS OF LYMPHATIC TUMOR SPREAD IN BREAST CANCER: RETRACTION CLEFTS, CELL POLARITY AND LYMPHANGIOGENESIS

Acs, G.

Women's Pathology Consultants, Ruffolo Hooper & Associates and Department of Pathology, Florida Hospital Tampa, Tampa, FL



Geza Acs, MD, PhD

Medical Director, Women's Pathology Consultants, Ruffolo Hooper & Associates, 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 in Cellular and Molecular Biology from the University of Debrecen School of Medicine. He served as Postdoctoral Fellow at the National Cancer Institute in Bethesda, MD and subsequently 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 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 College of Medicine, Tampa, FL. Dr. Acs is currently Medical Director of Breast and Gynecologic Pathology at Women's Pathology Consultants, Ruffolo Hooper & Associates in Tampa, FL. His research interests focus on the mechanisms of lymphatic tumor metastasis, and histologic and molecular prognostic/predictive factors in breast cancer. He has published over 100 peer-reviewed papers and book chapters.

Aim: The goal of this presentation is to describe our current understanding of the mechanisms of lymphatic tumor spread in breast cancer.

Methods: This presentation is based on a series of our studies and a review of the medical literature.

Results: In breast cancer the spread of tumor cells via the lymphatics to regional lymph nodes is an important early event in metastatic disease. Although tumor-associated lymphatic vessels are considered as the main route for tumor cell spread via the lymphatic system, little is known about mechanisms of this process. Our studies show that the extensive presence of retractions clefts around tumor cell nests correlates with the reversal of cell polarity, lymphangiogenesis and lymphatic vessel density in primary invasive breast cancers and metastatic tumor deposits in sentinel lymph nodes. These features in the primary tumors also predict the presence of lymphatic invasion, nodal metastasis and poor outcome. If present in metastatic tumor deposits in sentinel lymph nodes, they can predict the presence of additional positive lymph nodes.

Conclusions: The extensive presence of retraction clefts and the even focal reversion of cell polarity in breast cancers correlate with lymphangiogenesis and predict lymphatic invasion, nodal metastasis and poor outcome. Retraction clefts may represent an early stage of lymphatic invasion as part of the lymphangiogenesis process and lymphatic tumor spread.

MECHANISM OF THE PROTECTIVE EFFECTS OF IRISIN IN DIABETES MELLITUS

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Department of Anatomy, College of Medicine & Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates



Ernest Adeghate, MD, PhD, DSc

Professor and Chair, Department of Anatomy, College of Medicine & Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates

Professor Ernest Adeghate obtained his medical degree from Semmelweis University Medical School, Budapest, Hungary and his PhD and DSc from the Hungarian Academy of Sciences. He also has a master's degree in Family Medicine from Monash University, Australia. He is interested in the morphology of pancreatic grafts and the effect of neurotransmitters, neuropeptides and cytokines on parameters of metabolic disease, insulin release and on complications of diabetes mellitus. Prof. Adeghate has published more than 200 peer-reviewed articles. He is currently, the Editor-in Chief of The Open Medicinal Chemistry Journal published by Bentham Science Publishers. He serves in the

Editorial Boards of several scientific journals including World Journal of Diabetes, Current Diabetes Reviews, Neuroendocrinology Letters, Molecular and Cellular Biochemistry, and many others. He is currently the Chair of the Department of Anatomy, College of Medicine, UAE University.

Aim: Irisin is a novel adipocytokine and myokine, which has been implicated in the etiopathogenesis of several metabolic diseases including obesity, diabetes mellitus, ageing, and inflammation. Irisin has been shown to increase the tissue expression of mitochondrial uncoupling proteins, which in turn helps in the conversion of white fat tissue into a brown type. Irisin improves glucose metabolism, insulin sensitivity, increases lipolysis with a concomitant reduction in food intake and body weight. Irisin has also been shown to improve bone structure, function and density. It has been localized to different organ systems and tissues, including but not limited to cardiovascular system, nervous system (brain, cerebrospinal fluid), skin, retina, and many others. The blood level of irisin is dependent on variety of factors such as food type and intake, nutritional status, physical exercise, medication such as fenofibrate and statins and the overall health of the whole body. The aim of our study was to investigate the effect of irisin on metabolic and biological parameters in animal model of diabetes mellitus.

Methods: Morphological (light and electron microscopy), molecular biology and biochemical methods were used to characterize the effect of irisin on different molecules that have any impact on diabetes mellitus.

Results: Studies performed in our laboratory showed that irisin has a profound effect on several biological molecules that play a role in the etiopathogenesis of diabetes mellitus.

Conclusions: Increasing the blood level of irisin may help in the prevention and treatment of metabolic disorders such as obesity and diabetes mellitus.

THE INTERSECTION OF QUALITY AND VALUE: IS COST THE INDEPENDENT VARIABLE?

Alexander, J.

Steward Holy Family Hospital, Methuen, MA



John Alexander, MD, MHCM

Chief Medical Officer, Steward Holy Family Hospital, Methuen, MA and Assistant Clinical Professor, Tufts University School of Medicine, Boston, MA

Dr. Alexander is Chief Medical Officer for Steward Holy Family Hospital for the past 5 years. He is Assistant Clinical Professor at Tufts University School of Medicine, instructor for Foundations of Medicine curriculum. He is a practicing Emergency Physician, completed residency at University of Massachusetts Medical Center. Interests include health care economics, servant leadership, and palliative care.

Aim: For nearly two decades, Medicine in the United States has been challenged to identify ways in which safer, or higher quality, care is delivered at lower cost. Thought leaders in the industry have deemed this quotient to equal value. However, practical applications in organized health care arenas often observe a decrease in quality of care as expenditures, or costs, decrease. What are the effects on quality of care and financial performance as costs are tightly or loosely managed? Is there a set point at which reductions in total cost of care no longer drive value up, but rather drive it down? Can total cost of care and quality outcomes be used each independently to enhance value of care provided?

Methods: This presentation will discuss the shifting paradigm of valuing quality of care and total cost of care versus the quantity of care provided.

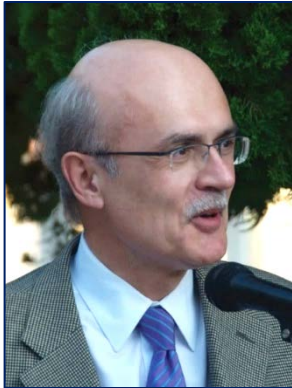
Results: The effects of a blended reimbursement model - i.e. value-based contracts - is to sacrifice short-term gains in quality for gains in efficiency and cost containment.

Conclusions: A model of reimbursement which stretches out costs over a longer period of time allows for improvements in quality through an overall cost-reduction model, namely reduction of unwanted variability in healthcare delivery.

GUT-LIVER AXIS: GUT MICROBIOTA AND NONALCOHOLIC FATTY LIVER DISEASE

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 is an Associate Professor of Medicine at Harvard Medical School and Chief of Gastroenterology at the VA Boston Healthcare System. He graduated from the Debrecen Medical School in Hungary and obtained his PhD from his studies on growth factor-mediated calcium signaling as an NIH Fogarty Fellow in the Department of Biochemistry and Biophysics at the University of Pennsylvania. He trained in gastroenterology at the University of Michigan and the Brigham and Women's Hospital. His current research interests are in various aspects of nonalcoholic fatty liver disease such as outcomes prediction and biomarkers. He has been part of clinical trials that pertain to colorectal cancer screening. He published 80 peer-reviewed papers and book chapters. In 2014, he was a Fulbright US Scholar at the University of Debrecen. He is the recipient of the Hetényi Medal and the Pro Optimo Merito in Gastroenterologia award of the Hungarian Gastroenterological Society.

Aim: To review the role of gut-liver axis, which is the sum of reciprocal interactions between the liver and gut microbiota, which is the largest collection of microorganisms in the human body.

Methods: Narrative review.

Results: NAFLD is a prevalent condition linked to obesity, insulin resistance, and endothelial dysfunction. The spectrum of NAFLD ranges from steatosis to steatohepatitis with a capacity to progress into cirrhosis. Dysfunctional host-microbiome interactions contribute to all stages of NAFLD. Excess caloric intake, obesity, and chronic liver disease all contribute to the development of dysbiosis, which is the breakdown of healthy composition and function of gut microbiota. NAFLD has been linked to decreased microbial diversity, weakened intestinal barrier, impaired bile acid metabolism and signaling, and altered release of gasotransmitters such as nitric oxide and hydrogen sulfide. These perturbations may alter liver sinusoidal homeostasis and splanchnic circulation by affecting energy metabolism, pathogen recognition, inflammation and vasoregulation. Dysbiosis is more prominent in cirrhosis, increasing the risk of clinically significant portal hypertension and leading to bacterial translocation, sepsis, and acute-on-chronic liver failure.

Conclusions: Several promising therapeutic strategies for the modification of host-microbiome interactions have been considered. Gut microbiota produce myriads of small molecules with key biological effects, but the majority of these metabolic signals remain unknown. Use of antibiotics, probiotics, fecal microbiota transplantation, and more tailored interventions to achieve specific configurations of bacteria or their metabolites are currently investigated.

THE RATIONAL ANTIBIOTIC USE AMONG RURAL TRANSYLVANIAN ADULTS

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Erika Gyongyi Ban, MD, PhD

Associate Professor, Department of Pharmacology, University of Medicine and Pharmacy of Targu Mures, Targu Mures, Romania

Dr. Ban is Associate Professor in the Department of Pharmacology, at the University of Medicine and Pharmacy of Targu Mures, Romania.

Aim: The antibiotic resistance is the global health issue of 21st century. The mortality and morbidity rates associated with infections due to multidrug-resistant pathogens are very high, and they represent a significant financial burden to the healthcare. The antibiotic resistance is directly correlated to the inappropriate usage of antibiotics. In order to have an optimal control over the antibiotic use and to prevent the development of antibiotic resistance, it is essential to have highly skilled general practitioners and average population comprehension about the correct use and the compliance with treatment. To promote a proper, rational use of antibiotics and to achieve an effective and efficient intervention, it is necessary to assess the attitudes, knowledge and behavior of the average population regarding the use of antibiotics.

Methods: We have performed an observational cross-sectional, epidemiological study based on questionnaires in the rural area of Transylvania. During the study we followed the Declaration of Helsinki. Statistical analysis was performed using Excel and GraphPad Prism. Our objective is to evaluate, with a questionnaire survey, the behavior and attitudes of the Transylvanian average population and to identify and analyze the factors that influence them.

Results: We accumulated a total of 98 questionnaires among adult rural area inhabitants in the period of April-May 2018. The average age is 52.2 years and the demographic distribution was 54% females 46% males. 83.67% used antibiotic only on the recommendation of a physician, but 41% used the medicine only during the presence of the symptoms. Among the asked persons the most frequent causes for antibiotic use are angina and fever.

Conclusions: It would be necessary to perform an adequate number, and a longer time survey, addressing the general population. Based on the analyzed questionnaires it would be suitable to provide awareness raising programs about the rational use of the antimicrobial agents and thus the prevention of bacterial resistance development.

REGULATORY ROLE OF PERIPHERAL PEPTIDERGIC SENSORY NERVES IN THE PROTEOGLYCANE-INDUCED CHRONIC AUTOIMMUNE ARTHRITIS MODEL

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Matyas Belak, MD

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Dr. Belak has just obtained his medical degree from the Medical University of Pécs and began to work as a resident at the Department of Urology in Pécs, Hungary.

Aim: The immunological aspects of rheumatoid arthritis are well-known, but there is significantly less information about the role of sensory-immune interactions in this condition. Capsaicin-sensitive sensory nerves densely innervating the synovium and the joint capsule, release pro- and anti-inflammatory neuropeptides which have important regulatory functions in various diseases associated with pain and inflammation. We investigated the role of capsaicin-sensitive sensory nerves in a translational mouse model of chronic autoimmune arthritis.

Methods: The capsaicin-sensitive sensory nerves were selectively inactivated by resiniferatoxin (RTX, capsaicin analog) pretreatment in female BALB/c mice (desensitization). Arthritis was induced by i.p. proteoglycan aggrecan obtained from human osteoarthritic cartilage (PGIA). Mechanonociception was measured by esthesiometry, paw volume by plethysmometry, arthritis severity by semiquantitative scoring, joint function by grid test, bone structure by micro-CT, myeloperoxidase activity by luminescence and plasma extravasation by fluorescence imaging during the 4-month experimental period.

Results: From the 7th week 30-35% decrease of mechanonociceptive threshold (hyperalgesia), 40-60% paw swelling, macroscopic arthritic signs and functional damage developed. The increase of myeloperoxidase activity and plasma protein extravasation also reached their maximum by this timepoint. Ankylosis was detected from the 12th week, and increased bone mass on the 17th week. Inactivation of the capsaicin-sensitive peptidergic nerves significantly decreased hyperalgesia, paw edema, arthritis score, functional damage, myeloperoxidase activity and the late pathological bone formation.

Conclusions: This is the first complex functional characterization of the proteoglycane-induced chronic autoimmune arthritis mouse model. We provided evidence that the capsaicin-sensitive sensory nerves increase edema, have a role in functional damage and mediate mechanical hyperalgesia. Identification of the released neuropeptides responsible for these actions provide novel insight in the pathophysiology of the disease and help to identify new drug targets.

ARE WE DOING TOO MANY CT-S IN HEAD TRAUMA PATIENTS?

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Alexander Benyovszky, MD

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Dr. Benyovszky is a graduate of the University of Pecs. Currently he is living in Ireland, working as a senior resident in Emergency Medicine. He is undertaking board exams with the ambition of obtaining an Anesthesiology Residency in the US.

Aim: Traumatic Head Injury causes significant morbidity and mortality; hence there has always been contention about whether to scan such a patient or not. The Royal College of Radiologists (RCR) has outlined guidelines for selecting trauma patients with clinically significant brain injury who may benefit from a head CT scan, while minimizing the radiation exposure/economic burden of scanning patients without injury. Our quality improvement study aims to assess compliance with the use of these guidelines in our Emergency Department.

Methods: Three cycles of retrospective/prospective data collection were performed. This included patients presenting with traumatic head injury out of hours to emergency department over 3 month periods. Criteria were established to assess indication for CT as per RCR guidelines. Patient notes and CT scan orders were assessed for indications for CT brain as laid out by RCR guidelines.

Results: Our initial study showed head injury guidelines were not being fully utilized in the Emergency Department resulting in 50% of patients getting CT without documented clinical justification. Results were discussed in multidisciplinary meetings involving departments of Surgery, Radiology, and Emergency Medicine. A form adopted from RCR guidelines was implemented as departmental protocol. Re-audits following this showed significant reductions.

Conclusions: Traumatic head injury and its emergency management remain a serious issue. After identifying a significant number of inappropriate out of hours CT requests within our ER, we created a new departmental protocol which resulted in clear and appropriate requests which were agreed upon by all stake-holding departments, as well as improved statistical outcomes in patient management.

EARLY- AND LONG-TERM PATENCY AFTER ENDOVASCULAR TREATMENT OF PATIENTS WITH INFRARENAL AORTIC STENOSIS

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Akos Berczi, MS

6th Year Medical Student, The Heart and Vascular Center of Semmelweis University, Budapest, Hungary

Akos Berczi is a 6th year medical student at the Semmelweis University, Budapest, Hungary. He finds radiology, especially interventional radiology extremely interesting, thus he would like to become one in the upcoming years. When he is not at the university, he likes to play tennis, run and be with his friends and family.

Aim: For patients with infrarenal aortic stenosis (IAS) the following endosurgical treatment options exist: 1. percutaneous transluminal angioplasty (PTA), 2. aortic stenting, and 3. aortobiliac stenting. The aim of this study was to determine the success of IAS interventions. The purpose of our study was to report our results on the patient characteristics, complications, long-term patency and clinical success rates we have written down during the last 17 years relating to endovascular treatment of patients with infrarenal aortic stenosis.

Methods: Fifty-two symptomatic patients (33 females; median age: 60 [56-67] years) with IAS who underwent endovascular treatment between 2001 and 2017 were retrospectively analyzed. Patient, vessel, lesion, and balloon/stent characteristics were examined. Follow-up included peripheral pulse palpation, ankle-brachial index measurement, and Doppler ultrasound examination. Kaplan-Meier analysis was used as statistical method.

Results: The cause of IAS was vasculitis in two patients (4%) and atherosclerosis in 50 (96%). Thirteen percent of the patients were ≤50 years, 73% were smokers, 88% had hypertension, 40% had hyperlipidemia, 33% had diabetes mellitus, 23% were obese (BMI≥30kg/m²), and 8% had chronic kidney disease. The median length of IAS was 17.6 (10.8-27.2) mm, while the grade of IAS was 70 (70-80) %. Severe calcification was present in 19% of the patients. In four cases (8%) PTA, in 34 (65%) aortic stenting, and in 14 (27%) kissing stenting was performed. Two puncture site complications and an aortic rupture requiring surgical repair occurred. The median follow-up time was 63 (18-96) months. The primary patency rate was 100% at 6 months, 96% at 12 and 24 months, and 83% at 60 and 120 months. Restenosis developed in six patients (12%); reintervention was carried out in four cases (8%).

Conclusions: Interventions in patients with IAS can be performed with excellent patency rates.

NOSTALGIA AND MENTAL HEALTH

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Gyula Julius Bokor, MD

Assistant Professor, Department of Psychiatry, University of Massachusetts Medical School, Worcester, MA

Dr. Gyula Julius Bokor, MD is Assistant Professor of Psychiatry at the University of Massachusetts Medical School. He did his post-graduate fellowship training at Harvard Medical School (2000 - 2004) in psychodynamic psychotherapy and psychosomatic illnesses and primary care in psychiatry.

Aim: Memories, Happiness, Social Adaptability, Nostalgia.

Methods: Historically, the emotion of nostalgia was seen as pathological, even being a symptom of depression or impaired attention. More systematic and recent research in neuroscience and psychology in the past 20 years demonstrates nostalgia's existential and social functionality in a healthy life. Functioning via the brain's "default mode network," nostalgia helps create continuity in the self narrative, social connections with others, and feelings of affection and prosociality with friends, family, and community. Nostalgia is a crucial part of a well functioning brain.

Results: Connection between nostalgia and mental function.

Conclusions: Nostalgia is beneficial.

FRAGILE LINK IN THE MEDICAL EDUCATION OF MAROSVASARHELY – PHARMACOLOGY

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Attila Brassai, MD, PhD

Medical Professor, Department of Pharmacology, University of Medicine and Pharmacy of Marosvasarhely, Marosvasarhely, Romania

Dr. Brassai is a University Professor of Pharmacology, a former Oxford University postgraduate student under professor dr. Péter Somogyi, and former research scientist at the National Institute of Health in Washington, DC (2002).

Aim: The University of Medicine and Pharmacy of Marosvásárhely started its activity in 1945. From the beginning pharmacology has been integrated into the basic study program of the medical school, but the path led through several obstacles during the last 73 years. The objective of our work is to relate to the members of the Hungarian Medical Association of America and any other interested persons the present situation of the education – full of hopelessness – at the – one and only Hungarian – Transylvanian medical school, which makes also impossible the training of new pharmacologists and clinical pharmacologists.

Methods: We intend to present the past, the present and a possible future of the education at our university.

Results: Past: The present lecturing community could continue the footsteps of quite famous and well-known professors. The founder of the department of pharmacology, Dr. sn. Obál Ferenc, was the founder head of department of pharmacology for 3 years, until 1948. Dr. Feszt György (now professor emeritus) was the head of our department for the longest period, and created a viable system, that became the basis of the pharmacology education. Following his leadership, the political circumstances brought a new situation, and professor Monea Marioara, pharmacist, became the new head of department until 2008, when again a medical doctor, professor Brassai Attila obtained the leadership. Present: The bumpy road of pharmacology training arrived at its hardest period, because the department lost its independency, and the Pharmacology Department ceased to exist at the Faculty of Medicine. Its remainings came under the control of the Faculty of Pharmacy. The present situation of pharmacology education consists of only one lecture of two hours a week, and a weekly – mandatory Romanian – two hours practical training, during only two semesters.

Conclusions: The future of the medical education at Marosvásárhely is uncertain. Unfortunately, clinical pharmacology specialists' training at our university center does not exist. Only two of the staff of the merged department are Hungarians, and two promising Hungarian medical students are helping their work.

VIRTUAL REALITY IN MEDICAL EDUCATION

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Tomas Brngal, MS

Medical Student, Institute of Anatomy, Comenius University, Bratislava, Slovakia
Winner of the 2018 Zoltan Gombos Travel Fund Award

Tomas Brngal, member of this year Forbes 30under30 (Slovakia) list received his MD degree at the Faculty of Medicine of Comenius University. He is the co-founder of start-up Virtual Medicine, which has been developing for almost three years the unique VR application called Human Anatomy VR. This medical educational app is designed for students of medicine and doctors, working on the principle of virtual reality. The application was downloaded by thousands of people in 149 countries of the world. Human Anatomy VR is making learning more effective, more interactive and more entertaining. It is the first and currently the only anatomical VR application on the Samsung GearVR and Google Daydream platforms in the world. Google even chose it among the top 3 apps in the store on Google Daydream and put it among "featured". Tomas represented Slovakia as the finalist of the Global Student Entrepreneur Awards 2017, Ideas from Europe 2017 and at Global Entrepreneurship Summit 2017.

Google Daydream platforms in the world. Google even chose it among the top 3 apps in the store on Google Daydream and put it among "featured". Tomas represented Slovakia as the finalist of the Global Student Entrepreneur Awards 2017, Ideas from Europe 2017 and at Global Entrepreneurship Summit 2017.

Aim: The aim of this work was to establish an innovative virtual anatomy classroom at the Faculty of Medicine of the Comenius University in Bratislava and to apply virtual reality learning to practice.

Methods: This work responds to new technologies in education process, that responds to the requirements of new generation of students. Didactive aids should be more interactive, playful and visually interesting. The paper consists of theoretical and practical part. The theoretical part provides and evaluates new trends in education. In the practical part of this work we analyze not only students' opinion on these innovations, but also on new technologies and games in general.

Results: The result of our long-time effort was the establishment of virtual anatomy classroom, many awards and the presentation of our alma mater all over the world and in media.

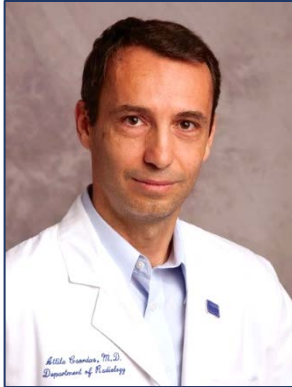
Conclusions: Students like this kind of education and would like to have more of these applications. Interestingly, a large proportion of students are interested in such development and want to actively participate, which can also be an important signal for the university.

EVOLVING TREATMENT OPTIONS OF LOWER EXTREMITY VENOUS INSUFFICIENCY

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Dr. Csordas spent three years in cardiac surgery at Zala County Hospital, Zalaegerszeg, Hungary. He completed his internship in surgery, a residency in radiology and a fellowship in interventional radiology at New York Presbyterian Hospital - Cornell and Memorial Sloan Kettering Cancer Center New York, NY. He served as Chief of Interventional Radiology at Creighton University for 11 years. Currently he works as an interventional radiologist at the University of Nebraska Medical Center.

Aim: To discuss newly developed options for endovenous ablation of superficial veins of the lower extremity and potential future treatment of deep venous insufficiency. Discuss the anatomy, physiology and pathophysiology of the lower extremity venous circulation.

Methods: Endovenous ablative techniques, Laser, cryo and RFA vs Glue Implantable venous valves (research only).

Results: Improving - already excellent - result using the widely available ablation techniques for superficial venous insufficiency. Difficult, often sub optimal result using current treatment options for deep venous insufficiency. Need for clinically usable implantable venous valve.

Conclusions: Wide variety of options available for superficial venous insufficiency, in an outpatient setting. Limited options for deep venous insufficiency - possible inpatient, multidisciplinary approach.

ADVANCES IN THE TREATMENT OF VARICOSE VEINS IN THE LAST 50 YEARS

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Steven T. Deak, MD, PhD

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Dr. Steven T. Deak was born in Budapest Hungary and came to the United States with his parents and sister Susan more than 50 years ago. He is a vascular surgeon practicing in New Jersey.

Aim: Review the diagnostic and therapeutic advances in the treatment of superficial venous insufficiency over the last 50 years. Review patient outcomes among symptomatic patients with superficial chronic venous insufficiency who were treated with retrograde ultrasound-guided polidocanol 1% in a community setting.

Methods: Between March 2015 and June 2017, 250 symptomatic patients with C2-C6 chronic venous insufficiency received polidocanol microfoam 1% and were followed for 16.6 +/- 7 months. Sixteen of the 250 patients (6.4%) had skin ulcers, and 56 (22.4%) were treated previously with thermal or surgical interventions. All patients underwent a duplex ultrasound venous incompetence study to map perforators and veins to be treated. Incompetent veins were accessed with a micropuncture needle distal to the mid-thigh perforator, approximately 10 cm above the knee fold. The leg was then elevated 45 degrees. Under ultrasound guidance, the incompetent greater saphenous vein was closed with polidocanol microfoam 1%. A second injection was administered through the same catheter directing the microfoam to flow in a retrograde fashion through the incompetent venous valves to the ankle.

Results: All patients completed the initial treatment; 55 (22.0%) required planned secondary treatment during the follow-up period for residual venous reflux in the below-knee greater saphenous vein. Complete elimination of venous valvular reflux and symptom improvement was documented in 236 patients (94.4%). Minor adverse events included asymptomatic deep vein thrombi (n = 2), common femoral vein thrombus extension (n = 1), and superficial venous thrombi (n = 4). Of the 16 patients with skin ulcers, 10 were C6 patients and 80% experienced wound closure within 4 weeks of treatment.

Conclusions: Retrograde administration of polidocanol microfoam 1% is a safe and effective treatment with important clinical benefit for superficial venous insufficiency.

REGRESSION GRADING OF RECTAL CANCER

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Dr. Dworak was born in 1951 in Budapest. He obtained his medical diploma from Semmelweis University and started to work at the 1st Department of Pathology at Semmelweis. He subsequently held positions the Departments of Pathology at Hospital Dusseldorf (1979-83), the University of Bonn (1983-89) and the University of Erlangen (1989-98). From 1998 till his retirement in 2016 he served as the Head of the Department of Pathology at City Hospital Fuerth. His main research interests include the pathology of rectal cancer and the standardization of tumor regression of rectal cancer.

Aim: Preoperative radiochemotherapy (RCT) is a standard therapy for advanced rectal cancer. For measuring of the biological response of tumor tissue the histological regression grade (TRG) can be used. The aim of this study was to describe distribution of TRG and its value as prognostic factor.

Methods: Specimens of 341 patients with rectal cancer who were treated with preoperative RCT were examined histologically. TRG was evaluated according to the recommendation of the German Guidelines for Colorectal Cancer. Also the tumor stage and survival data were determined. Statistical analysis with XLSTAT was performed.

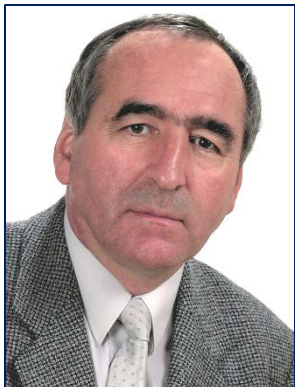
Results: TRG 0, 1, 2, 3, 4 was found in 9 (2.6%), 56 (17.0%), 149 (43.7%), 90 (26.4%) and 35 (10.3%) of the surgical specimens, respectively. In the Kaplan-Meier analysis best survival was observed in the patient group with TRG 4 (no vital tumor present) of the tumor tissue (median survival time 60 mo.). In contrary in the group with no tumor regression median survival time was 19.8 mo.

Conclusions: TRG for rectal cancer, which was firstly described in 1997 is a simple method for estimating tumor response after RCT and is widely used with different modifications. The small number of total tumor regression in our material underlines the importance of minacious pathological workup. Our survival analysis supports the observation that TRG may be an important factor for the estimation of tumor prognosis. Classifications with less TRG groups may simplify the pathological workup and increase the reproducibility of the regression grading.

PROTEIN PHOSPHATASE ACTIVATION AS POSSIBLE THERAPEUTIC TOOL IN DISEASES AND CANCER

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Dr. Ferenc Erdodi graduated from the University of Debrecen as a chemist in 1979 and received his PhD degree in medical biology in 1983 at the University Medical School of Debrecen. Currently he is full professor in the Department of Medical Chemistry, Faculty of Medicine at the University of Debrecen. He does research on the roles of protein phosphorylation-dephosphorylation in the regulation of cellular processes. He worked in the USA as a postdoctoral fellow and as a visiting professor at the University of Illinois and at the University of Arizona. He participated in international research collaboration with scientists in the USA, Germany, Japan and Canada. He has published over 90 peer-reviewed papers and 4 book chapters so far and his publications have been cited more than 2500 times. He has been the advisor for 7 successfully defended PhD thesis and the tutor for many students' research projects. He has been the Chairman of the Council of Students' Research Society since 2013.

Aim: It is well established that sustained phosphorylation of several key signaling proteins facilitates cancer cell survival and proliferation. Disease and cancer therapies mainly involve protein kinase inhibitors, while interventions via stimulation of protein phosphatases have received less attention. Our research focuses on protein phosphatase-1 (PP1) and -2A (PP2A), which dephosphorylate numerous regulatory proteins and the aims are to identify activators of these enzymes with possible pharmacological applications.

Methods: Leukemic, endothelial and mesenchymal stem cells were cultured and following different treatments changes in cell viability, protein expression, phosphorylation, formation of signaling molecules and lipid accumulation were determined by established protocols.

Results: Epigallocatechin-3-gallate (EGCG), a green tea ingredient, activates PP1 and PP2A via the 67 kDa laminin receptor (67LR) $\rightarrow$ cyclic-AMP $\rightarrow$ Protein kinase A $\rightarrow$ PP2A $\rightarrow$ PP1-type myosin phosphatase activation pathway. This EGCG induced phosphatase activation results in: (i) dephosphorylation and activation of endothelial NO synthase and myosin-II thereby improving the barrier function of endothelial cells, (ii) dephosphorylation of retinoblastoma protein increasing the chemosensitivity of leukemic cells to chemotherapeutic agents, and (iii) suppression of the adipogenic differentiation of mesenchymal stem cells. Searching for phosphatase activators we have identified several selenoglycosides which activated both PP1 and PP2A in vitro and to a moderate extent in cells. These molecules may serve as lead compounds to develop more potent activators with cellular effectiveness.

Conclusions: Our results indicate the important roles of PP1 and PP2A in cellular regulation and imply that phosphatase activation is a promising therapeutic approach for the treatment of distinct diseases and cancers.

HIDDEN CARDIOTOXICITY: PARADIGM CHANGE IN CARDIAC SAFETY TESTING IN ISCHEMIC AND COMORBID CONDITIONS

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Dr. Peter Ferdinandy is a professor of pharmacology and clinical pharmacology, director of the Department of Pharmacology and Pharmacotherapy, Semmelweis University, as well as the vice-rector for science and innovations of Semmelweis University. He received an MD diploma in 1991 and a PhD degree in 1995 from the University of Szeged. He became a registered clinical pharmacologist in 1999 and obtained a DSc degree of the Hungarian Academy of Sciences in 2004. He completed MBA studies in Finance and Quality Management in 2004 at the Budapest University of Technology and Economics. He was a postdoctoral fellow of MRC Canada for 2 years at the Department of Pharmacology,

University of Alberta, Edmonton, Canada. He is the founder and CEO of Pharmahungary Group, a group of R&D companies. He consulted hundreds of preclinical and clinical drug and medical device development projects for several pharmaceutical and medical device companies all over the world in the last 20 years. He published over 200 papers in international peer-reviewed journals and he is listed among the most influential scientists in the field of pharmacology on HighCited 2014 and HighCited 2017. He is member of the editorial boards of J Mol Cell Cardiol, and J Pharmacol Toxicol Methods. He was the president of the International Society for Heart Research, European Section, and currently the past chair of the Working Group of Cellular Biology of the Heart, European Society of Cardiology. The areas of his expertise include infarction, heart failure, cardioprotection, their interaction with co-morbidities and co-medication, transcriptomics, translational studies and clinical pharmacology.

Unexpected cardiac adverse events are one of the leading causes of interruption of clinical trials and drug withdrawals. It has been shown that cardiovascular risk factors and comorbidities (such as aging, metabolic diseases, etc.) and their medications (e.g. nitrates, antidiabetic drugs, statins, etc.) may interfere with cardiac ischemic tolerance and molecular signaling of endogenous cardioprotection. Indeed, certain drugs may exert adverse events on the diseased heart that is hidden in the healthy myocardium. Hidden cardiotoxic effects of drugs may occur due to (i) enhancement of unwanted signaling due to ischemia/reperfusion injury and/or the presence of risk factors and/or (ii) inhibition of cardioprotective signaling pathways, both of which may lead to ischemia-related cell death and pro-arrhythmic events. This led to novel concept of “hidden cardiotoxicity”, i.e. cardiotoxicity seen only in the diseased heart (i.e. ischemia/reperfusion injury and/or its major comorbidities). Hidden cardiotoxicity cannot be revealed by the routinely used cardiac safety testing methods in “healthy” test systems, moreover, the mechanism of hidden cardiotoxicity is largely unknown. Therefore, here we summarize the current knowledge on hidden cardiotoxicity and urge the need for development of novel cardiac safety testing platforms for early detection of yet “hidden” cardiotoxicity.

USE OF PROTEOMICS TO IMPROVE THE ASSESSMENT OF DRUG SAFETY

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Peter Ganz, MD

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Dr. Peter Ganz is the Chief of Cardiology at the Zuckerberg San Francisco General Hospital and Maurice Eliaser Distinguished Professor at UCSF. Dr. Ganz has been a pioneer in translational cardiovascular research. He was the first to publish on vascular endothelial function in health and its dysfunction in atherosclerosis in humans. Currently, Dr. Ganz is making important discoveries in the field of proteomics - using modified aptamers as binding reagents to quantify proteins in blood. Relevant to his presentation, he is improving assessment of drug safety through proteomics. Dr. Ganz received his M.D. from

Harvard, completed his residency at the Massachusetts General Hospital and cardiovascular fellowship at the Brigham and Women's Hospital. He spent 25 years directing cardiovascular research in the cardiac catheterization laboratories at the Brigham and Women's Hospital and Harvard Medical School, prior to arriving to UCSF in 2008.

Aim: Early detection of adverse effects of novel therapies and understanding of their mechanisms could improve the safety and efficiency of drug development. We have retrospectively applied large-scale proteomics to blood samples from ILLUMINATE (Investigation of Lipid Level Management to Understand its Impact in Atherosclerotic Events), a trial of torcetrapib (a cholesterol ester transfer protein inhibitor), that involved 15067 participants at high cardiovascular risk. ILLUMINATE was terminated at a median of 550 days because of significant absolute increases of 1.2% in cardiovascular events and 0.4% in mortality with torcetrapib. The aims of our analysis were to determine whether a proteomic analysis might reveal biological mechanisms responsible for these harmful effects and whether harmful effects of torcetrapib could have been detected early in the ILLUMINATE trial with proteomics.

Methods: A nested case-control analysis of paired plasma samples at baseline and at 3 months was performed in 249 participants assigned to torcetrapib plus atorvastatin and 223 participants assigned to atorvastatin only. Within each treatment arm, cases with events were matched to controls 1:1. Main outcomes were a survey of 1129 proteins for discovery of biological pathways altered by torcetrapib and a 9-protein risk score validated to predict myocardial infarction, stroke, heart failure, or death.

Results: Plasma concentrations of 200 proteins changed significantly with torcetrapib. Their pathway analysis revealed unexpected and widespread changes in immune and inflammatory functions, as well as changes in endocrine systems, including in aldosterone function and glycemic control. At baseline, 9-protein risk scores were similar in the 2 treatment arms and higher in participants with subsequent events. At 3 months, the absolute 9-protein derived risk increased in the torcetrapib plus atorvastatin arm compared with the atorvastatin-only arm by 1.08% ($P=0.0004$). Thirty-seven proteins changed in the direction of increased risk of 49 proteins previously associated with cardiovascular and mortality risk.

Conclusions: Heretofore unknown effects of torcetrapib were revealed in immune and inflammatory functions. A protein-based risk score predicted harm from torcetrapib within just 3 months. A protein-based risk assessment embedded within a large proteomic survey may prove to be useful in the evaluation of therapies to prevent harm to patients.

PATHOGENESIS OF ANEMIA OF INFLAMMATION, AKA ANEMIA OF CHRONIC DISEASE

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Tomas Ganz, MD, PhD

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Dr. Ganz is a Distinguished Professor of Medicine and Pathology at the David Geffen School of Medicine at University of California, Los Angeles (UCLA). He received his BS in Physics from UCLA, PhD from the California Institute of Technology in Applied Physics and MD from UCLA. He trained in Internal Medicine and Pulmonary/Critical Care Medicine at the UCLA Medical Center. His research focus is on the biological role of peptide mediators in innate immunity and iron metabolism. He has investigated the pathogenesis of anemia of inflammation and iron overload states, and developed hepcidin agonists and antagonists. He has authored more than 250 publications in refereed journals and more

than 30 book chapters. Dr. Ganz has served as an Associate Editor of Blood (1998-2007), President of the International Bioiron Society (2009-2011) and has been a member of the Erythrocyte and Leukocyte Biology (ELB) Study Section of the National Institutes of Health. He has helped start three biotechnology enterprises.

Aim: 1) Define anemia of inflammation, the context in which it develops and its impact on patients; 2) Explain the pathogenesis of anemia of inflammation; 3) Discuss current and future treatments.

Methods: The presentation is based on original discoveries made in my laboratory and a review of the many contributions made by others.

Results: Anemia of inflammation is a mild-to-moderate, usually normocytic, normochromic anemia that develops in the context of chronic inflammatory diseases. Its three recognized pathogenic components include 1) iron-restricted erythropoiesis from hypoferremia of inflammation, 2) diversion of hematopoietic precursors from erythrocytic lineage to leukocytic lineages, 3) shortened erythrocyte lifespan. The mediators of these effects are cytokines (mainly IL-6 and interferon-gamma) and the iron-regulatory hormone hepcidin. Current treatments include the combination of erythropoietin and IV iron. Future treatments will target the cytokines and hepcidin.

Conclusions: Anemia of inflammation is a common condition that can cause important morbidity in some patients. It is best treated by ameliorating the underlying disease but when this is not possible, specific treatments are available and more are in the pipeline.

TRANSCRANIAL DOPPLER MONITORING FOR CAROTID ARTERY INTERVENTIONS: TCAR IS A NEW KID ON THE BLOCK

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Zsolt Garami, MD

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Board Member and Chair of the Fellowship Committee, HMAA

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.

Aim: Carotid artery stenting (CAS) with an embolic protection device (EPD) has become a common treatment alternative to carotid endarterectomy (CEA) for prevention of stroke in patients with severe carotid artery stenosis. Although distal embolization is a well-recognized complication during carotid interventions, only clinically evident embolization resulting in neurologic sequelae is routinely used as an outcome measure; subclinical microemboli have not been fully assessed. Our studies have shown microembolization identified on diffusion-weighted MRI (DWI) in up to two-thirds of patients undergoing CAS despite an absence of clinical symptoms. Nevertheless, the clinical significance of acute DWI abnormalities is largely unknown because the stability of cognitive function in patients with subclinical microembolization has not been fully evaluated using comprehensive cognitive assessments.

Methods: Transcranial Doppler (TCD) is the "doctor's stethoscope for the brain". TCD can also detect potential collateral flow signals in the ophthalmic, anterior communicating, and posterior communicating arteries caused by hemodynamically significant carotid stenosis. TCD remains the only method to detect asymptomatic embolization but does even more. TCD provides essential "real time", hemodynamic information about the intracranial circulation compared to "static" brain imaging modalities.

Results: New promising cerebral protection is using active ICA flow reversal during Trans Carotid Artery Revascularization (TCAR). TCAR is an option for patients with carotid artery disease who are considered high-risk for conventional carotid endarterectomy (CEA). The TCAR is performed through small incision above the clavicle and ICA flow is temporarily from the brain. The debris from plaque is filtered out and flow reinserted into femoral vein.

Conclusions: TCAR makes carotid stent placement possible without any distal embolization.

INNOVATIONS AND THE HIPPOCRATIC OATH

Gloviczki, P.

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Peter Gloviczki, MD

Professor and Chair Emeritus, Division of Vascular and Endovascular Surgery, Mayo Clinic, Rochester, MN

Peter Gloviczki, MD, FACS, is the Joe M. and Ruth Roberts Professor of Surgery and Chair, Emeritus, Division of Vascular and Endovascular Surgery. He is Director Emeritus of Mayo Clinic's Gonda Vascular Center and serves as Editor-in-Chief of the Journal of Vascular Surgery Publications. He is married to Dr. Monika Gloviczki, has two children, Peter and Julia, a son-in-law, Ben, a grand-child, Katherine and a stepson, Michael. He lives with Monika in Rochester, MN.

Aim: The goal of this lecture is to examine what role inventions and innovations played in the development of modern day vascular surgery and minimally invasive endo-vascular interventions.

Methods: The manuscript recalls major innovations and innovators in vascular surgery, examines challenges innovators and those who adopt innovations face and discusses modern meaning of the Hippocratic Oath.

Results: The lecture remembers Professor Nicolai Volodos, a pioneer innovator and a giant in vascular and endovascular surgery from Ukraine, who performed the first endovascular repair of a thoracic aneurysm in 1986. It also recalls the pioneer work of the Argentinian Juan Parodi, who started the endovascular revolution using transfemoral endovascular repair of abdominal aortic aneurysms, as early as 1990. Medical innovations today face major challenges, including skyrocketing costs, difficulty obtaining funding, complicated regulations and bureaucracy, inertia in the academic environment and a lack of mentorship. Innovators and those who adopt innovations must adhere to basic principles of the Hippocratic Oath, follow modern ethical considerations, protect the human subjects of research and above all, protect the safety and well-being of the patients they treat.

Conclusions: Surgical innovations are essential to advance cost-effective care and shared decision making on adopting new therapies by an ethical surgeon and a well-informed patient is the cornerstone of ethical patient care.

INTRODUCING WHOLE HEALTH AND INTERGRATIVE MEDICINE IN THE VA HEALTHCARE SYSTEM

Halasz, I.

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Ildiko Halasz, MD

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Board Member, HMAA

Dr. Ildiko Halasz is President of HMAA New England Chapter and member of the HMAA Board of Directors. She received her MD from the University of Debrecen School of Medicine in 1980 and then certified in anesthesiology and intensive care at the Department of Surgery under the tutelage of Arpad Peterffy, one of the founders of modern cardiac surgery in Hungary. Dr. Halasz moved to the US in 1990 where she obtained additional clinical training in internal medicine. In 2000 she joined the primary care group at the VA Boston Healthcare System and became Assistant Professor at Harvard Medical School. Her academic interests focus on the comprehensive management of obesity and associated disorders among veterans. She is currently involved in several multicenter clinical research projects such as the Million Veterans Program and the CONFIRM study on colorectal cancer screening.

Aim: Biomedical research in the past 150 years has witnessed a roller coaster between reductionist and holistic efforts: from discoveries on microbes and immunity by Koch and colleagues through the integrative concepts of homeostasis (Cannon) and stress (Selye) to an unprecedented progress in molecular biology and finally to systems biology revolution. Aristotle already recognized how “the whole is more than the sum of its parts.” While detailed and mechanistic knowledge is critical, human life as a complex system has emergent properties that cannot be understood just by looking at the individual components.

Methods: The success of reductionist medicine led to a disease-driven approach to care and resulted in spiraling costs and a fragmented health system that is reactive, episodic and impersonal. By recognizing this, the VA has initiated a new model that focuses on compassionate aspects of patient care. The “whole health” program calls for strategies that strengthen the person's innate capacity for health and healing, such as mind-body approaches and other methods of complementary and alternative medicine (CAM). There is a perceptual barrier to the framework of Integrative Health (IH) as some clinicians are concerned that it may be “non-scientific.”

Results: To better understand the perception of medical community on IH, a survey has been initiated among Primary Care practitioners at VA Boston. The results of this survey will be briefly presented and analyzed. Personal views and professional experience of clinicians vary widely and implementation depends on local efforts and leadership. Most stakeholders agree that IH has great promises for US veterans who have a number of chronic conditions and may return to civilian life with complex service-related injuries. Putting these individuals at the center of care and exploring their values and their vision of health is intended to enhance the power of self-care strategies and strengthen innate healing capacities.

Conclusions: Supporting a holistic approach of healing that addresses all aspects of life may have a beneficial impact on disease outcomes, well beyond what conventional medicine can offer in the current health care system.

PRECISION ONCOLOGY MEETING LUNG CANCER MANAGEMENT

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Dr. Balazs Halmos is an active clinician/clinical and translational investigator and is currently Professor of Clinical Medicine and Chief of Thoracic/Head and Neck Oncology and Clinical Cancer Genomics at Albert Einstein College of Medicine/Montefiore Medical Center. He has spearheaded several key discoveries in the area of biomarker driven precision cancer medicine, in particular in EGFR and MET-mutated lung cancers and also has been overseeing a large clinical trials program including multiple key immunotherapy studies.

Aim: To provide an overview of recent advances in the management of advanced lung cancer highlighting original work by the presenter leading to transformational changes in the use of molecular and immune biomarkers to guide targeted and immunotherapies to optimize patient outcomes.

Methods: Basic technology of molecular, immune and liquid biopsy based biomarkers and key clinical trials leading to practice changing results will be discussed.

Results: A stepwise summary will be provided of major milestones reached over the last decade in lung cancer management through the introduction of molecular biomarkers to identify molecularly defined subsets of non-small cell lung cancers as well as the development of sequential generations of agents yielding dramatically improved outcomes in the treatment of patients with such tumors, for example EGFR/ALK/MET-positive lung cancers. Then research into understanding acquired resistance and development of novel, liquid biopsy based biomarkers and new agents to address resistance will be discussed. Lastly, more recent discoveries leading to the rapid incorporation of immune biomarkers and immune checkpoint inhibitors will be discussed that have led to a complete transformation of the treatment landscape.

Conclusions: The last decade has led to dramatic advances in lung cancer management now yielding further dividends through expansion to earlier stages of lung cancer as well as informing research of other cancer types.

ASSOCIATIONS BETWEEN THE EPICARDIAL FAT VOLUME AND THE VULNERABILITY GRADE OF CULPRIT CORONARY PLAQUES IN PATIENTS WITH UNSTABLE ANGINA

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Mihai Iuliu Harsa, MS

5th Year Medical Student, Medicine and Pharmacy of Targu Mures, Targu Mures, Romania

Winner of the 2018 Marosvasarhely HMAA Student Award

Mihai Iuliu Harsa is a 5th year medical student at the University of Medicine and Pharmacy of Targu Mures. He was the first prize winner on the 2018 TDK conference in Marosvasarhely in 2018, in the cardiology section and winner of the HMAA Student Award.

Aim: The role of the epicardial fat tissue, as an inflammatory mediator, is well known, but its physio-pathological role in acute coronary syndrome is not yet clarified. The aim of our study is to determine the association between the epicardial fat volume (determined with angio-CT) and the vulnerability parameters of culprit coronary plaques in patients with unstable angina.

Methods: We observed the coronary plaques and epicardial fat volume of 85 patients with unstable angina with the help of angio-CT. We studied the following vulnerability parameters: >70% narrowing, low plaque density of < 30 HU and size >20 mm³ on CT, positive remodeling index (RI > 15%) and spotty calcifications. The first group of 52 patients had at least 2 vulnerability markers on the culprit lesion. The second group of 33 patients had less than 2 vulnerability markers on the culprit coronary lesion.

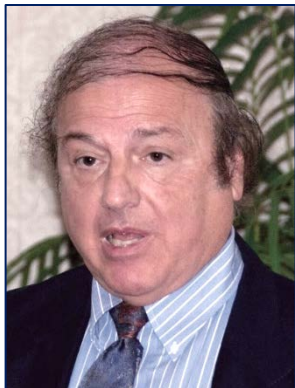
Results: The main epicardial fat volume was 102,0 ml. The first group had a volume of $113,2 \pm 17,0$ ml (95% CI: 108,5 – 118,0), whereas the second group a volume of $87,8 \pm 8,7$ ml (95% CI: 84,7 – 90,9) ($p < 0,0001$). The number of vulnerability markers was significantly higher in the group with an epicardial fat volume >100 ml, than in those with < 100 ml: (61,5% vs. 36,3%, $p = 0,02$ at plaque narrowing, 86,5% vs. 36,3%, $p < 0,0001$ at low plaque density, 73,0% vs. 42,4%, $p = 0,006$ at spotty calcifications, and 67,3% vs. 39,3%, $p = 0,01$ at remodeling index). The ROC analysis showed a good sensitivity at epicardial fat volume >100 ml as plaque vulnerability predictor (AUC=0,68, sensitivity: 78%, specificity: 67%).

Conclusions: Patients with unstable angina and culprit coronary lesions, who have more than 2 vulnerability markers present a higher epicardial fat volume. The epicardial fat tissue is in direct correlation with the vulnerability grade of culprit atheromatous coronary plaques and may represent a new imaging biomarker for plaque vulnerability determination and forecasting acute coronary events.

NUTRITIONAL DEFICIENCIES: IDENTIFICATION, TREATMENT AND MANAGEMENT IN THE WEIGHT LOSS SURGERY PATIENT

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Edward Hatchigian, MD

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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 illustrate how nutrient and vitamin deficiencies can occur after weight loss surgery. Some of the deficiencies are common and mild and can be overcome even prevented with adequate nutrient and multivitamin supplementation. Other nutrient deficiencies can cause significant clinical manifestations. Nutrient deficiencies such as iron, vitamin B12, vitamin D, calcium and thiamine as well as copper and vitamin A are reviewed and how treated and managed.

Methods: Weight loss surgery has increased dramatically from 1992 when 16,200 procedures were performed to 228,000 in 2017. The potential health benefits have been well established with reduction of co-morbid conditions such as type 2 diabetes, obstructive sleep apnea, gastroesophageal reflux, hypertension and musculoskeletal conditions. The 2 most common procedures - Roux-en-Y gastric bypass and the sleeve gastrectomy can cause nutritional deficits. Review of patient's chart including laboratory results, the type of deficiencies, treatment plan and outcome were assessed.

Results: Nutrient deficiencies were most common with the Roux-en-Y gastric bypass because of the malabsorptive component. The sleeve gastrectomy does not include intestinal bypass yet can lead to certain nutritional deficits. Iron deficiency with associated anemia was the most common (20–49 percent). Vitamin B12 deficiency was seen in 25–35 percent of patients but clinical symptoms were not common. Vitamin D was very common when checked pre-operatively and its deficiency along with calcium following surgery was associated with risk of osteoporosis. Thiamine deficiency was concerning for risk of developing Wernicke's encephalopathy. Severe copper deficiency manifested by myeloneuropathy in one patient responded nicely to supplementation. Vitamin A deficiency in another patient who had the sleeve gastrectomy developed decrease in visual acuity and night blindness.

Conclusions: Besides maximizing weight loss, reduce and co-morbid conditions, improving quality of life maintaining or achieving nutritional health by preventing/treating nutrient deficiencies is a major goal of weight loss surgery.

DIFFERENTIAL DIAGNOSTIC AND THERAPEUTIC DIFFICULTIES IN AN ADOLESCENT PATIENT WITH ACUTE LYMPHOBLASTIC LEUKEMIA – FUNGAL INFECTION VS METHOTREXATE-INDUCED SUBACUTE ENCEPHALOPATHY

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Gabor Horvath graduated from the University of Pecs, Faculty of Medicine in 2011. He received Pro Scientia Award of the Hungarian Academy of Sciences in 2009. He performed research in the Department of Anatomy at the University of Pecs and obtained his PhD degree in 2016. He is currently a 4th year pediatric resident at the University of Pecs and would like to specialize in pediatric oncology in the future. He has been a member of the HMAA Hungary Chapter since 2007 and became a Hungary Chapter Board member in 2010. He worked as a local representative of the HMAA HC in Pecs for 5 years (2010-2014). Dr. Horvath serves on the HMAA Board of Directors as one of the Liaisons for Hungary.

Aim: Acute lymphoblastic leukemia (ALL) is one of the most common malignancies of childhood, which is treated with high doses of methotrexate (MTX), as it crosses the blood-brain barrier to eradicate leukemic cells from central nervous system (CNS). Pediatric invasive aspergillosis (IA) has a rising incidence due to the increasing number of immunosuppressed children. Differential diagnostic difficulties in ALL intracranial abscesses are rare in immunocompromised patients. Intracranial abscesses may develop from pyogenic or fungal agents. IA is the most common and the most threatening fungal infection in patients with hematologic malignancy. In patients with invasive fungal infections, the CNS is an uncommon site of involvement, potentially resulting from systemic circulation and disseminating throughout the body. We would like to draw attention to a differential diagnostic difficulty we have experienced during a fungal infection under chemotherapeutic treatment which consists MTX.

Methods: A 16-year old common ALL patient received chemotherapeutic treatment (protocol ALL IC BFM 2009, intermediate risk). 4 months after the beginning of treatment a grand mal seizure occurred, and CT scan showed a pathological change which was suspicious to a right frontal lobe aspergilloma. Neurosurgical operation and histological examination proved the diagnosis. Elongated intravenous antifungal treatment was administered and chemotherapeutic treatment was continued based on the protocol with MTX. We noticed multiple acute neurological symptoms (transient numbness, sudden flexion in the elbow and joints of the fingers, increased muscle tone of the upper limb), simplex partial convulsion was suspected, and we presumed it was related with the CNS aspergillosis. EEG was negative, MRI showed no novelty since the last examination. The neurological symptoms persisted and showed undulating pattern. 2 months later retrospective investigation showed that these neurological signs occurred 7-10 days after MTX administrations. Transient MTX-induced leukoencephalopathy was suspected. EEG examination proved the suspected encephalopathy and based on international recommendations intravenous aminophylline administration was applied which gradually decreased the symptoms.

Results: Although, standard treatment protocol for ALL includes multimodality therapy, MTX could be associated with neurotoxicity and affects periventricular deep white matter region. MTX-induced acute toxic leukoencephalopathy has varying clinical manifestations ranging from acute neurological deficit to seizures or encephalopathy. Subacute encephalopathy occurs in relatively older pediatric patients and early in the course of treatment with MTX. Laboratory evaluations disclosed nontoxic plasma MTX levels at onset of symptom and not detected in liquor.

Conclusions: In conclusion, clinicians must be vigilant about fungal brain abscess in immunocompromised patients. Antifungal treatment must be applied without discontinuing planned chemotherapy, if possible. We would like to emphasize that beside a CNS fungal infection the patient could have comorbidity as chemotherapeutical side effect like MTX-induced acute toxic leukoencephalopathy and even if the neurological symptoms looks like related with the fungal infection or postoperative neurosurgical symptoms, we must think on other entities even if the laboratory, EEG and MRI, examinations show no typical pictures for a second entity in the background.

SCREENING AND HETEROGENEITY OF ALPHA-1 ANTITRYPSIN DEFICIENCY AMONG PATIENTS WITH COPD

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Professor Horvath is a pulmonologist currently working as medical director and department head at the National Institute for Pulmonology in Budapest. She is one of the pioneers in exhaled breath research and takes great pleasure in combining research, education and clinical care. She has more than 200 publications and an H-index of 32. She serves in the leadership of different scientific organizations including the executive management board of the European Respiratory Society and being the president of the Hungarian Respiratory Society and a Vice President of the Hungarian Association of Medical Societies (MOTESZ). She enjoys her family life with her husband and their 4

children with the addition of Böbe, a "magyar vizsla".

Aim: Development of chronic obstructive pulmonary disease is genetically influenced. Alpha-1 antitrypsin (A1AT), an enzyme that has an important role in the integrity of lung parenchyma, is coded at a single locus on chromosome 14. A1AT deficiency (A1ATD) is a genetic disorder linked with the mutation of the SERPINE1 gene resulting in decreased production of A1AT. The polymorphic gene may present different alleles from the normal MM to MZ, MS, SS, SZ, ZZ and other rare mutations. The disease is seriously underdiagnosed. Albeit the World Health Organization recommends that COPD patients should be screened at least once in their lifetime, this is not carried out regularly. We have run a pilot screening program in patients with COPD aiming to assess the presence of A1ATD among them.

Methods: 288 patients with different severity of the disease have been screened by dry blood spot sampling. A1AT phenotyping was based on isoelectric focusing. In case of abnormal findings genetic analysis was performed.

Results: Abnormal phenotypes were found in 32 cases (10.8%). There were 13 MS, 2 M0, 9 MZ and 1 MZ Pratt phenotypes. Genotyping was completed in 9 cases. Mutation was confirmed in 3 cases: one heterozygous 739C > T c (p.Arg247Cys) mutation (PiF phenotype) and two 863A > T (Glu288Val) (rs117580) mutations (S- allele) have been identified. The clinical phenotypes varied widely among these patients.

Conclusions: Our study shows that A1ATD is underestimated in COPD patients and that screening may have increasing relevance in the improvement of COPD care.

TREATMENT OF BILE DUCT GALLSTONES BY EXTRACORPOREAL LITHOTRIPSY: CLINICAL CASE AND LITERATURE REVIEW

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Zsafia Horvath, MD

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Zsafia Horvath was frequenting University of Pecs and after finishing her studies she moved to Switzerland for the residency. Actually, she is on her fourth year of residency in general surgery. After obtaining general surgery in the future she would like to specialize in abdominal surgery.

Aim: In 2 to 5% of cases of cholelithiasis, common endoscopic technics fail to completely release the bile ducts. The presence of multiple voluminous gallstones and the hard consistency of the those decrease the chances of getting a complete extraction. Extra-corporeal lithotripsy (ECL) is the simplest and less expensive technique for treating these large stones.

Methods: Young patient presenting to the emergency department with jaundice and pain. After additional examinations, a diagnosis of bile duct stones is made. ERCP with endoscopic sphincterotomy is inefficient because of the large diameter and polygonal shape of the stones. A naso-biliary probe is set up for drainage.

Results: Taking into account the impossibility of performing the clearance of the main bile duct, it is decided to do an ECL treatment for the fragmentation of bulky gallstones. An ERCP control confirms the complete clearance of the biliary tree. Finally, the patient underwent laparoscopic cholecystectomy during the same recovery.

Conclusions: The ECL is a valid alternative for the treatment of biliary gallstone, which allows a clearance of the bile duct in 85 to 95% of cases with a low rate of complications. This technique avoids the need for surgery often difficult and burdened with significant morbidity.

ACUTE AND PREVENTIVE TREATMENT OF MIGRAINE IN CHILDREN

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Peter Huszar, MD

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Dr. Huszar obtained his medical degree from the University of Szeged. He completed his residency in Pediatrics and a fellowship in Child Neurology at SUNY Health Science Center at Brooklyn, NY. He is a pediatric neurologist at the Johns Hopkins All children's Hospital with special interest in pediatric headache disorders. He is also involved in pediatric migraine research at the Johns Hopkins All Children's Hospital.

Aim: The lecture aims are that the audience should be able to diagnose, characterize specific migraine syndromes in pediatric population, achieve knowledge of basic treatment options for acute and preventive migraine management, and learn new experimental treatment methods.

Methods: The lecture is based on review of contemporary relevant publications and clinical experience.

Results: Pediatric headache is one of the most common complaints in pediatric office and the most common referral to pediatric neurology office. Pediatric migraine is the most common primary migraine syndrome. Although most of the clinical knowledge of pediatric migraine management is based on adult data, and the applications for the pediatric population is significant, the increasing results from pediatric migraine studies fundamentally changing the approach to the pediatric migraine and offer new and most efficient way to treat pediatric migraine.

Conclusions: Recent development in pediatric migraine management significantly improved the quality of migraine treatment in pediatric population, both increased the numbers of headache free days, and decreased the severity and duration of the acute migraine attacks.

AEROSOL EXPOSURE TO INTERMEDIATE SIZE NIPAH VIRUS PARTICLES INDUCES NEUROLOGICAL DISEASE IN AFRICAN GREEN MONKEYS

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Dr. Huzella is a biocontainment research pathologist for the NIH/NIAID at the IRF at Ft. Detrick, MD. He provides pathology support in all levels of bio-containment, 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 bio-containment.

Aim: Nipah virus (NiV) infection can cause severe respiratory or neurological disease in humans and occurs through contact with virus contaminated fomites or consumption of contaminated food. Using the African green monkey (AGM) to model NiV infection identifies aspects of infection that are similar to, but don't fully recapitulate disease. By creating a method for aerosol exposure to deposit virus in the upper respiratory tract may mimic human exposure routes. Computed tomography (CT) evaluation showed development of pulmonary parenchymal disease including consolidations, ground-glass opacities, and reactive adenopathy in some AGMs. There were no clear clinical neurological signs, but magnetic resonance imaging (MRI) identified brain lesions in three animals, similar to those previously reported in NiV-infected patients. Immunological characterization suggested a local pulmonary inflammatory response, but a limited neurologic response. These data provide evidence of neurological involvement in the AGM that reflects the human condition and provides an avenue for development of therapeutics aimed at virus-induced neuropathogenesis.

Methods: Two groups of three AGMs were exposed to either a low dose (group 1, 100 pfu target dose) or high dose (group 2, 1000 pfu target dose) dose in a medium-large particle (target 7 µm) aerosol challenge of NiV-Malaysia using a 16 Liter, head-only aerosol exposure chamber. Animal subjects underwent imaging on Philips Precedence SPECT/CT and Achieva 3 Tesla MR clinical scanners (Philips Healthcare, Cleveland, OH). For brain MRI studies, all animals underwent a 65-minute long series of scans using a Pediatric Head/Neck coil. Structural, quantitative and functional measures were obtained and all slices were acquired in the axial plane. Imaging sequences obtained included T1- and T2-weighted fast field echo (FFE) sequences, magnetization-prepared rapid gradient echo (MPRAGE) and principle of echo shifting (PRES). The FLAIR and T1-weighted FFE sequences were performed both pre- and post-contrast. Necropsies were performed on each subject with tissues collected from the same region in each individual animal.

Results: The data presented here demonstrate that NiV infection in AGMs can mimic human disease given an appropriate exposure route and viral dose. While these findings are helpful in understanding NiV induced disease, the infection in this model is still more lethal than reported in humans.

Conclusions: These studies are the first to directly identify neurological abnormalities in the AGM model that are consistent with what has been seen in humans. Furthermore, these studies are the first to report specific immunological changes within the brain and lungs following NiV infection that may be indicative of mechanisms of virus-induced pathogenesis. Further work is required to fully understand the critical components of disease progression and to identify specific correlates of disease that may allow identification of successful treatment options for NiV infection.

IMPACT OF THE FULBRIGHT PROGRAM ON COOPERATION IN THE MEDICAL AND ALLIED SCIENCES BETWEEN HUNGARY AND THE UNITED STATES

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Fulbright Commission Hungary, Budapest, Hungary



Karoly Jokay, PhD

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An expert in municipal finance and bankruptcy, Jokay taught municipal finance, public budgeting and public management in the Department of Public Policy at Central European University between 2005 and 2017. Jokay has extensive experience in Central and Eastern European countries, including Serbia, Bosnia-Herzegovina and Macedonia, completing projects on municipal bond disclosure standards, public utility transformation and regulation in the municipal services sector, as well as municipal debt regulation. He was born in Chicago to Hungarian DP parents, earned a BA in Economics from the University of Michigan and has an MA and PhD in Political Science from the University of Illinois. Jokay, who moved to Hungary in 1994, active in several civil society organizations, established a family foundation to support the education of poor, rural children in the High School of the Reformed Church in Pápa. Jokay has been Executive Director of the Fulbright Commission in Hungary since November 1, 2012.

The Hungarian-American Fulbright Commission and its antecedent bilateral educational exchange program started in 1992 and 1978 respectively. While I cannot comment on specific scientific and medical advances supported by the Fulbright Program, one can identify several types of long-term impacts that are clearly visible and replicable. These include:

- collaboration on scientific articles, outreach beyond the medical community and suggestions for policy changes
- research exchanges beyond the Fulbright framework that span generations of senior and junior medical professionals and scholars from both countries
- involvement of young Hungarian MDs in first rate research at the best US universities, and increasingly, attracting US natural science students to do research at Hungary's medical schools
- spin-off enterprises and two-way technology transfer
- improvement of medical practices based on observations in both countries
- attraction of related fields to the Fulbright program, such as sustainable hospital design and architecture, software development, biomedical engineering, human-computer interfaces, diagnostic methods and equipment etc.
- sustained professional contact between, and the holistic, cultural enrichment of the medical-scientific communities of both countries

I will defer to my esteemed colleagues to demonstrate the significant and lasting impact of their Fulbright grants.

FUNCTIONAL AND MORPHOLOGICAL CARDIAC ADAPTATION IN YOUNG COMPETITIVE ATHLETES

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Vencel Juhasz is a 6th year medical student at Semmelweis University. He is particularly interested in sport cardiology and will be spending his surgery rotation at Houston Methodist Hospital.

Aim: In order to diagnose pathological changes in athletes, normal upper limit of physiological cardiac adaptation should precisely defined and reliable normal values are required. Despite the numerous available data on adult elite athletes' cardiac parameters, there is considerably less information known about youth athletes. Our goal was to measure physiological cardiac adaptation in young competitive athletes and to determine the relationship between CMR parameters, clinical and spiroergometry data.

Methods: By the evaluation of morphological and functional parameters by CMR and spiroergometry, we studied comprehensively the degree and quality of cardiac adaptation in asymptomatic young athletes (n=84; 68 male; 16.6±2.3 ys; 13.1±6.5 training hours/week) performing sports with high dynamic component (football n=48, water polo n=22, swimming n=14) and healthy non-athletes (n=30; 17 male; 18,4 ys, <5 training hours/week). Using CMR we evaluated left (LV) and right ventricular (RV) ejection fraction (EF), body surface area related end-diastolic (EDVi), end-systolic (ESVi), stroke volume (SVi) and mass (Mi). Maximal oxygen uptake (VO₂max) as a generally accepted indicator of endurance capacity was assessed using spiroergometry.

Results: The young athletes showed significantly higher LVEDVi (109.6±13.4 vs 92.3±9.4 ml/m²), RVEDVi (110.1±15.3 vs 94.1±10.9 ml/m²), LVSVi (65.2±8.9 vs 54.4±7.3 ml/m²), RVSVi (63.6±9.1 vs 53.4 ml/m²), LVMI (70.0±11.0 vs 48.9±9.4 g/m²) and VO₂max (3.7±0.8 vs 3.1±0.8 l/min) compared to the non-athlete group. VO₂max showed a positive correlation with LVEDVi (p<0.0001; r=0.41), RVEDVi (p<0.0001; r=0.41) and LVMI (p<0.0001; r=0.56), RVMI (p<0.01; r=0.34). Analyzing age, gender, training hours/week and sports type gender and training hours/week seemed to be an independent predictor of elevated LVEDVi (p<0.05 beta=-0.31; p<0.01 beta=0.65), elevated RVEDVi (p<0.01 beta=-0.35; p<0.05 beta=0.50) and elevated LVMI (p<0.0001 beta=-0.677, p<0.0001 beta=0.67).

Conclusions: Youth competitive athletes have remarkable cardiac adaptation with an apparent correlation between morphological and functional changes. In young athletes gender and training hours seem to be an independent predictor of morphological changes called athlete's heart.

DATA ASSESSMENT OF ACUTE DESOBLITERATION THERAPY AND CLINICAL PROGNOSIS IN ACUTE STROKE – REGIONAL REGISTRY AT OUR STROKE CLINIC

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Dr. Zsolia Nozomi Karadi is currently a second year resident in Pecs, Hungary. Her primary interests include acute stroke care, neurointervention and global health.

Aim: Acute stroke has an outstanding role in current health policy due to being one of the leading causes of death and disability. Risk factors for stroke show similarity with other cardiovascular diseases, moreover, recent literature emphasizes the role of genetic factors in the pathogenesis of stroke. Our goal is a prospective data gathering from patients suffering of acute stroke in a form of a registry in order to offer a platform for the better understanding of this disease.

Methods: Our registry includes every adult patient admitted to our ward with the diagnosis of acute ischemic stroke. Uniformized questionnaires including modified Rankin Scale and NIH Stroke Scale are used to assess the medical condition on admission and information on the patient's medical history. Apart from gaining information on desobliteration therapy, we also count door-to-needle times and disease time-window. We collect two vials of blood samples of all of the included patients in our designated biobank, in order to perform genetic profiling for polymorphisms and allele variants, which may contribute to developing stroke.

Results: We maintain our data in our online system, which offers individual platforms for all of our partner institutions. All data including medical history, treatment and prognosis are uploaded to the online system, which offers immediate providing of cleaned data.

Conclusions: The acute stroke registry contributes to not only the better understanding of stroke epidemiology and pathomechanisms, but also plays an essential role in the quality management of the stroke care in our facility.

RULE OUT TRANSCATHETER AORTIC VALVE THROMBOSIS WITH POST IMPLANTATION COMPUTED TOMOGRAPHY (RETORIC STUDY) – INITIAL RESULTS

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Dr. Julia Karady is currently a PhD student of the Doctoral School of the Semmelweis University, Budapest, Hungary. She has been awarded the Fulbright Scholarship that allowed her to start a research fellowship at the Massachusetts General Hospital - Harvard Medical School, Boston, MA, from 2017 September where she studied the prognostic value of coronary computed tomography angiography derived imaging features in patients with coronary artery disease. She enclosed a successful year of research work thereby she was offered to extend her stay with another year in order to continue her efforts to identify patients at high risk to suffer future myocardial infarction.

Aim: Transcatheter aortic valve implantation (TAVI) is an alternative to surgical valve replacement in high-risk patients with aortic stenosis. Hypo-attenuated leaflet thickening (HALT) of the prosthetic valve detected with multidetector computed tomography (CT) is a recently described phenomena. The RETORIC (Rule Out Transcatheter Aortic Valve Thrombosis with Post Implantation Computed Tomography) study aims to define the prevalence and the predictors of HALT following TAVI.

Methods: Patients who underwent TAVI procedure between 2011 September and 2016 October were recruited into this prospective single-center observational clinical study. Exclusion criteria were defined as contraindications of cardiac CTA or documented infective endocarditis since TAVI placement. At the time of inclusion, patients underwent cardiac CTA, transthoracic echocardiography (TTE), brain magnetic resonance imaging (MRI) and neurological evaluation. If CTA revealed the presence of subclinical HALT, transesophageal echocardiography (TEE) was performed within 5 days following CTA evaluation and OAC therapy was initiated. Following 4 months of OAC treatment patients were followed up with cardiac CTA, TTE, TEE, brain MRI and neurological evaluations. The presence of HALT during the follow up after OAC treatment was judged using cardiac CTA.

Results: 144 patients were included (81.8 ± 8.6 years, 36.7% females). Between the TAVI procedure and the inclusion into the RETORIC study, a mean of 1.8 ± 1.1 years passed. Cardiac CT was performed altogether in 128 cases. HALT was detected in 9 patients (7%). With univariate analysis the maximal aortic velocity ($1.9 [1.6-2.2]$ vs $2.6 [1.8-3.2]$ m/s) and the mean aortic gradient ($15.0 [10.0-20.0]$ vs $27.5 [13.3-38.8]$ mmHg) as measured by echocardiography showed significant association with HALT ($p=0.009$ and $p=0.013$, respectively). These differences remained significant in the multivariate analysis (OR:8.13, 95%CI: 2.48-26.61; $p=0.001$; OR:1.12, 95%CI: 1.05-1.19; $p=0.001$). After 4-month OAC therapy in 7 patients (6%) of HALT resolved.

Conclusions: In the RETORIC study we found a 7% prevalence of HALT. 78% of HALT resolved OAC therapy, suggesting an agreement with the supposed thrombotic origin. Maximal aortic velocity and the mean aortic gradient were found to be significant predictors for the presence of HALT. (Rule out Transcatheter Aortic Valve Thrombosis with Post Implantation Computed Tomography; NCT02826200).

THE ROLE OF MIR-455-3P AND MIR-224-5P IN GASTROINTESTINAL CANCERS

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Aim: MicroRNAs are short non-coding nucleotides, the most notable role of which is negative regulation of gene expression by interfering with the process of protein translation, primarily through interaction with mRNAs. Therefore, microRNAs can potentially suppress the expression of anti-oncogenic proteins, and/or disinhibit the expression of oncogenic factors, contributing to the genesis of numerous malignancies. In one previous study, we observed decreased surface expression of claudin-3 (CLDN3) in colorectal carcinomas (CRC) in comparison to normal colorectal mucosa samples of matching patients, accompanied by increased miR-455-3p expression in tumor tissue when compared with normal mucosa. CLDN3 is a tight junction protein, the altered expression of which is associated with tumorigenesis and possible epithelial-mesenchymal transition in colorectal tissue. Another study examining hepatocellular carcinoma (HCC) patients described elevation of miR-224-5p expression before multi-kinase inhibitor (MKI) treatment being associated with higher patient survival. Platelet-derived Growth Factor Receptor Beta (PDGFR β), one of the most important targets of MKIs such as sorafenib used in the treatment of unresectable HCCs, is also a potential target of miR-224-5p. Our aims were to prove the regulatory effect of miR-455-3p on CLDN-3 expression in CRC cell lines and that of miR-224-5p on PDGFR β expression in HCC cell lines.

Methods: Quantification of microRNA expression was performed using TaqMan miRNA Assays (Life Technologies, ID: 002099). Exiqon miRCURY LNA Power Inhibitors were miR-455-3p and miR-224-5p knock-out tumor cells (4104843-111, 5 nmol and 4100825-111, 5nmol). Control cell lines were transfected with Negative Control A (199006-111, 5 nmol). Western blot analysis was performed to quantify CLDN3 and PDGFR β expression, both of which were normalized to the level of ACTB. CLDN-3 expression of HT29, SW1417 and HCT116 cell lines was measured following inhibitor treatment. Evaluation of the miR-224-5p-PDGFR β axis was performed using HepG2, HLE, and HLF cell lines. CLDN3 protein detection was performed using rabbit polyclonal antibodies (Life Technologies, 34-1700, 1:350), while mouse polyclonal antibodies were used for PDGFR β (Novus Biochem, NBP2-46361, 1:800). ImageJ2 software was used for measuring signal intensity during Western Blot analysis.

Results: Inhibitor-treated miR-455-3p knockout cells showed moderately increased CLDN3 expression, with an increase of CLDN3-to-ACTB ratios being 1.07, 1.44 and 1.62 in HT29, DLD1 and SW1417 cells, in comparison to the CLDN3-to-ACTB ratios measured in controls. Marked elevation of PDGFR β expression was observed in HepG2 HCC cells, with a PDGFR β -to-ACTB ratio of 14.9 compared to controls, while HLE cells also showed a less prominent 1.8-fold increase in PDGFR β levels. The addition of a miR-224-5p inhibitor seemed to have no effect on PDGFR β expression in HLF cells, with PDGFR β -to-ACTB ratios being virtually same in the treated cells and controls.

Conclusions: Both microRNAs examined seem to have a role in regulating the expression of their suspected targets. Treatment of CRC with miR-455-3p antagomiRs could potentially lessen the reduction of claudin-3 expression, contributing to an intercellular adhesion protein profile less favorable to the evolution of malignancies. Elevated levels of miR-224-5p in HCC is associated with lower PDGFR β expression, which was described as leading to reduced tumor angiogenesis and higher overall survival in patients with unresectable HCC.

UNCOVERING THE SECRETS OF ANCIENT HUMAN REMNANTS BY RADIOLOGIC INVESTIGATIONS

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Aim: Corpses of deceased persons can be mummified differently, depending on their environment or even by sophisticated mummifying methods for preparing them for their perennial lives. Egyptian mummification is a well known procedure, however it was modulating from time to time.

Methods: We investigate regularly different type of mummies and other small osseous parts of humanogenic archeological remnants. The leading method of our investigations is the computerized tomography (CT), sometimes completing with high resolution CT (HRCT) or even with of finest resolution cone beam CT (CBCT).

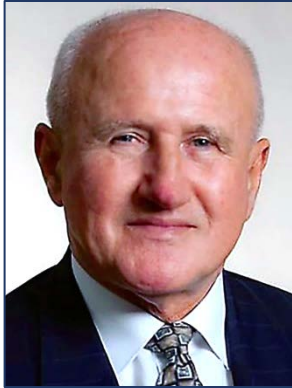
Results: In this presentation I would like to demonstrate the investigation of four complete mummies of ancient Egyptian origin placed in the collection of the Hungarian Museum of Fine Arts. There were mummies of two women and two men. The sarcophagus was preserved for two of them, but the other two corpses were found in the collection without any closer informative signs. Even one of them was totally denudated, because of his bandages were removed sometimes in the past. Their estimated time range was V.-I. century B.C. Beside of the radiological investigations there were microbiological, chemical, spectroscopical, and textile analysis performed. By the aid of radiology we could gain /extend anthropological, paleopathological and dental information.

Conclusions: Our conclusion was, that by the aid of a CT-data, analyzing by postprocessing methods and performing 3D reformations of those, we could tell not only the abovementioned data, but even we could help to analyze the embalment chemicals and methods of them, which are aids for estimating the place and period of their descends.

ROLE OF WATER STRUCTURING IN GENE REGULATION

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Dr. Miklos Kellermayer is an Emeritus Professor of Clinical Biochemistry at the University of Pecs. His research concerns the organization of water and potassium inside the living cells. Currently he serves as the President of the Hungarian Society for Healthcare (Magyar Egészségügyi Társaság, MET).

Aim: I dedicate my presentation to the memory of Dr. Barna Andrásföszky, founder of the Hungarian Society for Healthcare (Magyar Egészségügyi Társaság, MET) 25 years ago, who deceased this February at the age of 94 years. MET has become one of the most important societies interconnecting and assisting Hungarian physicians around the world and most notably in the Carpathian basin; thus, it is most appropriate to commemorate MET's founder at this forum. Water is the most abundant and most important chemical in living systems, yet it is the most neglected and ignored. According to Albert Szent-Györgyi, however, "life is water dancing to the tune of solids." My lifelong research is in accord with this statement as I have consistently found that gene regulation is most likely associated with the structuring of water which is regulated mainly by loosely bound nuclear proteins.

Methods: Ever since cell nuclei and chromosomes have been investigated, in the beginning by light microscopy, it has been conclusively thought that water structures play an important role in chromatin organization hence gene regulation. Water content of mitotic chromosomes is the lowest among the organelles. By contrast, the density of active and inactive chromatin regions of the interphase nucleus varies greatly, suggesting that the water content and water structuring in these regions are dynamically regulated, possibly by loosely bound nuclear proteins.

Results: We have previously demonstrated that the SV40 large T antigen, an oncoprotein derived from the polyomavirus SV40, is a member of the loosely-bound nuclear protein family. In hybrids of SV40-induced tumor cells and chicken erythrocytes, strong correlations could be observed between the nuclear volume, hence gene activity, and the presence of the large T antigen.

Conclusions: Thus, the important life process of gene regulation is indeed chromatin-associated structured water dancing to the tune of loosely bound nuclear proteins.

NANOMECHANICS OF NUCLEIC-ACID AND NUCLEOPROTEIN SYSTEMS

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Aim: Genetic information is encoded in DNA. Various protein systems are involved in the packaging, replicating, decoding and housekeeping of DNA in processes involving mechanical events. For example, viral DNA is packaged into the capsid against force, and the accumulated pressure is used later to eject DNA into the host. Furthermore, chemical modifications may alter the mechanics of DNA with not fully understood mechanisms. Our aims were: 1) to uncover the mechanical consequences of DNA methylation, which is one of the key mechanisms of epigenetic regulation; 2) to investigate the mechanisms of DNA ejection from a viral capsid, which is one of the most complex nucleoprotein systems.

Methods: We measured methylation-induced nanomechanical changes by manipulating, with optical tweezers, a DNA molecule with the sequence of a CpG island. Viral DNA ejection was followed by tapping T7 phage particles with an oscillating atomic-force-microscope cantilever.

Results: Contour length, bending rigidity and intrinsic stiffness decreased in hypermethylated DNA. Increased forces were required to convert hypermethylated DNA into an extended S-configuration. Tapping the T7 capsid wall triggered rapid DNA ejection via the tail complex. Triggering rate increased exponentially as a function of force, following transition-state theory.

Conclusions: The high structural stability of methylated DNA probably has significant consequences on the packaging, recognition, replication, transcription and reparation of hypermethylated genetic regions. Triggering of viral DNA ejection involves a mechanically sensitive conformational switch.

THE DEVELOPMENTAL ORIGINS OF INFLAMMATORY BOWEL DISEASES AND COLON CANCER

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Richard Kellermayer was born and raised in Hungary. He is currently an Associate Professor of Pediatrics at Baylor College of Medicine, Houston, Texas. He is the medical director of the Pediatric Inflammatory Bowel Disease and Fecal Microbiota Transplantation Programs at Texas Children's Hospital.

Aim: Intestinal mucosal epigenetic (including DNA methylation) changes have been implicated as important elements in the developmental origins of inflammatory bowel diseases (IBD; including Crohn's disease [CD] and ulcerative colitis [UC]), which are linked to young-onset colorectal cancer (YCRC). Parental exposures prior to conception, post-fertilization biochemical influences, and the environmentally responsive postnatally evolving gut microbiome may play a key role in modulating intestinal mucosal epigenetic patterning and consequent susceptibility to IBD and YCRC.

Methods: High throughput 16S rRNA gene sequencing and RNA sequencing was used to examine the mucosal microbiome and gene expression changes in pediatric ulcerative colitis patients after a series of fecal microbiota transplantation (FMT).

Results: Epithelial proliferation was dampened upon FMT with suppression of genes relevant for cell cycle control. The abundance modification of some bacterial species correlated with these changes.

Conclusions: Our recent findings in children without identifiable gastrointestinal pathology (controls), and with UC support the potential importance of gut bacteriome and mucosal epigenome interactions in the developmental origins of both UC and YCRC.

NEW DEVELOPMENTS IN THE DIAGNOSIS AND TREATMENT OF LYMPHANGIOLEIOMYOMATOSIS

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President, HMAA

Andras Khoor is the current President of the HMAA. He is Consultant and Chair of the Department of Laboratory Medicine and Pathology at Mayo Clinic Florida (Jacksonville, Florida) and Associate Professor of Laboratory Medicine and Pathology in the Mayo Clinic College of Medicine. Dr. Khoor received his medical degree from Semmelweis University, Budapest, Hungary. After some initial training in pathology and pediatrics at Semmelweis Medical University, he researched lung development with Dr. Mildred Stahlman at Vanderbilt University, Nashville, Tennessee. This was followed by residency in pathology at Vanderbilt University and a fellowship in pulmonary pathology at Mayo Clinic, Rochester, Minnesota. Dr. Khoor's research interests include multiple areas of pulmonary pathology with a special focus on the expression of airway epithelial cell markers in pulmonary neoplasms. He has authored more than 50 publications on pulmonary pathology and is a section editor for the Archives of Pathology & Laboratory Medicine.

Aim: Lymphangioleiomyomatosis (LAM) is a rare multisystem disorder with a strong female predilection, manifesting primarily as a progressive, diffuse cystic lung disease. Symptoms are generally due to obstructive lung disease; however, pleural complications such as pneumothorax and chylothorax may also occur. The lung cysts are related to proliferation of immature smooth muscle cells of perivascular phenotype (LAM cells) and LAM is now considered as a low-grade neoplasm of the perivascular epithelioid cell tumor family. The term sporadic LAM is used for patients without the tuberous sclerosis complex (TSC), while TSC-LAM refers to LAM that occurs in the setting of TSC. Both forms are primarily caused by TSC1 or TSC2 gene mutations. These mutations lead to hyperactivation of the mammalian target of rapamycin (mTOR) and subsequently proliferation of LAM cells.

Methods: This is a review of the recent literature including the author's own publication (Krencz et al. Hum Pathol. 2018 [Epub ahead of print]).

Results: The purpose of our recent study was to assess the significance of mTORC1, mTORC2 and various metabolic pathways (including glycolysis, oxidative phosphorylation, glutaminolysis, fatty acid β -oxidation, and acetate utilization) in the pathogenesis of LAM, using semiquantitative immunohistochemical methods on formalin-fixed paraffin-embedded human lung tissue. Expression of p-S6, Rictor, GAPDH, GLS, MCT1, ACSS2 and CPT1A was significantly higher in LAM cells than in bronchial smooth muscle cells ($P < 0.01$). No significant differences were found between LAM cells and normal bronchial smooth muscle cells in GLUT1 and ATPB expression.

Conclusions: Our results were uniquely derived from human tissue and indicated that, in addition to mTORC1, mTORC2 may also play an important role in the pathobiology of LAM. Furthermore, glutaminolysis, acetate utilization and fatty acid β -oxidation appear to be the preferred bioenergetic pathways in LAM cells. mTORC2 and these preferred bioenergetic pathways appear worthy of further study as they may represent possible therapeutic targets in the treatment of LAM.

PRESENT ROLE AND FUTURE PERSPECTIVE OF INTERVENTIONAL ONCOLOGY

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Dr. Kis is an Associate Professor in the Diagnostic Imaging & Interventional Radiology at Moffitt Cancer Center in Tampa, FL. He earned his MD and PhD from the University of Szeged in Hungary. He spent 2 years in the Department of Physiology at UOEH, in Kitakyushu, Japan as a post-doctoral fellow. He was a postdoctoral fellow then junior faculty in the Department of Physiology and Pharmacology at the Wake Forest University in Winston-Salem, North Carolina. He completed a surgery internship at the Wake Forest University Baptist Medical Center and Radiology Residency and Interventional Radiology Fellowship at Brigham and Women's Hospital, Harvard Medical School, where he also

served as Chief Resident. Dr. Kis' clinical interests include image-guided tumor therapy including transcatheter chemo- and radio-embolization, percutaneous and intraoperative tumor ablation (NanoKnife, cryo- and radiofrequency ablation) and image guided biopsies.

Aim: Interventional oncology, a subspecialty of interventional radiology, uses image-guided minimally invasive procedures to target tumors. It has experienced an exponential growth in recent years due to the development of new technologies and precise image guidance. The aim of this presentation is to introduce the audience to the latest advances and future trends of interventional oncology.

Methods: Presentation of interventional oncology procedures through index cases from the clinical practice of a National Cancer Institute-designated comprehensive cancer center. Patient selection, procedure outcomes, limitations and complications are discussed based on our experience and literature data.

Results: Compared to traditional surgery, interventional oncology is minimally invasive, therefore, it reduces risks for patients, is cost effective, can often be performed in outpatient settings, allowing for shorter recovery time and minimal hospital stay. Interventional oncology has the capacity to replace surgery in small renal and liver cancers with equivalent survival outcomes, yet with less impact on quality of life and overall economic burden. As a result, interventional oncology is growing in popularity with both referring medical and surgical oncologists and with patients.

Conclusions: In recent years, interventional oncology has become the fourth pillar of cancer therapy alongside medical, surgical, and radiation oncology. New image guiding platforms and embolization and ablation techniques contribute to improve the effectiveness and safety of interventional oncology procedures.

ALTERED PATTERN OF TIGHT JUNCTION COMPONENTS AND MICRORNAS IN PRIMARY AND METASTATIC LIVER TUMOR

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After graduation from medical school, Dr. Andras Kiss spent one year at the Institute of Pathology in Freiburg, Germany and three years (1994-1997) in Bethesda at the National Cancer Institute, NIH, MD, USA. He was trained and works as a pathologist and became the director of the 2nd Department of Pathology at Semmelweis University Budapest. His research area is the molecular aspects of carcinogenesis, especially, hepatocarcinogenesis.

Aim: Altered expression of tight junction (TJ) components, such as claudins, occludin and tricellulin plays role in the histogenesis of human malignancies. This involves carcinogenesis, differentiation and progression of tumors. Altered expression of microRNAs (miR) might exert regulatory effect on aforementioned processes. Our aim was to reveal characteristic TJ and microRNA expression patterns in normal liver, chronic hepatitis, cirrhosis and hepatocellular carcinoma (HCC), cholangiocarcinoma as well as in hepatoblastoma.

Methods: Immunohistochemistry (IHC), Western blotting, in situ hybridization and qRT-PCR techniques were used to reveal expression patterns.

Results: Expression of claudin-1 and -7 was significantly elevated in cirrhosis and in HCC when compared with normal liver while HCV infection did not show correlations with elevated claudin expression. HCCs in cirrhotic livers revealed significantly more claudin-1 protein in comparison to cirrhosis. Strong claudin-1 immunohistochemical reaction was found in liver metastasis of colorectal carcinoma (CRLM) as well, while liver metastasis of pancreatic ductal adenocarcinoma (PLM) and HCC revealed significantly lower expression. CRLM and PLM was strongly positive for claudin-4 while HCC did not express it. CRLM was characterized by strong and significantly higher claudin-3 and -7 IHC positivity when compared with HCC and PLM. Altered mRNA expression pattern of claudins were majorly similar to the IHC results. Claudin-4 expression was significantly elevated in cholangiocarcinoma (CC): 75-100 % of tumor cells showed membrane positivity. Differentiation of CCs did not influence the strength of staining. Protein expression of claudin-1, -2 and tricellulin was significantly higher in hepatoblastoma (HB) samples, when compared with non-tumorous liver tissue. Well differentiated fetal subtype revealed higher claudin-1, -2 protein and mRNA levels as well as tricellulin expression in comparison to poorly differentiated embryonal components. HBs with low tricellulin expression showed significantly shorter overall survival than cases with high tricellulin expression. Intrahepatic CCs showed decreasing expression with dedifferentiation. Survival of cholangiocarcinoma cases with „tricellulin high” expression was significantly longer when compared with „tricellulin low” cases. HCCs with „tricellulin high” protein expression showed significantly lower overall survival. Elevated miR-21 and low miR-222 and miR-224 levels were associated with significantly increased overall survival in HB patients treated by SIOPEL protocol.

Conclusions: Increased expression of claudin-1 as being one of the receptors of HCV might support entry of HCV into hepatocytes, therefore, enhance and maintain chronic HCV infection leading to cirrhosis and HCC. Primary and metastatic liver tumors are characterized by specific, altered claudin expression pattern which reflects tissue origin and histogenesis of malignancies. Claudin expression pattern might better differentiate biliary tract tumors from HCCs than cytokeratins. Claudin-4 expression might help to distinguish CC from anaplastic HCC, however, not from metastatic adenocarcinomas. Expression of claudin-1, -2 and tricellulin might be regarded as differentiation marker of HB, further, tricellulin expression bears with prognostic value in HB, CC and HCC. miR expression pattern in HB and sorafenib treated HCC might possess diagnostic and predictive value.

GENE THERAPY: THE NEXT FRONTIER OF MANAGEMENT OF NEOVASCULAR AGE-RELATED MACULAR DEGENERATION AND OTHER ACQUIRED AND

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Dr. Kiss's training began in New York City where he received his undergraduate degree with honors from Columbia College and medical school training at Columbia University College of Physicians & Surgeons. He then moved to Boston to complete his ophthalmology residency and surgical vitreoretinal fellowship, both at Harvard Medical School and the Massachusetts Eye & Ear Infirmary. At Harvard, Dr. Kiss was select by the faculty to serve as the Chief Retina Fellow. Dr. Kiss was then recruited back to New York City to join the vitreoretinal faculty at Weill Cornell Medical College and assume the role of Director of Clinical Research in the Department of Ophthalmology. Dr. Kiss was then named the Director of the Retina Service, overseeing and guiding all clinical, research and education activities within the retina division at Weill Cornell Medical College. More recently, Dr. Kiss was named the Director of Tele-Ophthalmology, spearheading the department's telemedicine and outreach efforts.

Aim: As the eye is an ideal site for gene therapy, considerable advancement has been made in the treatment a variety of retinal diseases with a single administration of a gene therapy vector. In retina practices, the burden of intravitreal injections is significant. Studies suggest that, compared with clinical trials, real-world patients are monitored less frequently, receive fewer injections, and may have inferior vision results. Moreover, most inherited dystrophies do not currently have any therapy. Our purpose is to assess ocular gene therapy as an approach to a variety of inherited and acquired retinal disorders.

Methods: For nAMD there are several anti-VEGF gene therapy approaches. Our group constructed an AAV rhesus serotype rh.10 vector to deliver bevacizumab (AAVrh.10BevMab). Genzyme evaluated a novel chimeric anti-VEGF molecule, sFLT01, in an AAV2 vector (AAV2-sFLT01). Avalanche Biotechnologies developed AVA-101, an AAV2 vector expressing sFLT-1, a naturally occurring anti-VEGF protein with high affinity for VEGF. Target for retinal dystrophies include Leber's congenital amourosis (LCA, SPK-RPE65) and choroideremia (AAV.REP1), among others.

Results: Preclinical evaluation, by our group, of an injection of AAVrh.10BevMab shows long-term efficacy in a mouse and primate AMD models. In Genzyme's phase 1 study, intravitreally injected AAV2-sFLT01 was safe and well tolerated. Biological activity was noted in 4 of 19 subjects, 11 of whom were deemed expected responders. In phase 1 study, AVA-101 (Avalanche) was well-tolerated with no significant vector- or procedure-associated safety concerns. All 6 subjects required numerous anti-VEGF injections prior to enrollment; during 12-month study period, 4 of 6 AVA-101 treated subjects required no injections, whereas 2 of 6 required only a single rescue injection. In completed clinical trials for LCA, SPK-RPE65 (Spark), was well-tolerated and improved vision and patient quality of life following sub-retinal administration, leading to FDA approval earlier this year. Similarly, AAV.REP1 (NightstaRx), was well-tolerated, increased retinal sensitivity in the treated eyes of choroideremia patients in phase 1 testing.

Conclusions: Preclinical and clinical data suggest that gene therapy for the long-term treatment of a variety of retinal disorders is practical and well-tolerated. With the initial successes in nAMD and LCA, the spectrum of retinal disorders amiable to gene therapy will undoubtedly continue to expand. The encouraging early results need to be followed up with long-term safety, tolerability and efficacy studies.

HEMODYNAMIC VASOMOTOR MECHANISMS ELICIT ADAPTATIONS OF CORONARY CIRCULATION TO SPORT

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Dr. Koller investigates the role of microvessels, (endothelium and smooth muscle) in the regulation of blood flow, in healthy and diseased conditions. He conducts his research at several Universities in Hungary and the USA. Dr. Koller had participated and organized symposia at the HMAA Conferences in Balatonfüred and Sarasota several times.

Aim: Exercise training elicits time-dependent adaptations of coronary vessels enabling the coronary circulation to provide greater blood flow during sports activities. Systolic and diastolic blood pressure and flow greatly increase during exercise. Thus, we hypothesized that short-term daily exercise induces biomechanical and functional remodeling of the coronary resistance arteries related to blood pressure and flow/shear stress.

Methods: Male rats were subjected to progressively increasing four-week treadmill exercise program (over 60min/day, one mph in the final step EX) whereas the other group remained sedentary (SED). Coronary arterioles were isolated and their diameters were measured by television-microscopy (~120 μm in diameter at 50 mmHg intraluminal pressure). The biomechanical characteristics, the magnitude of myogenic and flow/shear stress responses and the contribution of endogenous nitric oxide and prostanoid production to diameter were assessed.

Results: Arterioles isolated from exercised animals - compared to their sedentary mates - had thicker walls (~10 μm), increased distensibility (0.5 vs. 0.8 kPa⁻¹), and decreased elastic modulus (at lower pressure range) as a result of reduced wall stress (by ~ 15%). Arterioles of exercised rats exhibited a significantly greater myogenic constriction (SED: 102.1 vs. EX 80.1 μm) and flow/shear stress-induced dilation (diameter increase: 52.4 $\pm$ 7.8 vs. 30.3 $\pm$ 3.9 μm). Inhibition of nitric oxide synthase and cyclooxygenases reduced the diameter at the lower pressure range and eliminated flow/shear stress-induced dilation. Indomethacin (a COX1/2 inhibitor) increased the diameter of arterioles at higher pressure range.

Conclusions: Short-term daily exercise induces morphological and functional remodeling of rat intramural coronary arterioles resulting in a greater constrictor and dilator reserves, which extend the range of coronary autoregulation contributing thereby to the optimization of coronary blood flow during exercise and sports activities.

Acknowledgments: This work has been supported by the Hungarian Scientific Research Funds (OTKA- K108444) and National Institutes of Health (HL-46813).

CAUSES BEHIND THE INEFFICIENT HYPERTENSION TREATMENT IN RURAL TRANSYLVANIA

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Zoltan Kollo is a Hungarian student undertaking General Medicine Degree at the University of Targu Mures (UMF), starting year five in September 2018. Recently he has been undertaking his next study about hypertension in rural Transylvania and feels that the results would provide some great insights that he could share at your conference. He hopes the experiences of the Annual Scientific Meeting of HMAA will greatly benefit his professional development.

Aim: We commissioned a survey about hypertension in an isolated Transylvanian settlement called Varmezo, with the aim of undertaking a comparative retrospective study, and finding out how the status of hypertension (including epidemiology, diagnosis, severity, treatment, and outcomes) has changed in the past 15 years in rural Transylvania. We observed and evaluated the pharmacological treatment of hypertension and used our results to make conclusions.

Methods: Our survey is an observational, epidemiological questionnaire and physical examination based study. We gathered information regarding the hypertensive people, to compare with our previous study. Besides the basic information, we also asked about their health, symptoms, medication, education, habits, and social background. The statistical analysis was performed using Excel and GraphPad Prism softwares.

Results: In the past 15 years, the percentage of hypertensive patients decreased with only 10%, and more than 50% had high blood pressure at random measure. In less than 10% of the hypertensive patients can the prescribed medicine keep the blood pressure within the normal range. The most commonly used antihypertensive drug is Enalapril. 80% of the inhabitants must leave the neighborhood to acquire their medication. Long-term medical supports are needed.

Conclusions: Doesn't matter how huge steps are made in advancing medicine, many people cannot reach these beneficial improvements. And despite the globally emerging medical technologies, education, and easily accessible information, hypertension still remains a significant problem in these isolated small rural communities, due to lack of sufficient medical help.

MOLECULAR AND FUNCTIONAL ANALYSIS OF ALL-TRANS RETINOIC ACID-INDUCED CHANGES IN HUMAN GLIOBLASTOMA

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Winner of the 2018 HMAA Student Scientific Travel Award

Zsuzsanna Kolostyak is a 6th-year medical student from the University of Debrecen. Her affinity for natural sciences appeared during her elementary school years. In high school, she was a participant of numerous scientific competitions and she joined Prof. László Nagy's Laboratory during the preparation period of the European Union Science Olympiad and International Biology Olympiad. She became familiar with molecular biological techniques and took an active part in a research project about the effect of ascorbic acid in adipocyte differentiation. As a result of this work she is a co-author of an article published in the journal Stem Cell Research. At the beginning of her medical studies she

started to examine the potential therapeutic role of nuclear hormone receptors, especially the retinoic acid receptor in glioblastoma. She presented her work in national and international conferences. Among these events she earned many awards such as 2nd prize in the National Conference of Students' Research Societies.

Aim: Glioblastoma (GBM) is a malignant tumor of CNS. The clinical therapy of this cancer creates challenge, the identification of novel drugs is essential to increase therapeutic efficiency. All-trans retinoic acid (ATRA) is an active form of vitamin A which activates retinoic acid receptor (RAR) and retinoid x receptor (RXR). The activated nuclear receptors induce the transcription of their targets which influence different cellular functions and show cell type specificity. In our study, we aimed to investigate the molecular background of ATRA-dependent regulation of cell proliferation and differentiation in GBM.

Methods: As model systems, we applied U251 human GBM cell line and human primary astrocytoma samples. To analyze the cell proliferation we combined MTT assay and trypan blue staining. The GBM stem cell formation was followed in cell culture. We performed mRNA-sequencing to describe the transcriptomic changes and we used RT-qPCR to measure the mRNA and eRNA levels. Protein expression changes were identified by Western Blot. We mapped RXR cistrome applying ChIP-sequencing.

Results: Our studies proved the action of ATRA in regulation of cell proliferation and differentiation. We found significant alteration in more than 900 genes mRNA expression. The pathway analysis of involved genes revealed that TGF β signaling pathway is significantly affected. We described the activated RAR:RXR-mediated regulation of SMAD3 transcription factor. Finally, both Smad3 mRNA and eRNA of Smad3-linked enhancer showed grade dependency in primary samples.

Conclusions: These findings indicate an alternative pathological effect of aberrant RAR:RXR activity in GBM and support our hypothesis about the potential benefits of ATRA in this malignancy.

CEREBRAL MICROBLEEDS MAY TEMPORARILY DISAPPEAR IN SUBACUTE SUSCEPTIBILITY WEIGHTED IMAGING IN RATS

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Aim: Our study aims to reveal subacute temporal microbleed appearance alterations in susceptibility weighted imaging (SWI) in an experimental model.

Methods: To elicit microbleed formation brains of 19 male Sprague Dawley rats were pierced in a depth of 4 mm, in a parasagittal position bilaterally using 34 G and 26s G needles. Rats underwent 4.7 T MRI acutely, then at 12 h, 24 h, 48 h, 96 h, and 125 h. Volumes of hypointensities consistent with microbleeds in SWI were measured using intensity threshold-based approach. Microbleed volumes across time points were compared using repeated measures ANOVA. Microbleeds were assessed by Prussian blue histology at different time points. In vitro MRI examinations of blood samples of different oxygenation and hematocrit were performed.

Results: Microbleed volumes were significantly decreased (corrected $p < 0.05$) at 24 h compared to the acute, 96 h or 125 h time points. By visual inspection, microbleeds were similarly detectable at the acute, 96 h and 125 h imaging, but were decreased in extent or completely invisible at 24 h or 48 h. Histology confirmed the presence of microbleeds in all animals.

Conclusions: Our study presents evidence of subacute temporary decrease or disappearance of microbleeds in SWI in rats. Clot retraction related biophysical features are suggested as the primary cause of this phenomenon. Such temporal dynamics of microbleeds should be considered when using SWI as a diagnostic tool for microbleeds in various diseases.

THE IMPACT OF LEFT VENTRICULAR LEAD POSITION ON LONG-TERM CLINICAL OUTCOME: A HIGH VOLUME, SINGLE CENTER EXPERIENCE

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Dr. Kosztin has been working in the Semmelweis University, Heart and Vascular Center for 7 years. First as a PhD student, then after completing the clinical education, as an assistant professor. Her field of interest is chronic heart failure and cardiac resynchronization therapy.

Aim: We evaluated the mid-term echocardiographic response and long-term survival of patients who underwent CRT implantation by LV lead non-apical positions and further characterized them by right to left ventricular activation delay (RV-LV AD).

Methods: In our retrospective registry patients who underwent CRT implantation from 2004 to 2017 were registered. Those with non-apical LV lead location was classified into anterior (n=30), posterior (n=154), and lateral (n=370) positions. Primary endpoint was all-cause mortality assessed by Cox regression analyses. Secondary endpoint was echocardiographic response within 12 months.

Results: From 554 patients 291 (53%) reached the primary endpoint during the mean follow up time of 4.3 years. Univariate analysis showed patients with lateral position had significantly better outcome compared to others (HR 0.78; 95% CI: 0.61–0.98; p=0.04), which was also confirmed by Cox regression analysis (HR 0.79; 95% CI: 0.62–1.01; p=0.05) after adjusting for RV-LV AD. The mean value of RV-LV AD was significantly longer in the lateral group and showed a U-shaped curve by LV lead location. When echocardiographic response was evaluated in the lateral group, 100 ms as the optimal cutoff value (AUC 0.60, 95% CI: 0.51–0.69; p=0.03) was found by ROC analysis.

Conclusions: Mortality benefit derived from CRT is associated only patients with lateral LV lead location, moreover the most beneficial echocardiographic response could be expected when RV-LV AD is longer than 100ms in this group.

PAINFUL SHOULDER IN THE COMPETITIVE SWIMMER

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Aim: "Swimmer's shoulder" has been used as a general phrase to describe and diagnose shoulder injury in swimmers. In this presentation we will discuss the complexities of the diagnosis and ideal treatment procedures.

Methods: Though swimming is often considered to be easy on the joints, research has found specific shoulder injuries often sustained by professional swimmers. Included in the differential diagnosis for shoulder pain suffered by swimmers are labral damage, suprascapular nerve entrapment, hyperlaxity, glenohumeral rotational imbalances, os acromiale, subacromial impingement, and scapular dyskinesis. To appreciate, diagnose, and successfully treat "swimmer's shoulder" one must take into account the complex anatomy of the shoulder as well as the mechanics of the swim stroke.

Results: It is essential to understand the nuances of the potential injuries encompassed in swimmer's shoulder.

Conclusions: Moreover, cooperation between the athlete, coaching staff, and physician can enhance speed of recovery. In this presentation we will discuss the complexities of the diagnosis and ideal treatment procedures.

DETECTION OF PRECLINICAL DIABETIC RETINOPATHY BY USING OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY

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Dr. Illes Kovacs is Associate Professor of Ophthalmology at Semmelweis University. He served as a Fulbright Scholar at the Weill Cornell Medical College in New York, NY.

Aim: Diabetic retinopathy is a common microvascular complication of diabetes that develops in almost 80% of diabetic patients after 15 years. DR can significantly affect quality of life, particularly at the vision-threatening stages, with substantial public health implications in terms of resources allocated to screening and management. Better identification of diabetic patients at high risk of vision-threatening complications is crucial for the prevention of vision loss. Ocular imaging by fluorescein angiography and optical coherence tomography has been playing a significant role in the visualization of retinal vascular perfusion and macular edema, respectively. Optical coherence tomography angiography (OCTA) is a new, non-invasive imaging technique that is able to visualize separately the different retinal and choroidal vascular layers using motion contrast technology to detect blood flow without intravenous dye injection. In this presentation, we summarize our results on the reproducibility and the predictive accuracy of quantitative retinal microvascular parameters using OCTA in patients with non-proliferative diabetic retinopathy.

Methods: The reproducibility of OCTA imaging was evaluated by calculating measurement error for different OCTA parameters. The effect of risk factors on retinal microvascular alterations and the accuracy of these parameters in the prediction of clinically detectable diabetic retinopathy were assessed in multivariable regression models.

Results: We found that measurement error is substantially larger in scans with lower image quality compared to those with better quality. We determined the optimal image quality cutoff values for different OCTA parameters to provide reliable measurements. We found, that macular vessel density was significantly decreased in diabetic patients without clinically detectable diabetic retinopathy compared to healthy controls ($p < 0.001$). Decreased retinal vessel density in these eyes was an independent predictor of later development of diabetic retinopathy (OR: 1.24) and vision loss (OR: 1.15).

Conclusions: Retinal vessel density is decreased in patients with diabetes in comparison to healthy subjects. Microvascular changes are related to the duration of diabetes and can be detected even before the presence of clinically detectable diabetic retinopathy. These data suggest that OCT angiography shows excellent repeatability in diabetic patients, indicating that this non-invasive technology might be suitable for longitudinal assessment of microvascular complications. The quantification of retinal microvascular changes using optical coherence tomography angiography might help clinicians to avoid the development of clinically significant diabetic retinopathy and vision loss.

PAST, PRESENT AND FUTURE OF COMENIUS UNIVERSITY BRATISLAVA

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Doc. MUDr. Eliska Kubíková, PhD is the Head of Anatomical Department LF UK and Study Vice Dean for 1st-3rd year for General Medicine in the Slovak language program, quality and innovation in education. Her expertise and awards include: Attestation in surgery and clinical oncological department; Management in financing and healthcare; Assistant Professor at Trnava University; Assistant Professor in surgical discipline and Doctor of philosophy LF UK. She received the Slovenka roka (Slovak Woman of the Year) and Absolutna Slovenka rola (Absolute Winner) 2013 in healthcare category, Metropolitan Figure of Year 2016 - healthcare category. Since 2010, she has been included in the WHO is WHO encyclopedia (Slovak edition) and in 2013 she was cited in Oxford encyclopedia. She is the author of 5 monographies and over 300 scientific publications; she has been cited over 200 times. She had participated in research fellowships at the Mayo Clinic, USA, in Zagreb, Croatia, in Belgium, as well as in Hungary at Semmelweis University.

Aim: The aim of the presentation is to show the past, present and future of Comenius University's Faculty of Medicine in Bratislava.

Methods: Overview study describing the history of Comenius University which was established based on more than 600 years old tradition of Charles University in Prague. The Medical faculty is the eldest out of 13 faculties of the Comenius University. The upcoming September of 2019 signifies its 100th anniversary.

Results: The result is to point out the achievements of the medical faculty from history to present and outline the vision for the future.

Conclusions: Ever since its establishment, the university has been considered to be a well known science-research institution that provides education, with stable bases for clinical practice. The numerous nationalities of students (United States, Serbia, Greece, Vietnam, Japan, Syria, Germany etc), undoubtedly contribute to the multinational spirit of the Comenius University.

BREAST CANCER SCREENING WITH MR-MAMMOGRAPHY – SCRIMS PROJECT: PRELIMINARY OUTCOMES OF PILOT STUDY IN WOMEN WITH GENETIC MUTATIONS

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Aim: In Slovakia Project SCRIMS was introduced in October 2015 and it focuses to the role of MR-mammography in breast cancer detection rate in gene mutation carriers according to their age, type of mutation and breast density. The aim of study is to analyze preliminary outcomes of project SCRIMS.

Methods: Between 10/2015 and 10/2017 103 women (median 41.76 years) with mutations (BRCA1, BRCA2, BRCA1+2, CHEK2, BLM) underwent MR-mammography. Suspicious lesions were analyzed by core cut or vacuum assisted biopsy. 42 carcinomas were diagnosed. Comparative analysis of patients divided into two groups according their age at the time of diagnosis was performed.

Results: In group 1 - 16 out of 41 patients under 40 and in group 2 - 26 out of 62 of the age 40 and older were diagnosed with breast carcinoma ($p=0.78$). Invasive ductal carcinoma (IDC) appeared in 14 patients in group 1, in 20 in group 2 ($p=0.39$). Triple negative (TN) IDC was presented in 7 from group1, in group2 in 2 patients ($p=0.005$). Breast carcinoma was associated with BRCA1 mutation in group 1 in 12 out of 16, in group 2 in 11 out of 26 ($p=0.038$), BRCA2 in group 1 in one case, in group2 in 12 cases ($p=0.006$). Dense breast was typical for group 1 (13/16; 81.25%), in group 2 scattered fibroglandular tissue (10/ 26; 38.46 %).

Conclusions: MR-Mammography could be considered as important part of high-risk women management, especially in patients under 40 with dense breast. Since aggressive TN carcinoma is typical for these women, the potential of MR to depict carcinomas in dense breast makes this method crucial for prognosis improvement.

VASER HI DEF LIPO, THE ART OF BODY SCULPTING

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Dr. Marosan was born in Nagyvarad, Romania and emigrated to the US at the age of 15 with his family. His undergraduate education was at SUNY at Buffalo with a BA in microbiology. He received his MA degree from Roswell Park Cancer Institute in experimental pathology and completed medical school at Rush Medical College of Rush University in Chicago. He went on into a general surgery residency for 5 years and a plastic surgery fellowship for two years and became board certified in both. He served in the USAF for ten years and resigned his commission at the rank of Lieutenant Colonel. He has been in solo private practice for the past 22 years. For the last 14 years, he specialized in breast and body cosmetic surgery.

Aim: Familiarize the other medical specialties about the latest advances in the field of cosmetic plastic surgery of the body.

Methods: Present the author's personal experience in the art of body sculpting. Will discuss technical and surgical nuances to achieve the best outcomes based on the muscle and bony anatomy.

Results: Presentation of cases of varying degrees of difficulty and complexity.

Conclusions: The author's vast experience in body sculpting will give an insight into this rapidly expanding field of plastic surgery.

MOLECULAR MECHANISMS OF LYMPHOMA TRANSFORMATION AND PROGRESSION

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Dr Matolcsy is a pathologist, hematopathologist and Head of the 1st. Department of Pathology and Experimental Cancer Research at Semmelweis University.

Aim: In the natural history of low-grade non-Hodgkin's lymphomas (NHL) a prolonged indolent phase of the disease may be followed by clinical progression toward intermediate and high-grade disease. The most interesting and highly debated question of lymphoma transformation is the molecular mechanisms associated with the lymphoma transformation.

Methods: Sequential cytogenetic, molecular and mutation analyses were done to demonstrate the molecular alteration associated with lymphoma transformation and progression.

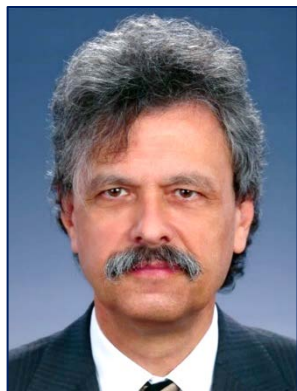
Results: It has been demonstrated that the transformation of the neoplastic cells frequently acquires additional genetic abnormalities at cytogenetic and molecular levels. Molecular lesions of regulators of tumor suppression (p53, Rb), cell proliferation (RAS, MYC, BCL2, BCL6) and cell cycle (p16INK4A) have been detected.

Conclusions: The heterogeneous cytogenetic and molecular aberration suggests that genetic instability can be a pathogenic factor in histologic transformation, which was also supported by the results of next-generation sequencing.

CELL SURFACE ORGANIZATION OF IL-9 AND IL-2 RECEPTORS ON HUMAN T LYMPHOMA CELLS

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Dr. Matyus graduated as a medical doctor at the University Medical School of Debrecen in 1980. Since then he has been working in the Department of Biophysics and Cell Biology of the University of Debrecen, currently as Full Professor (since 2007) chairman of Biomathematics Division (since 2009). His research interest is the cell surface organization and dynamics of cell-surface receptors. After having received a habilitation degree in 1998, he became the Doctor of the Hungarian Academy of Sciences in 2005. He is the President of the Hungarian Biophysical Society and serves as the Dean of the Medical Faculty since 2013.

Aim: IL-9 is a multifunctional cytokine with diverse cellular targets including immune and non-immune cells as well, thereby regulating a variety of cellular processes. The heterodimeric IL-9R consists of the cytokine-specific α subunit and the common γ_c chain. Expression of IL-9R α is mainly restricted to T cell subsets expressing the heterotrimeric IL-2R as well, where IL-2 has a crucial regulatory role. The two receptor kinds share the signaling γ_c chain, therefore the question arises what their spatial relationship is and how it is affected by the cytokine milieu.

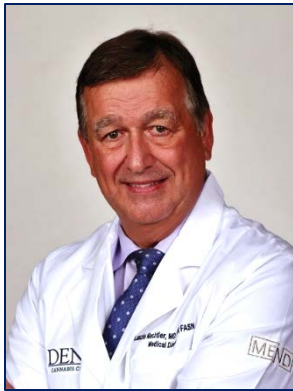
Methods: Confocal microscopy and FRET experiments.

Results: We demonstrated the bipartite spatial relationship of IL-9R with IL-2R in human T lymphoma cells: a considerable fraction of IL-9R and IL-2R was in spatially segregated membrane areas. The presence of distinct IL-9R domains is not mutually exclusive; they may co-exist on the same cell. IL-2 deprivation reduced slightly the overlapping fraction of the receptors, implying that IL-2 may have a regulatory role in the cell surface organization of IL-9R. Short-term exposure to IL-9 did not cause significant rearrangement of the receptors at the few-hundred-nanometer scale, but changed FRET efficiencies between the subunits of the IL-9/2R system, i.e. IL-9 binding either alters the conformation of the IL-9/2R complex or causes lateral redistribution of the receptor chains on the nanometer scale.

Conclusions: It is hypothesized, that by sequestering receptor subunits in common membrane areas, the overlapping domains of IL-9R and IL-2R provide a platform enabling both the formation of the appropriate receptor complex and subunit sharing between related cytokines.

MEDICAL CANNABIS TREATMENT IN A COHORT OF CHRONIC MIGRAINE PATIENTS

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Dr. Mechtler is the Medical Director of the Dent Neurologic Institute. He is a past president and past secretary of the Hungarian Medical Association of America (HMAA). He dedicates a great deal of his time being the Chair of the HMAA Student Exchange Program.

Dr. Mechtler is publishing some of the first major retrospective research trials on Medical Marijuana in Headaches and other neurologic disorders. Dr. Mechtler lectures both nationally and internationally and is recognized as a leader in the fields of Neuroimaging, Headache Medicine, Medical Cannabis and Neuro-Oncology. He is the Director of the DENT Cannabis Clinic, which has over 5,000 patients certified through the NYS MMJ program. His recent awards include 2016 Medical Leader of the Year Award from the MDA Association, 2016 Business First's Lifetime Achievement Award, 2017 Business First's Power 250 WNY's Most Influential People; Rank 155, and 2018 Business First's Power 250 WNY's Most Influential People; Rank 156.

Aim: To examine the efficacy of medical cannabis in a cohort of chronic migraine patients in reducing migraine frequency and severity and correlating those improvements with specific dosages.

Methods: This study uses a retrospective chart review of chronic migraine patients, as defined by the International Headache Society. Three hundred and sixteen patients seen at Dent Neurologic institute over the age of 21 with the diagnosis of chronic migraine were included in the study. Chronic migraine was defined as having over 15 headache days a month, of which 8 or more were migraineous, for a period of at least three months.

Results:

1. 83.2% (263 patients) of patients reported subjective improvement in their headache profile.
2. 54.1% (171 patients) of patients reported improvement in the overall frequency of their headaches. Of those 171 patients:
 - a. 80.1% (137 patients) reported $\geq 30\%$ improvement in average monthly headache day frequency.
 - b. 63.2% (108 patients) reported $\geq 50\%$ improvement in average monthly headache day frequency.
 - c. 25.7% (44 patients) reported $\geq 75\%$ improvement in average monthly headache day frequency.
3. 41.4% (131 patients) of patients reported improvement in severity of their headaches.
4. Average initial headache frequency reported was 25 per month, and the average post medical cannabis treatment headache frequency was 16.3 per month which amounts to a 34.8% overall decrease in headache frequency per month.
5. Average initial migraine frequency reported was 12.7 migraines per month, and the post medical cannabis treatment frequency was 7.4 migraines per month which represents a 42.1% average decrease in migraine frequency.
6. Seventy-three patients used opioid pain medications at the start of MC treatment, of those 51% (37 patients) reduced their opioid consumption. 42 charts contained evidence comparing the effects of MC to the effects they experienced on opioids. 81% (34 patients) reported that MC was the same or better than opioid pain management effectiveness and 80% (33 patients) reported that the side effects of MC were more tolerable than that of opioids.
7. 38.3% (121 patients) reported improvement in sleep, 30.7% (97 patients) reported improvement in anxiety, and 24.7% (78 patients) reported improvement in mood.
8. 23.1% (73 patients) reported side effects, while 76.8% (243 patients) denied having any adverse side effects. The most common side effects reported were fatigue (12 patients), poor taste (9 patients), and increased appetite (8 patients). Only four patients (1.4%) discontinued due to side effects.

Conclusions: These results suggest that when used in conjunction with other migraine regimens medical cannabis may prove a useful treatment for those suffering from chronic migraines. The frequency of headaches and migraines per month was decreased through the use of medical cannabis, and almost half of all patients reported a decrease in

the severity of their headaches. In addition, a significant portion of patients were able to reduce or completely eliminate their consumption of prescription opioids. These results support the analgesic and anti-inflammatory properties of medical cannabis and make it a remarkable candidate for treatment of chronic migraine.

FORCEPS ASSISTED VAGINAL DELIVERY: A DYING ART

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Dr. Mechtler was born in Sydney, Australia and moved to Buffalo, New York in 1969. He attended Canisius College premed and graduated from Semmelweis University in 1984. He completed his OB/GYN residency at SUNY Buffalo in 1991. Currently Dr. Mechtler is Associate Professor in the Department of Obstetrics and Gynecology at SUNY Buffalo, NY and President of Snyder OBGYN, PC. His professional interests are high risk obstetrics as well as daVinci Gynecologic surgeries. Dr. Mechtler is Member of the Board of Directors and Chair of the Membership Committee of the HMAA.

Aim: The aim of this presentation is to explain what forceps assisted vaginal delivery is, to show the different kinds of forceps, and when were forceps used first. Differentiate between high, mid, and low forceps.

Methods: The author will go over the history of forceps, review the different papers on forceps and show examples of when to use it, and when not to. The advantages and disadvantages of forceps use will be discussed, as well as the possible complications that may arise.

Results: Explain the reasons why forceps usage has declined over the years not only here in the US but other parts of the world. Also, able to show the Cesarean section rate has risen at the same time forceps have decreased.

Conclusions: Forceps assisted vaginal delivery may be a safe alternative to Cesarean section in experienced hands.

HOW ADAPTATION TO HYPOXIA INFLUENCES TREATMENT RESPONSE IN CANCER: LESSONS LEARNED FROM AGGRESSIVE LYMPHOMAS

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Professor Mehes is the Head of the Department of Pathology at the Faculty of Medicine, University of Debrecen, Hungary for more than 11 years now. He graduated and obtained his PhD at the University of Pecs, Hungary. Between 1997 and 2007 he worked as a consulting pathologist and research fellow in Vienna, Graz (Austria) and Bonn (Germany). From 2016 he is Doctor of the Hungarian Academy of Sciences. He is specialized in hematopathology and molecular pathology, runs several resident and PhD programs.

Aim: Intensive tumor growth requires increasing oxygen supply that is supported by the continuously expanding capillary perfusion system. In spite of this, a significant part of the cancer tissue is exposed to hypoxia resulting in cell death or in metabolic reprogramming and functional diversity. As a major effect, hypoxia induces intracellular lactate acidosis through increased glucose utilization. Neutralization is enabled by parallel adaptive mechanisms, one of which is the upregulation of membrane carbonic anhydrases IX and XII (CAIX, CAXII). The restoration of the intracellular pH and consequential extracellular acidosis favors cancer cell survival and supports migration/invasion of the cells but has direct adverse effects on the treatment response as well. The acidic microenvironment inhibits the access of drug molecules and therapeutic antibodies and further, influences local immune cell interactions. Information regarding these aspects of cancer phenotype are limited.

Methods: According to earlier observations, hypoxia related features can be studied both by histological and molecular biological methods. Immunohistochemistry using antibodies specific for individual pH regulators present prominent changes in aggressive forms of lymphoma (e.g. diffuse large B-cell lymphoma, anaplastic lymphoma, lymphocyte depleted Hodgkin's lymphoma).

Results: Our recent studies showed that hypoxia related CAIX and CAXII may be highly expressed in a subgroup of aggressive lymphomas. CAIX was particularly associated with tissue necrosis and hypoperfusion and presented with a characteristic tissue distribution. While CAXII was expressed by both lymphoma and stromal cells, CAIX was found exclusively in the neoplastic cell compartment in a larger series of cases. Especially CAIX cancer cell expression could be associated with a statistically significant unfavorable response to the standard therapy applied.

Conclusions: Hypoxia related cancer phenotype - including CAIX upregulation - is proposed as a conceptual marker for therapy resistance and as an indicator for frontline therapy intensification.

CAROTID STENOSIS TREATMENT: INTERNATIONAL VARIATIONS

Menyhei, G. on behalf of the ICVR Collaboration

Department of Vascular Surgery, University of Pecs, Pecs, Hungary



Gabor Menyhei, MD, PhD

Professor and Head, Department of Vascular Surgery, University of Pecs, Pecs, Hungary

Scientific Advisor, HMAA Hungary Chapter

Dr. Gabor Menyhei is Head and Professor of Vascular Surgery at the University of Pecs Medical School. He also serves as Scientific Advisor to the Hungary Chapter of the HMAA.

Aim: To analyze current praxis and international variations in treating patients for carotid disease in countries of the International Consortium of Vascular Registries.

Methods: Collected data from the national vascular registries of Vascunet collaboration and from the VQI of Society of Vascular Surgery from the United States were analyzed to draw conclusions with regard to international variations in the treatment of symptomatic and asymptomatic carotid disease among countries and centers.

Results: Among 58,607 procedures, octogenarians represented 18% of all patients, ranging from 8% (Hungary) to 22% (New Zealand and Australia). The proportion of carotid artery stenting among asymptomatic patients ranged from 0% (Finland) to 26% (Sweden) and among symptomatic patients from 0% (Denmark) to 19% (USA). The overall proportion of asymptomatic patients was 48%, but varied from 0% (Denmark) to 73% (Italy). There was also substantial center level variation within each country in the proportion of asymptomatic patients, most pronounced in Australia (0-72%), Hungary (5-55%), and the United States (0-100%). Countries with fee for service reimbursement had higher rates of treatment in asymptomatic patients than countries with population based reimbursement.

Conclusions: The proportion of asymptomatic patients, treatment modality, and the proportion of octogenarians vary considerably among and within countries. There was a significant association of treating more asymptomatic patients in countries with fee for service reimbursement. The findings reflect the inconsistency of the existing guidelines and a need for cooperation among guideline committees all over the world.

SPORTS CARDIOLOGY SCREENING IN ELITE ATHLETES

Merkely, B., Sydo, N., Csecs, I., Erdi, J., Major, D., Csulak, E., Czimbalmos, C., Lakatos, B., Kovacs, A., Kiss, O., Kovacs, T. and Vago, H.

The Heart and Vascular Center, Semmelweis University, Budapest, Hungary



Bela Merkely, MD, PhD

Rector, Semmelweis University, Budapest, Hungary

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Dr. Bela Merkely is Rector of Semmelweis University. He is Professor and Director of the Heart and Vascular Center of Semmelweis University.

Aim: Due to the potential risk of acute cardiovascular events during extreme physical exertion, comprehensive sports cardiology screening of elite athletes is mandatory. Our main goal was to perform detailed sports cardiology screening of Hungarian athletes and to minimize the risk of unexpected life threatening cardiovascular events.

Methods: Since 2010, at the Semmelweis University Heart and Vascular Center, besides the basic cardiovascular exams (questionnaire, physical examination, laboratory tests, resting 12-lead ECG) most asymptomatic athletes also underwent 24-hour Holter monitoring, echocardiography, cardiac magnetic resonance (CMR) examination and cardiopulmonary exercise testing. Athletes with symptoms or pathology, moreover athletes after aborted sudden cardiac death were also investigated.

Results: We examined more than 500 athletes (male and female elite, young and masters athletes; mainly water polo players, soccer players, swimmers, kayak-canoers and rowers). Some athletes were diagnosed with hypertension (n=15) and antihypertensive therapy was initiated. In the lab results - mainly in women athletes - iron deficiency was the most common finding, which was corrected with oral iron supplementation. In our ECG study, physiological signs of athletic adaptation were more common in athletes but some potentially pathological ECG signs also occurred more frequently compared to controls: ST- (6.6% vs. 1.1%, $p<0.05$) and T-wave (15.0% vs 5.6%, $p<0.05$) alterations, signs of pathological left ventricular hypertrophy (5.3% vs 0%, $p<0.05$). In our Holter ECG project all studied heart rate variability parameters were higher in elite athletes compared to controls [SDNN 225.3 vs 158.6 ms; SDNN Index 99.6 vs 72.4 ms; pNN50 24.2 vs 14.4%; RMSSD 71.8 vs 50.8 ms; $p<0.001$]. We determined athletic normal HRV values. Comparing healthy athletes and sedentary controls left and right ventricular volume indexes by CMR, athletes had higher values in both gender ($p<0.001$). Left (111.8 ± 18 vs 87.6 ± 11 g/m² $p<0.001$) and right ventricular mass index (male athletes vs 33.6 ± 7 vs 22.5 ± 15 g/m² $p<0.01$) were also higher in male athletes as part of the athletic adaptation. Based on the ECG abnormalities and echocardiography results, 153 athletes were referred for CMR examination with suspected structural myocardial disease. CMR findings confirmed structural myocardial disease in 39 athletes, the most common cardiomyopathy (CMP) was HCM (23%, n=9). Among the aborted SCD cases (n=10) arrhythmogenic right ventricular CMP was the leading pathology (n=3).

Conclusions: Using conventional and advanced cardiac examination techniques, our study provides information of a unique and comprehensive cardiovascular screening program of the Hungarian athletic population. Exact definition and widespread knowledge of normal athletic parameters is vital and differentiating physiological athlete's heart from pathological alterations is essential in early recognition of high risk athletes and prevent acute cardiac event.

APPROACH TO CARTILAGE DEFECT: DIAGNOSTIC ALGORITHM AND TREATMENT OPTIONS

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Gergo Merkely, MD

Research Fellow, Center for Cartilage Repair, Brigham and Women's Hospital Harvard Medical School, Boston, MA

Dr. Gergo Merkely is finishing his PhD at Semmelweis University in Cartilage repair. Currently, he has been working as a research fellow at the Cartilage Repair Center, Brigham and Women's Hospital, Harvard Medical School.

Aim: Articular cartilage injuries are common and have the potential to progress to osteoarthritis if left untreated. Once articular cartilage is damaged, full recovery of its structure, function and biomechanical properties is unlikely. The diagnosis and treatment of symptomatic cartilage defects is challenging and requires attention to detail as both patient specific and cartilage defect specific factors need to be appreciated in order to obtain an accurate evaluation of the patient. Given the variety of therapies for the treatment of symptomatic cartilage lesions, one must consider the big picture to provide a long-lasting solution. The purpose of this presentation is to discuss the incidence, natural history, diagnostic process and the various treatment options of a symptomatic cartilage defect.

Methods: Available literature review.

Results: Our search obtained a total of 288 articles and was included in the current study.

Conclusions: Although the natural history of cartilage defects is not completely understood, patient specific background factors (genetic predisposition, age, BMI, smoking, compliance, duration of symptoms, previous surgeries, joint laxity, malalignment with subsequent overload of the tibiofemoral or patellofemoral compartment, meniscal insufficiency) and cartilage defect specific factors (depth, size, location, chronicity, and associated bony abnormalities) must be evaluated collectively in order to perform a successful biological joint reconstruction.

SPORT AND WOMEN

Merkely, P.¹, Sydo, N.², Sobel, G.¹, Varbiro, S.¹ and Merkely, B.²

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Petra Nora Merkely, MD

Resident Physician, ²nd Department of Obstetrics and Gynecology, Semmelweis University, Budapest, Hungary

Dr. Merkely is a resident physician at the 2nd Department of Obstetrics and Gynecology, interested in the effects of sport on female cardiovascular and metabolic system and its benefit on pregnancy.

Aim: Current American College of Obstetrics and Gynecologists guidelines recommend 30 minutes of exercise per day throughout pregnancy. This level of exercise might increase cardiorespiratory fitness and improves musculoskeletal conditions such as low back pain, prevention of urinary stress incontinence, depression, gestational diabetes and decrease gestational weight gain. While regular exercise training during pregnancy might lead to physical and psychological benefits, the potential benefits of high endurance physical training have not been evaluated before. Furthermore, little is known about the short- and long-term benefits of preterm period mild-moderate and high level of exercising for the newborn. Therefore, our aim is to assess the effects of high endurance training on both mothers and newborns.

Methods: Pregnant women at 6-10th week of gestational age are recruited into our prospective single-center study. The included patients then are divided up into three groups: the first group involves mothers with prior history of regular exercising undergo standardized training three times a week that comprises endurance and strengthening training, the second group consists mothers without prior history of regular training who undergo the same training throughout their pregnancy as in the first group. The third group is the control group where patients are not undergoing any exercise. Preterm period complications, such as gestational hypertension, preeclampsia/eclampsia, gestational diabetes are recorded, as well as gestational weight changes. In order to monitor the fetal environment changes the uterine artery flow are measured after every training. Furthermore, the gestational age by the end of pregnancy, natural born versus C-section, abnormal CTG, the Apgar score and the delivery weight of the newborn is recorded to allow us to monitor the effect of exercise on the baby.

Results: As of now, the patient recruitment is at an early stage.

Conclusions: Prenatal team should be familiar with exercise recommendations, taking advantage of this time of gestation to encourage women to begin an active lifestyle that could impact on long-term health and quality-of-life improvements. This study might provide valuable results in order to emphasize the importance of exercise throughout pregnancy.

FULLBRIGHT AND CARRIER

Nagy, K.

Department of Oral Surgery, University of Szeged, Szeged, Hungary



Katalin Nagy, DDS, PhD

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At present, Dr. Katalin Nagy serves as the Head of the Department of Oral Surgery at the University of Szeged. Previously she was the Vice President for Foreign Affairs, and she has also finished two cycles of Deanship (2006-2015) of the Faculty that she helped of making the foundation of becoming independent from the Faculty of Medicine in Szeged. As a former Fulbrighter, she was elected as President of the Hungarian Fulbright Alumni Association. She received the "Bólyai Award", a "Fulbright Research Fellowship" in 2002, USA, New York, NY, Memorial Sloan Kettering Cancer Center, a UICC Grant 2004, USA, UCLA. She received the "Batthyány-Strattmann László" Award (by the Hungarian Ministry of Health) for lifetime achievement in public service and professional excellence in 2014, the "Pro Urbe" Award from her city, Szeged, for promoting international relations of the city in 2014, and the "For the Internationalization of Higher Education" Award given by Tempus Public Foundation 2014. During her above mentioned activities, she has still been working as a practicing dentist.

Aim: One of the fundamental aims of my academic carrier at the University of Szeged was to enhance the relationship between the University and other countries.

Methods: The main focus has always been the USA, based and relying on my Fulbright Scholarship in 2012. Luckily enough I had also received a UICC fellowship in 2004 at UCLA Los Angeles.

Results: Those two study trips determined my future carrier and allowed me to gradually develop myself from the University teacher position through the full professorship until my position as vice rector of the University of Szeged.

Conclusions: In my presentation I will emphasize the dominating role and importance of the US fellowships, and consequently the different ways to foster the Internationalization process of the University of Szeged, one of the most important higher education institutions of our country.

UNDERSTANDING AND HARNESSING THE HEALING POWER OF MACROPHAGES USING MULTI-OMICS APPROACHES

Nagy, L.

Johns Hopkins University/Johns Hopkins All Childrens' Hospital, St. Petersburg, FL



Laszlo Nagy, MD, PhD

Professor and Co-Director, Johns Hopkins University/Johns Hopkins All Childrens' Hospital, St. Petersburg, FL, Professor and Director, Sanford Burnham Prebys Medical Discovery Institute, Orlando, FL and Professor, University of Debrecen Faculty of Medicine, Debrecen, Hungary

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 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. Studying these questions while evaluating the entire genome makes it more likely to discover key changes related to a particular disease and to find reliable biomarkers to monitor that disease. Those answers may lead to better diagnoses and novel therapies.

Aim: The incredible plasticity of macrophages required for their diverse activities is provided by gene expression and epigenomic mechanisms. However, it is not known how macrophages change their phenotypes and turn off inflammatory and turn on repair-type gene expression.

Methods: In the past several years we have been studying these processes using unbiased, global transcriptomic, epigenomic and lipidomic approaches with the goal to identify regulatory and effector mechanisms, allowing the macrophage to support tissue growth and repair.

Results: Using a mouse model of acute sterile inflammation and skeletal muscle regeneration and by systematically mapping the gene expression changes, epigenomic alterations and lipid signaling, we were able to identify regulatory and effector mechanisms; including signaling and effector lipids and secreted proteins contributing to tissue repair. In the presentation we will show examples of macrophage-derived lipid and protein effector molecules and describe how these can be used to improve tissue regeneration.

Conclusions: The identified mechanisms will allow us to reprogram macrophages and to exploit them to promote anti-tumor activities and enhance tissue regeneration.

SPECIAL NEUROSURGICAL INDICATION OF LOW LEVEL LASER THERAPY

Olah, C.

Borsod County University Teaching Hospital, Miskolc, Hungary



Csaba Olah, MD

Consultant neurosurgeon, neuroradiologist and Scientific Director, Borsod County University Teaching Hospital, Miskolc, Hungary

Dr. Olah is a consultant neurosurgeon, neuroradiologist, clinical pharmacologist and scientific director of the largest hospital in Hungary.

Aim: In our presentation we would like to introduce the general neurosurgeon indications, effects and results of low level infrared laser treatment. Besides this we demonstrate a special laser treatment in a very serious neurosurgical situation.

Methods: Low level laser therapy is an important part of a physiotherapy treatment. For years, we have been using soft laser therapy on cervical, thoracic, and lumbar segments of the spine to relieve pain, to relax muscles and to control inflammation. A number of Hungarian academic researchers and rheumatologists have contributed to the development of soft laser treatments. The term 'biostimulation' was coined by Prof. Endre Mester 50 years ago to describe specific phenomena underlying the healing processes observed during soft laser therapy.

Results: Our team have finished a preclinical animal (beagle dogs) prospective, controlled pilot study. We have confirmed that ganglion pterygopalatine stimulation by low level infrared laser could cause brain arteries' effective dilatation. This effect can be very important after subarachnoid hemorrhage caused vasospasm.

Conclusions: We are developing a special laser optical unit that can be used to perform ganglion therapy easily and painlessly.

THE PREDICTABILITY OF INSULIN RESISTANCE AND FAT OXIDATION CHANGES FROM SERIAL MEASUREMENTS OF WEIGHT AND FAT MASS

Ori, Z.P.

Ori Diagnostic Instruments, LLC, Durham, NC



Zsolt Peter Ori, MD

Internist at Ori Diagnostic Instruments, LLC, Durham, NC

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.

Aim: The goal is to show the predictability of insulin resistance and fat oxidation changes from serial measurements of weight and fat mass by meta-analysis of clinical trial data aiming to gauge insulin resistance changes during any type of sustained dietary and exercise changes. We would like to demonstrate to the medical community how our Metabolic Health Monitor app could be used to track and predict changes of metabolic data such as insulin resistance, fat oxidation rates, body weight, lean mass, fat mass, utilized macronutrient energies and burning rates. Further we want to show how these metabolic data could be used to display metabolic trends for real time control for goal directed self-management and guided therapy and improvement of mortality indicators.

Methods: We calculated the dynamic changes of R-ratio (defined as the ratio of lean mass change to fat mass change) R%, in 40 studies from 11 clinical trials and correlated this with the percent change of the HOMA-IR, H% across these studies perturbing the energy balance with diet and exercise.

Results: We found excellent correlation between R% and H% -0.8510 , $P = 0.0036$. The correlation between weight change W% and H% was 0.8929 with $P = 0.0012$; fat mass change F% and H%: 0.7915 $P = 0.0011$.

Conclusions: Based on the excellent correlation between R% and H% and based on principles of indirect calorimetry we can confirm a very strong predictability of insulin resistance change, change of the carbohydrate to fat oxidation and a strong relationship between the R-ratio and respiratory quotient RQ and food quotient FQ.

NEW HOPES IN THE TREATMENT OF SMALL CELL LUNG CANCER

Ostoros, G.

National Koranyi Institute of Pulmonology, Budapest, Hungary



Gyula Ostoros, MD, PhD, Med. Habil.

National Koranyi Institute of Pulmonology, Budapest, Hungary

Dr. Gyula Ostoros is the Head of the 8. Department at the National Koranyi Institute of Pulmonology in Budapest, Hungary.

Aim: To review novel therapeutic approaches of immunotherapy and other targeted therapies in the treatment of SCLC.

Methods: In Hungary, each year, around 1,500 people are diagnosed with SCLC. This number represents 15% of all newly diagnosed lung cancer cases. My home institute, the National Korányi Institute of Pulmonology, admits 300 newly diagnosed SCLC patients on annual basis. This presentation reviews the results of recent clinical trials that have evaluated targeted and novel cytotoxic agents alone or in combination with standard chemotherapy in SCLC.

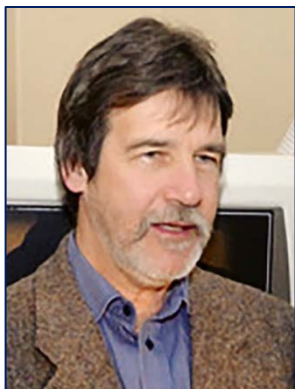
Results: SCLC usually has a very aggressive course and is characterized by early development of lymphatic and organ metastasis. Platinum compounds have been used in SCLC treatment and remain the backbone for current combination strategies. Modest advances in SCLC therapy in the past 3 decades involves the discoveries that prophylactic cranial irradiation (PCI) improves survival in patients responding to initial chemotherapy and, moreover, that second line therapy (e.g. topotecan) is superior to best supportive care. There is no standard third line regimen approved in SCLC. In the phase 3 single arm Trinity study, patients with DLL3-expressing SCLC who had undergone at least 2 previous treatment regimens were treated with rovalpituzumab tesirine (a DLL3-targeted antibody-drug conjugate). Although the first results were promising, the primary endpoint (response rate) was not reached. Somatostatin receptors are often expressed in SCLC. Accordingly, lanreotide (a somatostatin analog) maintenance treatment showed activity in SCLC patients with somatostatin receptor-positive limited stage tumors. A confirmatory phase 3 study is needed. Immunotherapy, especially immune checkpoint inhibition, has become a new hope for the future SCLC therapy. SCLC cells exhibit high numbers of acquired mutations that may generate several antigens, a condition thought to favor immunotherapy. The CheckMate 332 study - a phase 1/2 trial investigating the efficacy of Nivolumab with or without ipilimumab in advanced SCLC - demonstrated that patients with high tumor mutation burden had extreme long median overall survival (22 months) in the combination arm. Other SCLC trials are investigating immunotherapy in combination with platinum and etoposide in the first-line setting, after platinum and etoposide as maintenance therapy, and as a second-line option too. In our Institute, we investigate if and how antibiotic therapy influences the gut microbiome and the efficacy of immuncheckpoint inhibition.

Conclusions: Although several genetic and molecular alterations have been reported, our current knowledge on these molecular features of SCLC is, however, not yet sufficient to affect diagnosis and therapy. Nevertheless, the aforementioned approaches offer new treatment options for SCLC, indicating a new era in SCLC therapy.

MODES OF MEDICAL SUPPORT PROVIDED TO BELEAGUERED MEDICAL INSTITUTIONS AND TO DESPAIRING PATIENTS IN THE SUB-CARPATHIAN UKRAINE/TRANSCARPATHIA

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¹Sharing America's Resources Abroad Foundation, OH and ²The Rovt-SARA International Teaching and Consultation Centre, Tiszalok, Hungary



I. David Pandy-Szekeres, BSc, MSc, Doctorat de l'Université

Sharing America's Resources Abroad Foundation, OH

Dr. Pandy-Szekeres obtained BSc and MSc degrees in organic and biochemistry, served as instructor and research fellow at the University of Toronto. He obtained his doctorate in organic chemistry at the Université de Bordeaux I and served as research fellow at CNRS (France). He completed Reformed Church seminary studies in Budapest, served as a teacher at Reformed Church Secondary School and seminary in Sárospatak and at Reformed Church seminary in Kolozsvár. He is director and instructor at Reformed Church Missionary Training School in Transcarpathia (Ukraine) and missionary of the Presbyterian Church in Canada posted to the Reformed Church in Transcarpathia. He is executive director of SARA the Foundation.

Aim: After the collapse of the Soviet Union in 1991, the "state" of Ukraine declared independence. Among other consequences, the newly-established country fell into a downward spiral of economic turmoil which persists to this day, this being further exacerbated by general endemic corruption and by the eruption in 2015 of a "civil" war in the country's eastern reaches. Having been underfunded for more than two decades, state-operated institutions, such as schools, medical clinics and hospitals, have been continually hard-pressed to provide services even at nominally acceptable levels.

Methods: Providing 1) medical instruments, equipment, materials and supplies to the hospitals/clinics in Beregszász, Munkács, Ungvár and Tiszaújlak; 2) opportunities for further training for healthcare professionals; 3) medical care support and diagnoses at reduced prices for patients from Transcarpathia for whom a precise diagnosis or prescribed medical care is not available in Transcarpathian clinics/hospitals; 4) access to individual healthcare monitoring, consultation and diagnosis or emergency alert via an Information Technology (IT) system functional in any country; 5) emergency evacuation/ambulance service from Transcarpathia to hospitals in Hungary.

Results: 1. One example: in September 2016, S.A.R.A. organized the equipping with appropriate instruments one of the operating rooms in the Munkács Children's Hospital so that child patients with scoliosis could undergo corrective surgery. The surgeons performing the operations were trained through education programs sponsored by S.A.R.A. 2. Since 1991, S.A.R.A. has organized and sponsored 34 healthcare professionals from Transcarpathia and 31 from Hungary to travel to the USA and participate in further training programs at renown American healthcare institutions; surgeons from USA and Hungary have travelled to Transcarpathia to carry out operations and teach their Ukrainian colleagues. 3. The Rovt-S.A.R.A. Centre in Tiszalök (Hungary) offers low-cost diagnoses and organizes hospital care for patients from Transcarpathia. 4. The IT monitoring healthcare system has already been accessed by more than 300 individuals living in various countries throughout the world; it can also assist in the organization of medical care in Hungary for ex-patriots. 5. The Centre in Tiszalök can provide ambulances to ensure emergency transportation to hospitals in Hungary.

Conclusions: All the methods mentioned have provided positive results in achieving designated aims and will continue to be applied in the future. Emphasis hereon, however, will be placed on expanding and developing IT Moni-system sites which will allow individuals to personally access and enroll in the IT healthcare monitoring program. Where there are no doctors on site, the IT Moni-system will prove to provide the most cost-effective method of quality medical care.

ION CHANNELS IN HUMAN CHORIONIC MESENCHYMAL STEM CELLS: PHYSIOLOGICAL ROLES AND PHARMACOLOGICAL PROFILING

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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: Mesenchymal stem cells (MSCs) are multipotent cells with intensive proliferative capacity and ability to differentiate into various cell types. The chorionic plate of placenta contains placenta-derived MSCs, thus, this tissue may be an attractive source for stem cells to be used in cell therapy and tissue engineering. Ion channels play a role in the regulation of various physiological processes, such as proliferation, differentiation and migration of many cell types. Our aim was to characterize the ion channel expression in cMSCs and determine their sensitivity to pharmacological agents.

Methods: CD73(+) and CD90(+) and CD34(-), CD45(-) cells were separated from the chorionic plate of human placenta using FCAS. RT-QPCR was used to identify the expression of the ion channels at mRNA level. Functional expression of the ion channels was studied using single cell (patch-clamp) electrophysiology, whole-cell currents were separated to individual components using biophysical (voltage protocols) and pharmacological (ion channel inhibitors) tools.

Results: RT-PCR of cMSCs showed the expression of Kv1.3, Kv4.2, Kv4.3, Kv10.1 of the voltage-gated potassium channels, KCa1.1 of the calcium-activated potassium channel genes. Interestingly, we have also found transcripts for Nav1.2 and Nav1.7 voltage-gated sodium channels along with the strong expression of 5 types of chloride channels (CLCN2, CLCN3, CLCN4, CLCN6 and CLCN7). Of the cation channels we confirmed the expression of Kv10.1 and KCa1.1 and Nav1.2 using electrophysiology and pharmacology but not those of Kv1.3, Kv4.2 and Kv4.3 or Nav1.7.

Conclusions: Our conclusion is that cMSCs express ion channels which may be used to manipulate selectively the function of these cells.

CLUSTER OF SYMPTOMATIC CHRONIC ARSENIC EXPOSED PATIENTS

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Tamas R. Peredy, MD

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Emergency Physician, Tampa General Hospital, Tampa, FL and Sarasota Memorial Hospital, Sarasota, FL
Past President, HMAA

Dr. Tamas Peredy is a past Secretary and President of the HMAA. He is currently the Medical Director of the Florida Poison Information Center in Tampa and works as an Emergency Physician in Sarasota, Tampa and Portland Maine.

Aim: The purpose of the study was to describe the effects of chronic arsenic exposure from highly contaminated drinking water in the US.

Methods: We performed a site visit, patient interviews, clinical examinations, photographs and laboratory tests of individuals suspected of chronic arsenic exposures.

Results: 5 of 9 possible patients were available for evaluation in 2 of 3 houses associated with contaminated drinking water with arsenic level of 2555 mcg/L. Inorganic arsenic levels from 24-hour urine collection ranged from 148-950 mcg/L. Most common symptoms included dermatological abnormalities (pigment changes, hyperkeratosis, pre-malignancies) and neurological (sensory neuropathy).

Conclusions: Chronic arsenic exposure from drinking water sources is a known global hazard but rarely occurs in the US. Classic findings of chronic arsenic poisoning were identified and correlated with urinary inorganic arsenic levels.

SEMMELWEIS MEMORIAL PRESENTATION 2018

Perenyi, A.

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Agnes Perenyi, MD

Physician at SUNY Downstate Medical Center – Northwell Health, Brooklyn, NY

Agnes Perenyi MD is a graduate of Semmelweis Medical School. Her specialty is pediatrics; her subspecialty is perinatal-neonatal medicine. Her academic title is Clinical Associate Professor of Pediatrics. She is on staff at SUNY Downstate Medical Center and at Northwell Health where she participates in clinical service, education and research. Her research interests include neurodevelopmental follow-up studies and neurodevelopmental outcome of preterm infants. She is a member of the American Academy of Pediatrics and an NRP (Neonatal Resuscitation Program) instructor certified by the American Board of Pediatrics.

Ignac Semmelweis is the most prominent Hungarian physician. He graduated from the Vienna and Pest-Buda Universities at the Faculty of Medicine. He started his medical career as an obstetrician/ gynecologist at the Allgemeines Krankenhaus in Vienna. Apart from clinical service he regularly performed autopsies and participated in educating medical students the Krankenhaus being a university hospital. Later he received the title of University Professor and continued to work at the St. Rokus Hospital in Pest-Buda.

His lifetime achievements include the discovery of the cause and prevention of the childbed fever (febris puerperalis) that took the life of many of his patients. He was also among the first to conduct experiments and laid the foundation of experimental medicine, pathophysiology and preventive medicine.

Despite of his apparently successful strategies to prevent childbed fever, the lack of support and acknowledgement by his colleagues and higher-ups soon took their toll. Dr. Semmelweis died of the same diseases that took the life of many of his patients.

20018 is The Semmelweis Year in Hungary commemorating the 200 years' anniversary of his birth. In this presentation we remember him recalling his achievements in medicine, in everyday life and in culture.

RESEARCH ACTIVITY OF TWO HUNGARIAN PEDIATRIC SURGEONS IN MANCHESTER THE UK

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¹Semmelweis University, Budapest, Hungary and ²Department of Pediatric Surgery and Urology, Central Manchester Children's Hospital, Manchester, United Kingdom



Gyorgy Rakoczy, MD, PhD

Deputy President of the Hungarian Medical Association of the United Kingdom

Dr. Gyorgy Rakoczy, as an experienced pediatric and thoracic surgeon had to leave Hungary in 2002, worked 3 years as consultant in Groningen, the Netherlands and 13 years in Manchester Children's Hospital. The number of his publications is 150 including a Hungarian textbook about pediatric surgery. He was the president of the Federation of Hungarians in the UK and he is the Deputy President of the Hungarian Medical Association of the UK.

Aim: I would like to present the extended research activity of two pediatric surgical consultant. What we achieved, what we have learned.

Methods: I will shortly present 10 different research activities what we were dealing with during the last 8 years in Manchester taking advantage of the possibilities of multi-center, international collaborations, first of all with Hungary.

Results: I will summarize the idea and the outcome of the following studies:

- Long term effect of the loss of ileo-cecal valve
- Development of the spiral intestinal lengthening (SILT)
- Application of SILT and alternative longer small bowel flap and the role of mucosectomy during Mitrofanoff operation
- Introduction of the in vivo microscopy in the clinical practice
- Rheological changes after splenectomy and 90% splenectomy
- Long term effects of vagotomy through the microbiome gut-brain axis
- Development of new acoustic diagnostic method of osteoporosis

Conclusions: This presentation summarizes our excellent opportunities to develop collaborations, our research efforts to improve patient care and our acceptance in the UK. We hope we will be able to develop organized training for Hungarian Pediatric Surgeons in the UK.

PACAP DEFICIENCY AS A MODEL OF ACCELERATED AGING

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Dr. Reglodi obtained her medical degree in 1994. From 1994 she has been working at the Department of Anatomy, University of Pecs, Hungary. At present she is Full Professor and Chair of the Anatomy department. She is Vice Dean of Science at the University of Pecs Medical School. She did her PhD research work at Tulane University, New Orleans and served as Visiting Professor at Ross University School of Medicine. Her research interests include neuropeptides, neuroprotection, neuroendocrinology, with special emphasis on PACAP (pituitary adenylate cyclase activating polypeptide).

Aim: Pituitary adenylate cyclase activating polypeptide (PACAP) is a potent cytoprotective peptide that provides an endogenous control against a variety of tissue-damaging stimuli. Dysregulation of neuropeptides may play an important role in aging-induced impairments. We hypothesized that the progressive decline of PACAP throughout life, the increased vulnerability to various stressors of animals partially or totally lacking PACAP and the well-known general cytoprotective effects of PACAP lead to age-related pathophysiological changes in PACAP deficiency.

Methods: Young and aging PACAP knockout mice were used. Detailed histopathological analysis was carried out from all organs with Kongo red staining followed by mass spectrometry analysis of the amyloid plaques. Serum laboratory tests, cytokine array, PCR and immunohistochemistry were used to analyze details about the amyloid depositions and underlying mechanisms.

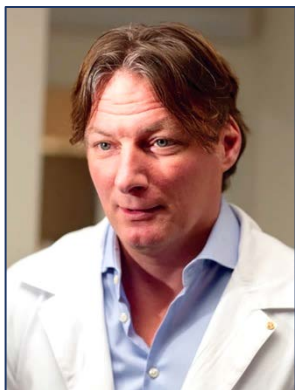
Results: Using young and aging CD1 PACAP knockout mice, we found pre-senile appearance of amyloidosis in young PACAP knockout (KO) animals and showed that senile amyloidosis in mice lacking endogenous PACAP appeared accelerated, more generalized, more severe and affected more individuals. Histopathological analysis showed a type of age-related systemic amyloidosis with mainly kidney, spleen, liver, skin, thyroid, intestinal, tracheal and esophageal involvement. Mass spectrometry-based proteomic analysis, re-confirmed with immunohistochemistry, revealed that apolipoprotein A-IV was the main amyloid protein in the amyloid deposits together with several other accompanying proteins. Although the local amyloidogenic protein expression is disturbed in the KO animals, no difference was found in lipid laboratory parameters, suggesting a complex pathway leading to increased age-related degeneration with amyloid deposit in the lack of PACAP.

Conclusions: In summary, here we describe accelerated systemic senile amyloidosis in PACAP gene deficient mice, which might indicate an early aging phenomenon in this mouse strain. Thus, PACAP KO mice could serve also as a model of accelerated aging, with human relevance.

LAUNCHING THE HUNGARIAN LUNG TRANSPLANTATION PROGRAM AND THE CURRENT RESULTS

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Dr. Ferenc Renyi-Vamos is a thoracic surgeon and Head of the Department of Thoracic Surgery at the national Institute of Oncology in Budapest, Hungary.

Aim: The number of lung transplant centers in Eastern Europe is still limited. In Hungary, all solid organ transplantation programs started with several decades delay, compared to Western countries. The Vienna Lung Transplant program was launched in 1989, and from 1996 in this center lung transplantation became available also for Hungarian patients. As a leading high volume center in this special geopolitical position, the Vienna Lung Transplant program provided support for several ongoing lung transplant programs in its region.

Methods: Within the framework of a “twinning agreement” between Budapest and Vienna, approved by Eurotransplant, distinct modules of an independent program have been stepwise introduced in Hungary. The goal of this type of cooperation was to provide lung transplantation for Hungarian citizens, enable access to Hungarian donor lungs for Vienna, and establish a training system for all essential specialist of the independent Hungarian lung transplant program. Lung procurement started in 2002, followed by post-operative long term care in 2005, and whole responsibility from pre-transplant evaluation and listing in 2008. Surgical training was started in 2003, and education for anesthesia and preoperative care was completed in 2013. Main catalyzing elements were the setup of the new OCO in 2007 and the Eurotransplant membership of Hungary in 2013. To finalize the process, in 2013 the Thoracic Surgery Department of Semmelweis University was founded and defined as the Hungarian center for lung transplantation. Reimbursement for lung transplantation was settled with 70.000 Euros per case. The government provided 3 million Euros specifically for infrastructural developments.

Results: Lung transplantation was first performed on a Hungarian patient in Vienna, in 1996. In the next 20 years 180 lung transplantation were performed on Hungarian patients, and during the same period more than 15 experts were trained in Vienna. The first Hungarian lung transplantation was done on the 12th December 2015. In the following period between 12th of December in 2015 and 15th of June in 2018 49 patients underwent LuTx in Budapest, from which 24 suffered from COPD, 7 from IPF, 12 from CF, 2 from IPH and 4 from other diseases. From these transplantations, there was a combined lung-kidney TX and a LuTx after ECMO-bridge therapy. Most of the patients received double LuTx (48), 1 patient had single LuTx, and 2 patients had one side lobar-Tx combined with whole lung Tx on the other side. We unfortunately lost 8 patients.

Conclusions: The early results of the program are comparable with those of other middle size programs in the world. The constant volume of patients transplanted in our center shows that this technique was successfully introduced in the Hungarian clinical practice. Stepwise and systematic approach in the preparation phase within a well defined cooperation framework is highly recommended for ongoing lung transplantation programs.

WHEN AN ABDOMINAL ULTRASOUND COULD HAVE SAVED THE DAY: MALIGNANT PHEOCHROMOCYTOMA AS A CAUSE FOR CHEST PAIN – CASE REPORT AND REVIEW OF THE LITERATURE

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Dr. Rosta has studied at the University of Szeged. During his studies he spent internships in Houston, TX and Buffalo, NY. In the last 2 years he has been working as a resident in St. Polten, Austria. His areas of interest include urological oncology and radiology.

Aim: Pheochromocytoma (PCC) is a rare catecholamine producing tumor, that arise from chromaffin cells of the adrenal medulla, occurring in less than 0.2 percent of patients with hypertension. They are mostly benign, but they may also transform into malignancy in 10% (8% to 12.5%) of the cases.

Methods: We present an interesting case of a 65 year old Caucasian male, who was initially admitted to our hospital for a heart-cath because of positive cardiac stress test. The patient suffered from night sweats and Raynaud syndrome too. The left circumflex artery was stented. One week after discharge, the patient presented with chest pain to our emergency room, and underwent another heart catheterization again, without finding any significant occlusion. An abdominal ultrasound revealed a left renal mass of 6 cm. Further diagnostic with contrast-enhanced CT has confirmed the perirenal mass and in addition it showed some para-aortic lymph node enlargement too. Extended tumor nephrectomy with para-aortic lymphadenectomy was carried out, with severe hypertensive crisis episodes during and after the surgery. Malignancy was difficult to diagnose microscopically, but after molecular pathologic and Next Generation Sequencing techniques a malignant pheochromocytoma pT3 pL1 pV1 pN1 (two from four lymph nodes positive) was histologically confirmed. A DOPA/PET revealed two suspicious lesions for bone metastases, one in the vertebral body and one in the 11th rib. Because of the implanted coronary stents, we were not able to perform a bone MRI, but a contrast enhanced CT Scan hasn't showed any abnormalities in these two lesions. 123I-MIBG scintigraphy showed also no increased activity. Normatenehrin plasma level was 290,7 pg/ml postoperative (normal range <200 pg/ml). Together with the radio-oncologists we decided to irradiate the two suspect areas with 43,01 Gy. The patient tolerated the therapy very well.

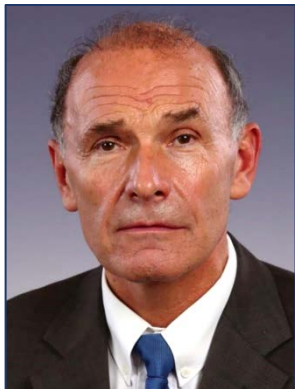
Results: After 3 months, the patient reported to control with normal blood pressure and a significantly better overall condition. There is no evidence of recurrence at the present time. Further DOPA/PET control is planned in the next month.

Conclusions: Dealing with pheochromocytomas can be challenging, by therapy resistant cardiac diseases abdominal ultrasound screening and hormone profile should be considered. Because of the rarity of malignant pheochromocytoma and the consequently limited number of patients available for clinical study, there is no good evidence for a standard of care, individual approach should be applied for each patient.

THE PREVALENCE AND ECONOMIC BURDEN OF OBESITY IN HUNGARY

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Aim: The prevalence of obesity is growing continuously worldwide, even in Hungary. Since 1988, when the first professional wide-range evaluation was performed, only limited data were available. Obesity could be considered as the main consequence of unhealthy nutrition, responsible for many pathological alterations in human. Obese patients usually need more health care services.

Methods: Anthropometric parameters were measured, presence of metabolic diseases were questioned in primary & community care settings and in workplaces. Age, BMI, waist circumference, educational level, presence of hypertension or/and diabetes were analyzed statistically and compared with previous data from 1988. Yearly data of the Hungarian National Health Insurance Fund Administration (NHIFA) were collected, regarding finances of secondary care, hospital services and health insurance reimbursement for medications, based on the International Classification of Diseases (ICD) codes of selected morbidities considering linked to obesity.

Results: Data of 0.55 percent of the population above 18 years were registered in all geographical regions of Hungary (43,287 persons; 17,901 males and 25,386 females), close to the proper national representativeness. The overall prevalence rate of overweight among men was 40%, while obesity 32%, by women both was close to 32%. In the different age groups of men, the prevalence of overweight and obesity was: 18–34 y = 32.7% and 18.2%, between 35–59 y = 40.1% and 34.4%, over 60 y = 43.5% and 38.8%. Among women, in the same age categories were: 19.6% and 5.7%, 36.8% and 38.7%, 36.5% and 39.7%. Data of BMIs and waist-circumference were presented according to age, by decades and by type of residency as well. The highest ratio of overweight was registered among men with the highest educational level, while highest ratio of obesity among women having the lowest education. Obesity according to BMI and abdominal obesity was the highest in the villages, especially among females. Registered metabolic morbidities were strongly correlated with BMIs and both were inversely related to the level of urbanization. The estimated total public health expenditures were 58,986 Million HUF (190.3 Million EUR) and the financial contribution of patients was calculated as 25,316 Million HUF (82 Million EUR). These data represent 9.3 % of the whole national health services budget (908,011 Million HUF - 2929 Million EUR) and 30 % of the whole drug-reimbursement budget (296,024 Million HUF - 955 Million EUR).

Conclusions: Over the previous decades, the ratio of the overweight and even the obese persons increased significantly, it was most prominent among males, mainly in younger generation. Expenditures for all obesity related pathologies could be estimated between 0.5 - 1 % of the national GDP. Obesity means a serious medical, public health and economic problem, requires higher public awareness and political support.

THE ROLE OF SELECTIVE PREOPERATIVE SPLENIC ARTERY EMBOLIZATION IN THE MINIMALLY INVASIVE SURGICAL MANAGEMENT OF MASSIVE SPLENOMEGALY

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Dr. Sandor graduated from Semmelweis University in 1992. He started his surgical career at the Postgraduate Medical University under Professor Janos Kiss. He moved to the United States in 1994, completed his general surgery residency and fellowship in minimally invasive and weight loss surgery at the University of Massachusetts. He is in private practice in Stoneham, Massachusetts and holds a teaching faculty appointment at Tuft University.

Aim: Massive splenomegaly (> 20 cm in largest diameter) often forms a surgical indication for splenectomy but minimally invasive surgical techniques have been associated with prolonged operative times and increased complication rates, such as bleeding and splenic laceration. Manipulation and removal of a giant spleen can be challenging with laparoscopic instruments. The aim of the study was to evaluate if operative risks can be reduced by selective preoperative splenic artery embolization.

Methods: A 58 year old women presented with abdominal pain and her CT demonstrated massive splenomegaly with the spleen measuring 22.4 x 19.7 x 7.3 cm and filling the entire left side of the abdomen from the left upper quadrant to the pelvis and crossing the midline with engorging of the splenic vein. She received immunization against encapsulated organisms 2 weeks prior to surgery. On the day of the surgery, the patient underwent selective splenic artery embolization with Gelfoam slurry and three Nester coils. No complication was noted. 2 hours later the patient underwent a laparoscopic splenectomy. The patient was placed in right lateral decubitus position, the operating table was flexed at the hip level.

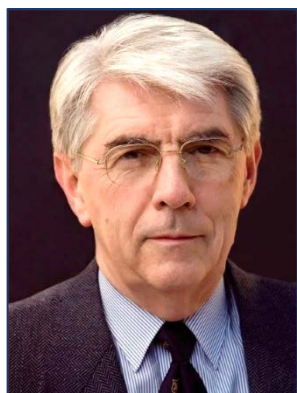
Results: Total operative time was 140 minutes, blood loss was 5 ml. Her drain was removed on the 1st postoperative day with minimal out. The postoperative course was complicated by fever, tachycardia, leukocytosis (without a left shift) and progressive thrombocytosis. Imaging studies did not reveal any surgical complication, the patient responded to beta blockers, acetaminophen and fluid therapy. She was discharged home on the fifth postoperative day. The final pathology revealed splenic marginal zone lymphoma.

Conclusions: The technical challenges of removing a massively enlarged spleen with minimally invasive techniques can be effectively reduced by preoperative selective splenic artery embolization. However, the sudden subdiaphragmatic volume change and the hematologic consequences of splenectomy require close postoperative observation and management and may warrant against early discharge.

IGNAC SEMMELWEIS – A MORAL ICON AND A PIONEER OF EVIDENCE BASED MEDICINE

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In the building of the International College of Surgeons in Chicago one can find the „Hall of Fame” where twelve statues were erected in 1954 to celebrate medical „immortals”. Among them we can see a Hungarian physician, Ignac Semmelweis’ full size statue – at his knee there is a young mother with a baby in her arms. Why is this special respect? The answer is: a hard life, the continuous fight for the truth, for his principles which influenced millions’ life.

He realized - forty years before Pasteur’s study of pathogenic role of bacteria - that some poisonous agent from the autopsy room can cause puerperal fever, i.e. sepsis. The next step was to find the method by which one can get rid of this „poison” – it was the proper handwashing with a proper solution. Semmelweis didn’t stop: he supported his theory by analyzing statistical data of different gynecological departments, furthermore, he performed animal experiments, by which he could prove the way of septic complications – this way he became a pioneer of evidence-based medicine.

He felt responsible for the death of many young mothers because his super activity in the autopsy room during the previous years. His death is like a classic Greek tragedy: he died as a consequence of a disease against which he was fighting all along his life: sepsis.

Semmelweis’ lesson represents the direct continuity of Hippocrates’ teaching: Primum nil nocere – do not harm during our medical activity in any respects.

THE ROLE OF STOOL GENETIC TESTING (SGT) FOR DIFFERENTIAL DIAGNOSIS OF EARLY STAGE IBD AND IBS

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Dr. Schwab is a physician-entrepreneur, practicing in the fields of internal medicine and gastroenterology. He started his career with Prof. Akos Pap and served ten years under his mentorship in GI referral centers in Budapest. He also gained significant experience in early stage development of drugable compounds and diagnostics as a co-worker of late Prof. George Keri. He is founder of diagnostic start-ups Oncompass Medicine targeting personalized therapy in oncology by molecular characterization of tumors and DiaVitas introducing personalized treatments based on genetic testing of the microbiome.

Aim: Retrospective analysis of stool microbiome samples of IBD and IBS patients to determine distinct patterns to guide differential diagnostics.

Methods: Stool samples were analyzed in 54 patients (14 IBD and 40 IBS) by standard 16S RNA sequencing and determined diversity index as well as relative ratios of distinct taxonomy classes of the stool microbiome.

Results: Clostridiaceae, Prevotellaceae, Verrucomicrobiaceae, Rhodospirillaceae Family of bacteria were by far less abundant in the IBD group (40%, 59%, 72%, 71% respectively), whereas Desulfovibrionaceae, Enterobacteriaceae, Sutterellaceae, Veillonellaceae, Acidaminococcaceae, Erysipelotrichaceae were less abundant in the IBS group (105%, 194%, 76%, 79%, 53%, 51%) respectively. There was no clinically significant difference in the microbiome diversity (Simpson's Score).

Conclusions: Stool Genetic Testing for determining changes in the microbiome is a potentially new and non-invasive method to help differentiating early/mild forms of IBD requiring early introduction of 5ASA therapy in adequate doses that can help restoring the gut mucosa barrier function. Detection of lower abundance of Prevotellaceae and Clostridiaceae family of bacteria in these patients as well as higher abundance of Enterobacteriaceae and Veillonellaceae may prove valuable tools for differentiation as shown already in recent publications also supported in our small pilot cohort. Furthermore, SGT results can help establishing personalized diet and probiotic recommendation for both patient groups. Prospective clinical trials are needed to prove the role of SGT in this respect but given its non-invasive nature, easy-to-repeat format and decreasing costs in the future make it a very appealing tool for the daily clinical setting.

CIRRHOSIS AS A POSSIBLE RISK FACTOR FOR DEVELOPING DIASTOLIC DYSFUNCTION

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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: Greater prevalence of diastolic dysfunction (DD) and association with severity of liver cirrhosis has been reported in different studies. We therefore hypothesize that cirrhosis may increase the risk for developing DD. We tested this hypothesis in a population of cirrhotic patients where demographic variables and diagnostic criteria were systematically controlled.

Methods: Prevalence of DD was measured in 102 cirrhotic patients with no independent risk factors for DD. Tissue Doppler Imaging (TDI) criteria with age correction were used to determine DD. Logistic regression analysis was used to find variables of liver disease that independently predicted DD. Patient death (Kaplan-Meier analysis) and graft failure were compared 3-7 years following evaluation.

Results: Diastolic dysfunction was diagnosed in 18% of our cirrhotic patients compared to published values of 6.4-11.8% in the general population. There was no association with severity of cirrhosis and no diastolic parameter was associated with a significant hazard ratio for death. The DD rate in our data varied (8-35%) depending on choice of TDI criteria of previous studies from the literature.

Conclusions: Our data suggests cirrhosis is a risk factor for DD. The higher rate of moderate to severe DD in cirrhotic patients without additional risk factors compared to randomly chosen study subjects from the general population supports this conclusion. It is important to standardize the measurement of DD to avoid significant variability between previous studies.

INTRODUCING NEW CURRICULA/UNIVERSITY OF SZEGED, COLLEGE OF DENTISTRY AND DEPARTMENT OF PSYCHOLOGY

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Professor Shedlin is a medical anthropologist involved in global qualitative research. Her work in reproductive health, substance abuse and HIV has focused on the behavioral issues of risk, context and prevention. She teaches research, narrative medicine and health disparities in the doctoral program in the NYU Meyers College of Nursing. She is also a University Professor (HON) at the University of Szeged and has dual US and Hungarian citizenship.

Aim: The aim of this Fulbright Scholar intervention at the University of Szeged was to introduce an innovative curriculum in the College of Dentistry for teaching humanistic medicine.

Methods: Teaching: seminar format.

Results: In 2013, as a Fulbright Scholar at the University of Szeged, I worked with Prof. Katalin Nagy and Dr. Gabor Braunitzer to develop a seminar on Narrative Medicine for the foreign students in the College of Dentistry. A syllabus was prepared for the semester course and readings were determined. Books and other readings were sent ahead from the US for the students. This presentation will discuss an innovative curriculum which introduced humanistic medicine to the College, and the impact on a cohort of students who have recently graduated. Work with the Department of Psychology on the development of Narrative Medicine will also be presented.

Conclusions: The international students benefited greatly from the readings and discussion. Their feedback demonstrated important new perspectives on the role of the provider and the cultural and psychosocial issues involved in delivering patient-focused care.

50 YEARS OF ADVANCES IN ASSISTED REPRODUCTIVE MEDICINE

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Aim: Understand the history of in vitro fertilization (IVF) and advances in Infertility treatments.

Methods: The spectrum of human assisted reproductive technologies available today will be presented.

Results: The genesis of in vitro fertilization has enabled millions to become parents that would otherwise have never succeeded. The original use of IVF for the treatment of tubal factor infertility has now expanded to include male factor with the use of intracytoplasmic injection of sperm (ICSI), endometriosis, recurrent miscarriage, ovulatory dysfunction and polycystic ovarian syndrome, advanced maternal age, and unexplained infertility. Genetic analysis of embryos using embryo biopsy prior to implantation (PGS/PGD; preimplantation genetic diagnosis and screening) enables the complete karyotype of an embryo (including the sex) to be determined to optimize a healthy outcome and exclude the transfer of aneuploidy embryos. Single gene disorders that are inheritable may also be tested for to prevent the transmission of the diseases including cystic fibrosis, sickle cell anemia, Tay Sachs, and over 200 other genetic based diseases.

Conclusions: Assisted reproductive technologies have enabled many to achieve parenthood that otherwise would never have. The development of genetic testing of embryos prior to implantation holds promise for higher pregnancy rates, lower miscarriages, and healthier babies.

IS IT TRUE THAT THE RISK OF ACUTE PANCREATITIS IS INCREASED IN INFLAMMATORY BOWEL DISEASE?

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Aim: Inflammatory bowel disease (IBD) is the chronic inflammatory disease of the intestines, its most common forms are Crohn's disease and ulcerative colitis. Acute pancreatitis (AP) is the acute morbidity of the pancreas which can have serious consequences. Based on researches investigating the relationship between IBD and AP it is possible, that the risks of developing AP in IBD patients are increased, but there is no accurate data.

Methods: In our research, we conducted a complex search in Embase, PubMed, Scopus, Web of Science and Cochrane Library databases using the filters 'human' and 'English'. For inclusion criteria, we defined the simultaneous existence of both pancreatitis and any form of IBD. The selection was done by two independent investigators, the questionable cases were dissolved by consensus. Meta-analysis and statistical calculations were done by a biostatistician using RevMan5 and STATA software.

Results: Following the data search, we found 2679 publications after removing the duplicates. After filtering based on title and abstract we analyzed the whole text of 649 publications. The 649 publications included more than 50 review and 200 case-control studies, we put these aside in the first phase of our research and worked only with the large-scale observational studies. Based on our provisional data, 2 case-control publication investigated the risk of AP in patients with IBD. Based on these meta-analyses the risk for AP is 3.14 times higher in IBD patients than in the non IBD population (OR=3,14; 95% CI=2,65-3,72; I²=0%; n=97434). Based on 7 further publication we concluded, that among those who suffer from pancreatitis for the first time, the incidence of IBD is greater than in the whole population (OR=2,13; CI=1,96-2,32; I²= 20; n=120 393).

Conclusions: After data analysis of the 641 observational articles, it looks obvious that the risk of AP is increased in patients with IBD, but there is no prospective, multicentric research yet. For these reasons, we start a prospective, international, observational study by the name: APRICOT (Analysis of Pancreatitis Risk in Paediatric Patient with IBD: a Clinical Observational Trial).

PLASMA SOMATOSTATIN INCREASES DURING SCOLIOSIS, BUT NOT DISCUS HERNIA OPERATIONS

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Dr. Suto graduated from the Medical School of the University of Pecs, Hungary in 1995 as a medical doctor and the following years he was trained as an anesthetist and intensivist both in Hungary and in the United Kingdom. To broaden his medical expertise, he also specialized in accident and emergency medicine. He works as a consultant physician at the Department of Anesthesia and Intensive Therapy and Accident and Emergency Medicine at the University of Pecs, Hungary. After graduation he left for the United Kingdom to gain more experience in the field of anesthesia/intensive therapy, acute care and then passed the international exam of Diploma of the European Academy of Anesthetists in 2003. To gain more experience in the economic aspect of modern health care and management he also enrolled for an international MBA program at the Faculty of Business and Economics of the University of Pecs. He earned his PhD in 2014; his research focused on the role and alteration of plasma somatostatin-like immunoreactivity during surgery in SIRS/septic patients and in an animal CLP model. His research field is sepsis and he has also published in international peer reviewed journals. He has been teaching medicine for 23 years, which includes seminars and practical trainings of first aid, ALS, ATLS, intensive therapy and anesthesia, emergency medicine for Hungarian and international medical students, and lectures, training courses for residents, anesthetic assistants, ICU nursing staff.

Aim: Somatostatin (SOM) is a neuropeptide released from the capsaicin-sensitive sensory fibers in response to stimulation and exerts anti-inflammatory and analgesic actions throughout the body. We earlier described plasma somatostatin elevations in patients during abdominal and thoracic surgeries that correlates with the tissue injury. In order to define whether it is a general protective mechanism, we now investigated plasma somatostatin concentrations during spine surgery in orthopedic (scoliosis) and neurosurgical (discus hernia) operations in comparison with the visual analogue pain scale (VAS) and in scoliosis also the correction angles (COBB angle).

Methods: Thirty spine surgery patients undergoing orthopedic and neurosurgical interventions were examined (9 orthopedics, mean age of 18.75±9.06 years, 2 males / 7 females, 21 neurosurgical, mean age of 55.2±14.13 years, 13 males / 8 females, 2 groups: microscopic 9, and traditional type of operation 12). Procedures were done under general anesthesia supplemented with parenteral opioids. Blood samples obtained from age and gender-matched healthy volunteers served as controls. We measured SOM concentrations in the serum in different phases of surgery (5 times all together: 1. before operation, 2. after exploration of soft tissues, 3. after osteotomy/heriotomy, 4. at the time of skin closure, 5. 1 day after operation).

Results: Significant increase of the plasma SOM level was detected during scoliosis surgery, but not in either conventional or minimal invasive discuss hernia operation in phases 3 and 4 compared to the initial level and then declined in phase 5. We found a significant strong correlation between plasma SOM increase and postoperative pain intensity (VAS1), which was higher in patients with higher degree of correction (COBB) in the orthopedic patients. Significantly greater plasma SOM increase was detected in patients with lower degree of initial deformity (COBB1).

Conclusions: It can be concluded that SOM is released during orthopedic spine operation presumably from the sensory nerve terminals in response to painful and/or inflammatory stimuli, as well as tissue damage. This release is determined by the type and extent of the surgical process, plasma SOM increase occurs during higher level of tissue damage in scoliosis patients, but not is discus hernia representing a smaller injury. SOM might exert endogenous analgesic and anti-inflammatory effects, but evidence has to be provided for this theory.

PERFORMANCE ASSESSMENT OF ATHLETES IN THE LAB AND ON THE FIELD

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Dr. Sydo is a cardiology fellow at Semmelweis University Heart and Vascular Center and a research collaborator at Mayo Clinic, Rochester, MN. Her main field of interests are sports cardiology, exercise testing and performance enhancement.

Aim: In athletes, performance assessment is essential in order to evaluate, maximize and follow-up exercise capacity, moreover it can help to exclude pathologic conditions. Sport specific training is a method of legal performance enhancement. To get accurate results of athletic performance and to develop training guidelines lab and field testing have to be combined and repeated. We aimed to complete our detailed sports cardiology screening program with exercise physiology assessment of youth soccer (SP) and water polo players (WP) and to provide individualized training recommendations. Our further objective was to create and evaluate a field testing method for SPs.

Methods: All athletes underwent basic examinations (questionnaire, resting ECG, body composition analysis, echocardiography) and treadmill cardiopulmonary exercise testing (CPET) with 2-minute lactate measurements. Field testing (Yoyo test with lactate measurements, 5 and 10 meter speed tests and body composition analysis) was performed at the beginning of the season. Based on the results, we recommended personalized running programs and retested every 8 weeks.

Results: We examined 221 athletes (183 male, 15.7±1.7years, 122 male SP). 74.2% had physiologic ECG changes, iRBBB being the most common (50.6%). On resting ECG, WPW syndrome was diagnosed in a WP; managed by ablation. Based on ABPM exams, hypertension was diagnosed in 3 cases, antihypertensive treatment was initiated. Apart from some minor changes, echocardiography exams were negative. No underlying structural heart disease was verified with cardiac MR. On the CPET one SP had SVT; electrophysiology exam identified AVNRT, slow pathway ablation was performed. Our field testing study included an U17 soccer team (n=17, 15.6±0.5years). On CPET they had excellent exercise time (15.6±1.6min), aerobic capacity (58.0±3.6ml/kg/min) and ventilation (146.2±18.0l/min). According to body composition analyses, mean fat was 9.6±1.9 kg (14.3±2.7%), lean mass was 14.8±7.6 kg (22.1±0.1%). On the first Yoyo test, average running distance was 2040±206m with peak lactate 11.3±3.1mmol/L. After the running program all SPs performed better; average distance increased by 745±295m (+37%, P<.0001), while peak lactate levels decreased by 2.1±3.4mmol/L (-14%, P<.05). On the second 10 meter speed test there was a -0.11±0.05s (-6.34±0.03%; P<.0001) improvement. According to lactate profiles, all players had improved metabolic status. Mean body fat decreased by 18.2% (-1.7±2.4kg, P<.05), while muscle mass increased by 5% (0.7±0.6kg, P<.05). However, on the third field test average running distance decreased by 671±380m. The indicated performance decrease may be explained by overtraining as a result of a different endurance training program initiated by a new coach. After discussing the results with the coaches they returned to our training program and the results exceeded the second measurements.

Conclusions: Combined lab and field testing are effective methods of athletic performance evaluation with the recognition of underlying cardiac abnormalities. Our new field testing method was able to identify the significant improvement of SPs who followed our training programs. Reduced fat and increased muscle mass proved to be good indicators of the effectiveness of our training recommendations.

THE ANTIARRHYTHMIC EFFICACY OF VERNAKALANT IN POSTOPERATIVE ATRIAL FIBRILLATION: AN ATTEMPT TO MAKE A META-ANALYSIS BASED ON INTERNATIONAL STUDIES

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Dorottya Kata Szabo is a 6th year medical student and student representative of the HMAA at the University of Pecs Medical School, looking forward to the conference.

Aim: Arrhythmias are common and undesirable consequences of cardiac and thoracic surgeries. Based on Hungarian and international publications the most prevalent one is the atrial fibrillation. For sinus rhythm restoration, intravenous vernakalant is a new member of the therapeutic regimes (non-pharmacological and pharmacological) available for cardioversion. Its remarkable atrial selectivity is beneficial, hence it has no serious pro-arrhythmic effect. Usage of vernakalant in postoperative atrial fibrillation is girdled with high international literary interest, our aim was to sum up the results of the available literature on the drug's efficacy.

Methods: We carried out PICO search strategy (Patient population, Intervention, Comparison, Outcome) in online databases (Embase, Pubmed) with which we looked for studies comparing adult patients with postoperative atrial fibrillation (POAF) treated with vernakalant to other patients with POAF but cardioverted with different common-used antiarrhythmic drugs (amiodarone, propafenone, flecainide) or placebo.

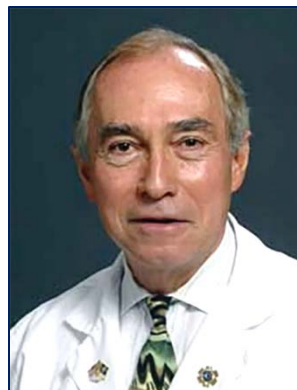
Results: Out of 159 search results of the two databases 15 analyzed the cardioversion's efficacy and were appropriately documented human pharmacological experiment, out of which only four reported adequate quality data of $\Sigma 267$ patients who underwent coronary bypass and/ or aortic/ mitral valve surgery. Studies reported 113/206 successful cardioversion with vernakalant (placebo: 7/50) but either the design and the inconsequent set up of control groups both restricted the comparative statistical evaluation of the data.

Conclusions: International literature is definitely in favor of vernakalant hydrochloride's efficacy in cardioversion, which would be advantageous in postoperative, often instable patients. However, the restricted number of available and quality publications comparing vernakalant to other drugs used for cardioversion draws attention to the importance of further well-organized clinical trials about this new drug.

FROM DISTRESS TO EUSTRESS: 80 YEARS OF STRESS RESEARCH & OTHER MAJOR DISCOVERIES OF HANS SELYE

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Sandor Szabo, MD, PhD, MPH, DSc(hc), FRCPath, AGAF, External Member of the Hungarian Academy of Sciences, after medical school in Belgrade, obtained PhD in the institute of Hans Selye (the 'father of biologic stress') at the Univ. of Montreal & continued with pathology residency at Harvard Med Sch, Boston, where he became assistant & associate professor. He also obtained an MPH at Harvard School of Public Health, & after 20 years at Harvard, became a professor of pathology & pharmacology at the Medical School of Univ. of California, Irvine, CA, where he is still teaching part-time & doing research in stress-related diseases, esp., GI ulceration. He also served as chief of Pathology & Lab. Med. Service as well as chief of staff for 12 years at a nearby VA Med. Center. Thus,

he has extensive experience in biomedical research & executive management, quality control & quality improvements as well as education & training.

Hans Selye (1907, Vienna - 1982, Montreal) first published his seminal papers in 1936 (Nature) & 1937 (in Science) that described the three stages of stress reaction (i.e., alarm reaction, resistance & exhaustion) in rats exposed to cold, immobilization or toxic agents. He identified the adrenals & the pituitary as the main endocrine glands involved in this nonspecific reaction. He also knew & documented that although the sudden release of epinephrine (adrenaline) from the adrenal medulla plays a critical role in the initial alarm reaction, but the long-term effects of stress reaction are due to the enhanced synthesis & release of glucocorticoids from the adrenal cortex. Based on this mechanistic reasoning he described in his first publications what has later become known the "morphologic stress triad": adrenal hypertrophy, gastric erosions/ulcers & thymo-lymphatic atrophy. Furthermore, what we call today 'stress-related diseases' in man, he described these in the 1940s & 1950s as 'diseases of adaption' in rats. In the last stages of his productive life, Selye realized that virtually all the stressors (i.e., stress-causing agents) he used in experimental animals were unpleasant, negative factors that caused 'distress'. Thus, in his last scientific book (1974) "Stress without distress" he called distress the stress reaction caused by negative, unpleasant factors & eustress (from 'euphoria') the similar reaction triggered by positive, pleasant factors like joy over major rewards, receiving surprising good news. Namely, we learned during the last about 40 years that our pituitary gland cannot distinguish between positive & negative stimuli to release ACTH (only our brain cortex, amygdala & hippocampus may perceive the difference). Because of these stress-related creative discoveries Hans Selye is known as 'father of biologic stress', but he also made numerous other major discoveries, e.g., he also introduced the first physiologically sound, structure-activity classification of steroids that was also based on the chemical structure of steroids in 1943. He not only introduced the names of glucocorticoids & mineralocorticoids but discovered the anti- & pro-inflammatory properties, respectively, of these steroids in animal models. Furthermore, he not only described the first stress-induced gastric ulcers in rats (1936 & 1937), but he also recognized the first human 'stress ulcers' during the air-raids in London during World War II (1943). Thus, Selye was a much more productive & creative scientist than it is generally considered.

IDENTIFICATION OF NOVEL TARGETS FOR THE PREVENTION AND TREATMENT OF HPV-ASSOCIATED MALIGNANCIES

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Anita Szalmas received her PhD in 2013 from the University of Debrecen and obtained board certification from Clinical Microbiology in 2012. She is currently an Assistant Professor in the Department of Medical Microbiology, in Faculty of Medicine at University of Debrecen. Her research work is focused on molecular virology with special interest in cellular targets of human papillomavirus oncoproteins and the effects of these oncoproteins upon cellular regulatory pathways.

Aim: Diseases caused by sexually transmitted oncogenic human papillomaviruses (HPV), particularly cervical cancer, represent a serious public health problem and a significant economic burden globally. Despite of the intensive research in this field, useful cellular markers for the prognosis of oncogenic HPV infections and pharmaceutical targets for the successful selective therapy of HPV-related diseases are yet to be found. The central aim of my research is to increase our understanding of the cellular processes that drive the malignant transformation of host cells infected with HPV.

Methods: With the support of the Fulbright Scholar Program, I had the unique opportunity to learn database analysis at the University of Texas MD Anderson Cancer Center in Houston, which is one of the most prominent cancer research centers worldwide. We applied a systematic approach that uses large, publicly available data sets to identify novel immunotherapy targets for the prevention and treatment of HPV-associated malignancies. We also analyzed the correlation of the expression of potential target genes with immune markers, immune suppressor markers, and clinical variables as well.

Results: This project provided new target candidates for the prediction of disease progression and formed the basis of specific immunotherapeutic approaches for the targeted prevention or treatment of HPV-associated cancers.

Conclusions: HPV infection provides a unique model system for investigating the key steps in cancer development, with E6 and E7 viral oncoproteins being perfect tools for dissecting relevant pathways, specifically those related to immune response.

ASSOCIATIONS BETWEEN VERTEBRAL ARTERY DOMINANCE, BASILAR ARTERY CURVATURE AND WHITE MATTER HYPERINTENSITIES

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Aim: The vertebrobasilar is a unique system in human anatomy in the sense that two arteries merge into a single vessel, and it is especially important because it supplies the posterior circulation of the brain. The diameters of the vertebral arteries (VA) are very often unequal. Therefore, this study investigated if unequal VA diameters contributes to the development of basilar artery (BA) curvature and if it is a link to the laterality of White Matter Hyperintensities (WMH) on magnetic resonance imaging (MRI) scans.

Methods: We retrospectively selected 300 patients (205 with WMH and 95 control patients without WMH lesions) with FLAIR and Time-of-Flight MRI scans who visited our clinic in 2017. We analyzed the circle of Willis with 2 vascular surgeons and WMHs with 2 radiologists. We reconstructed all patient's posterior circulation and analyzed VA: length, angle, dominance, tortuosity, torsion, BA: length, angle, dominance, tortuosity, torsion curvature and their directional relationships. The "dominant" VA side was determined by the volume of the VA divided with the length of the VA. WMH were counted, localized (supratentorial, brainstem or cerebellar), lateralized (left or right dominant) and scored with Fazekas score.

Results: Initial statistical analysis showed that the dominant VA was more frequent on the left side. Most patients had an opposite directional relationship between the dominant VA and BA curvature. Further in-depth statistical results will be revealed at the conference.

Conclusions: Unequal VA flow is an important hemodynamic contributor of BA curvature and development of MR White Matter Hyperintensities.

Support: Erasmus+ program scholarship.

THE USE OF A SMARTPHONE APPLICATION FOR FAST LUNG CANCER RISK ASSESSMENT

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Dr. Zalan Szanto is the Head of Thoracic Surgery at the University of Pecs. He introduced lung cancer CT screening at the University.

Aim: The early detection of NSCLC cases is still the key point of the surgical treatment of lung cancer, but 75% of the cases are still diagnosed in an advanced, inoperable stage. Screening with IdCT of the high-risk population can improve the early diagnosis, but it might be aggravated by the complex task of risk group selection and recruitment. The modern communication path of the mobile devices is enabling us a complete new communication and selection method which can effectively simplify the risk group identification and the suggestion of screening by the Screening Centers. The aim of our study was to determine the effectivity of a lung cancer risk assessment mobile application (LungScreen) in a localized setting.

Methods: We constructed a free lung cancer risk assessment application (LungScreen) for selecting high risk population in Baranya County, Hungary. for Android and iOS mobile platforms. The application calculates and shows individual NSCLC risk based on Bach's protocol after collecting demographic data, smoking status, possible environmental harms of the participant. Based on GPS coordinates the high-risk participant is navigated to the nearest Screening Center for further investigation. We analyzed the records of the application in a two month test period aided by an informative campaign in Hungary.

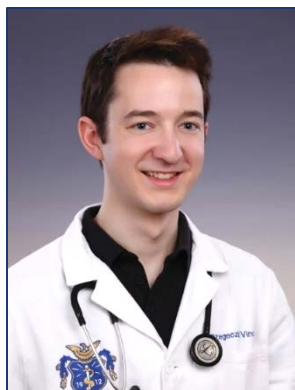
Results: In one year test period 12780 participants downloaded and completed the risk assessment test (Male/Female 58%/42%, Age range 9-92 years, mean age 38,2 year). 2750 participants were active smokers, high risk criteria were calculated in 789 cases, in which further screening investigation were suggested. 158 LDCT screening were performed, with 32 positive findings which required further investigations. In 9 cases Tumor Board decided to indicate surgery (7 cases NSCLC, 2 cases benign lesion). All the procedures were performed with VATS.

Conclusions: Lung cancer risk assessment via mobile devices allows free, fast and efficient way to select, manage and localize high risk population for NSCLC. By omitting the complex recruitment process, it can aid to initiate screening trials. Giving immediate personalized feedback and individual direction to diagnostic centers can facilitate early diagnosis of operable NSCLC cases.

EFFECTS OF PACAP IN ENDOMETRIOSIS

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Vince Szegeczki received his medical degree from the University of Debrecen in 2018. He is currently a PhD student at the Department of Anatomy, Histology and Embryology at the University of Debrecen Faculty of Medicine.

Aim: Pituitary adenylate cyclase activating polypeptide (PACAP) has been detected in the central nervous system, however it has effects in various peripheral organs, such as female genital tract. Despite the role of PACAP has been described in the development of gonads, in follicle maturation and in relaxation of uterus, there are no data about its function in endometrium and endometriosis. In our investigation the main goal was to set an in vitro model for maintaining endometriotic tissue in which the effect of PACAP can be investigated. In addition, we intended to analyze possible changes in the expression of Oct4 and Nanog transcription factors after PACAP treatment. These factors are presumed to be responsible for the migration and invasion capacity of endometrial cells in endometriosis.

Methods: First we cut the laparoscopically removed endometriotic cysts and put them into matrigel-covered plates, using HG-DMEM medium. Depending from the time of adhesion to the gel, half of the samples were dosed with PACAP solution. Samples were analyzed with RT-PCR, Western blot, immunohistochemistry, PCNA proliferation assay and H&E staining methods.

Results: In contrast with the untreated endometriotic tissues, in PACAP treated samples there was significant decrease in the expression of PACAP specific PAC1 receptor, P-PKA, Oct4, P-Oct4 and Nanog. Proliferation capacity and amount of glandular endometrial tubules were also reduced.

Conclusions: Based on our results it may be hypothesized that PACAP can reduce the proliferation of the ectopic endometrial tissue by regulating the expression of stem cell transcription factors.

ONCORHEUMATOLOGY: VARIOUS RELATIONSHIPS BETWEEN MALIGNANCY AND AUTOIMMUNE RHEUMATIC DISEASES

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Dr. Eva Szekanecz was graduated from the University of Debrecen Faculty of Medicine. First, she specialized in Otolaryngology but later she was board certified in Oncology. Currently she is working in the Department of Oncology in Debrecen, Hungary. She received her PhD degree on the basis of her research in the field of oncorheumatology.

Aim: Oncology and rheumatology may have several relationships. In this review talk we wish to demonstrate various aspects of these overlaps.

Methods: We have been conducting numerous studies on patients with autoimmune rheumatic conditions. We assessed the prevalence of secondary malignancies, the production of soluble tumor antigens, paraneoplasias, as well as the occurrence of autoimmunity in patients treated with checkpoint inhibitors.

Results: We found significantly higher prevalence of malignancies among patients with rheumatoid arthritis (RA), systemic sclerosis (SSc) and systemic lupus erythematosus (SLE). We will discuss the possible oncogenic effects of antirheumatic drugs. We detected increased levels of soluble tumor antigens in RA, SSc and SLE. On the other hand, malignancies may result in the development of paraneoplastic rheumatic syndromes. In addition, oncotherapy including checkpoint inhibitors may cause autoimmune rheumatic symptoms.

Conclusions: There are numerous relationships between rheumatic and malignant diseases. Our studies may draw attention to the importance of collaboration between medical specialties including rheumatology and oncology.

STROKE IN AUTOIMMUNE DISEASES: PATHOPHYSIOLOGY OF CEREBRAL VESSELS

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Aim: The prevalence of stroke is increased among rheumatoid arthritis (RA) patients. Vascular physiology should be assessed in the preclinical vascular state. Assessment of intracranial vessels includes transcranial doppler (TCD). TCD performance requires intact temporal acoustic windows (TAW). Failure of TAW (TAWF) is present in 8-20% of people. This may be due to pathological bone metabolism. We assessed RA patients and healthy controls by transcranial Doppler (TCD), carotid ultrasonography and brain MRI. We wished to determine preclinical pathophysiological changes in the cerebral vasculature.

Methods: TAWF, temporal bone thickness and texture were determined by ultrasound and CT. BMD and T-scores of multiple bones were determined by DEXA. Several bone biomarkers were assessed by ELISA. Altogether 63 female RA patients and 60 age-matched controls underwent TCD assessment of the medium cerebral (MCA), basilar and vertebral arteries. Pulsatility (PI), resistance (RI) indices and circulatory reserve capacity (CRC) were determined. The presence of carotid plaques and intima-media thickness (cIMT) were also determined. Intracerebral vascular lesions were investigated by brain MRI. RA subsets include MTX- and biologic-treated patients.

Results: In RA, the right and left TAW were undetectable in 35% and 53% of patients, respectively. In controls, TAWF was only present in 20% of subjects. Temporal bone was thicker, and texture was more heterogeneous in RA patients vs controls ($p < 0.05$). These TAW features were generally more common on the left side. There was close association between TAWF, bone thickness and texture ($p < 0.05$). These TAW parameters all correlated with age, however TAW failure and texture also correlated with serum osteoprotegerin. TAW bone thickness inversely correlated with hip BMD ($p < 0.05$). MCA PI and RI values at rest and after apnea are significantly increased in the total RA population vs controls. MCA PI(r) and RI(r) is also lower in biologic-treated patients. MCA CRC was also impaired and basilar artery PI was higher in RA. More RA patients had carotid plaques and had increased cIMT. Correlation analysis suggested multiple associations between right and left TCD parameters. There may be an association of TCD and carotid features with cerebral atrophy and age. Disease duration, disease activity and anti-CCP may influence left MCA PI and RI, as well as CRC. Lp(a) may also influence the development of carotid plaques.

Conclusions: TAWF, thicker and heterogeneous temporal bones were associated with RA. These features have been associated with bone loss and OPG production. Bone loss seen in RA may result in OPG release and stimulation of bone formation around TAW. This may be the first study to show increased distal MCA and basilar artery occlusion in RA as determined by TCD. RA patients also exert CRC defect. We also confirmed increased carotid plaque formation, increased cIMT. Biologics may beneficially influence some parameters in the intracranial vessels.

THE HISTORY OF THE CIRCUMCISION: AKA THE RAPE OF THE PHALLUS

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Dr. Szollar started his urological practice in 1972 at SOTE Urologiai Klinika as "tanarseged". His restless mind and body dragged his family though Nigeria, Ann Arbor, Buffalo to San Diego where he spent most of his carrier as chief of the urology department before retirement. He considers himself to be lucky being apprentice of Dr. Antal Babits and Dr. Imre Magoss. He is happily retired in Santa Rosa with his wife Zsuzsanna Molnar M.D., whom he met in Medical School at SOTE.

Aim: To explore the progression of the circumcision from circa 60 000 BC to the present days.

Results: Circumcision was practiced way beyond the perceived origin (Egypt 5000 Y BC) by the Australian indigenous people, followed by the Jews, Greeks, Muslims and African and people of the far East. The motivations were different from totemic genital surgery, to prerequisite for selection into the higher echelon of the secrets knowing society, via being one's covenant to God, or stopping the person's duality entering adulthood. Attempted behavior modifications: preventing masturbation to discouraging sexual activity to theoretical castration. Will learn how Dr. Sayre "science" introduced the circumcision as cure for all in America and the controversy between the believers and scientific evidence never stopped since.

Conclusions: In conclusion you will learn about the misconceptions of the foreskin care, about sexual differences, surgical techniques and the present recommendations from the USA and EU. You will be able to form your opinion, bit it maybe will be like Peer Gynt's onion...

PITUITARY ADENYLATE CYCLASE ACTIVATING POLYPEPTIDE (PACAP), AS A POTENTIAL BIOMARKER, IN HEART FAILURE PATIENTS

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The aim of the Hungarian PACAP Research Group in Pecs is to examine the role of this neuropeptide in physiological and pathological conditions in different in vitro, in vivo models. Andrea Tamas is the leader of the clinical researches which aim to examine the potential biomarker function of PACAP in different disorders.

Aim: Pituitary adenylate cyclase activating polypeptide (PACAP) is a pleiotropic and multifunctional neuropeptide having neurotrophic, neuroprotective, and general cytoprotective actions in a variety of tissues based on its antiapoptotic, anti-inflammatory and antioxidant effects. Several studies have demonstrated its cardioprotective effects in vitro and in various animal models. However, few data are available on the presence of PACAP in human cardiac tissues and its role in the pathomechanism and progression of different cardiac disorders particularly heart failure. Earlier our research group has shown PAC1 receptor immunoreactivity in human heart tissue samples and we have found significantly elevated PACAP27 and PACAP38-like immunoreactivity in ischaemic cardiac samples compared to valvular abnormalities with radioimmunoassay. In the last few years, numerous studies examined the presence and the changes of PACAP levels in different human tissue samples and biological fluids to show alterations in different physiological and pathological conditions. Therefore, the aim of the present study was to measure the alterations of blood PACAP levels in chronic heart failure caused by primary dilated cardiomyopathy or ischemic cardiomyopathy to examine the possible relationship between serum levels of PACAP, N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and systolic left ventricular function the most reliable biomarkers of heart failure.

Methods: In this experiment we examined peripheral venous blood samples of 42 patients with primary (n=9) and ischemic (n=33) dilated cardiomyopathy. From all patients two blood collection tubes (one 10 ml, one 5 ml) were taken for general laboratory examination. Other two 10 ml tubes including EDTA (Ethylenediaminetetraacetic acid) were taken – one for PACAP and the other one for NT-proBNP determination. Because of the polypeptide nature of PACAP we had to use protease inhibitor (200 µl aprotinin (1.4 mg/ml) into 10 ml blood) and ice water bath for storage the tubes to avoid peptide degradation. Radioimmunoassay (RIA) method was used for the analysis of the PACAP38-like immunoreactivity (LI) of blood samples.

Results: In the group of mild heart failure patients a significant strong negative correlation was detected. Furthermore, in moderate heart failure we found a significant moderate negative correlation between PACAP and NT-proBNP levels only in ischemic subgroup. Positive correlation was found between serum PACAP level and ejection fraction only in patients with heart failure due to ischemic cardiomyopathy but not in patients with primary dilated cardiomyopathy.

Conclusions: In summary, remarkable differences were observed between the ischemic and non-ischemic heart failure suggesting that PACAP might play an important role in the pathomechanism and progression of ischemic heart failure and it might be a potential biomarker of cardiac diseases in the future.

A PHASE 2, SINGLE-DOSE, OPEN-LABEL STUDY TO INVESTIGATE THE SAFETY AND EFFICACY OF OTL38 INJECTION (OTL38) FOR INTRA-OPERATIVE IMAGING OF FOLATE RECEPTOR-ALPHA POSITIVE OVARIAN CANCER

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Aim: OTL38 is a folate ligand conjugated with an indole-cyanine green dye. The objectives of this clinical trial were to assess the sensitivity and positive predictive value (PPV) of OTL38 in detecting Folate Receptor-alpha (FR α +) ovarian cancer during surgery and to assess the safety and tolerability of single IV doses of OTL38.

Methods: Patients with ovarian, tubal, or peritoneal cancer planned for primary, interval, or secondary cytoreductive surgery were eligible to receive a single dose of OTL38 (0.025 mg/kg) 2-3 hours preoperatively. Intraoperative near-infrared (NIR) imaging was used to visualize target FR α lesions for resection. Lesions were designated by the investigator as visible by normal light and/or by NIR imaging, and the presence or absence of malignant cells was subsequently examined by histology and FR α immunohistochemistry (IHC). A modified intent to treat (mITT) population of lesions from all patients who received OTL38-NIR imaging, underwent cytoreductive surgery, and had at least one FR α target lesion was used to determine sensitivity and PPV. Two generalized linear models were employed to evaluate sensitivity and PPV and to control for possible intrapatient correlations among lesions.

Results: A total of 48 patients were enrolled. A total 225 lesions from 29 patients in the mITT population were evaluated for sensitivity and PPV of OTL38 in detecting FR α ovarian cancer. Only those lesions that tested positive for both ovarian cancer (pathology) and FR α (immunohistochemistry), or a negative result for both tests were included in the primary analysis. The results of a GLMM analysis accounting for the possible correlation of lesions within patient (includes a random effect for patient) yielded an estimate for sensitivity of 97.97%, with a 95% lower one-sided CI = 87.75. The estimate for PPV was 94.93% with a 95% lower one-sided CI = 86.13. A GLM analysis assuming no correlation of lesions within patient (excludes a random effect for patient) resulted in an estimated sensitivity of 85.93%, with a 95% lower one-sided CI = 81.19. The estimate for PPV was 88.14% with a 95% lower one-sided CI = 83.59. A total of 48.3% (14/29, (95% CI 0.29-0.67)) of patients had at least one additional pathology-confirmed lesion detected by OTL38 that was not identified by normal light or palpation. There were 8 (18.2%) patients with a study drug-related adverse event which were mild or moderate in severity and resolved within 1 day of onset.

Conclusions: OTL38-NIR was a safe and efficacious intraoperative imaging tool in this preliminary phase 2 study and merits further evaluation in an upcoming phase 3 trial.

INTRACAVERNOUS ANEURYSMS OF THE INTERNAL CAROTID ARTERY – TREAT IT OR NOT?

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Timea Tarjan is a 6th year medical student at Semmelweis University, Budapest. She will be spending her Surgery and Neurology practice at Houston Methodist Hospital from September until December.

Aim: To analyze the clinical benefit of invasive therapeutic modalities for the treatment of saccular intracavernous internal carotid artery aneurysms (ICAICAs).

Methods: Prospectively collected clinical data of 23 patients with ICAICA treated endovascularly in the National Institute of Neurosurgery were retrospectively analysed as part of an international multicentre study. Multiple flow diverters were applied in 19 patients, single flow diverter in 2, stent assisted coiling in 1 and parent artery occlusion without bypass in 1 patient. We assessed

- A) the technical success rate,
- B) the periprocedural complication rate,
- C) the efficacy of treatment on clinical symptoms (48 months mean follow up).

Results:

- A) The treatment was technically successful in 22/23 patients with no residual flow in the aneurysm at the last imaging.
- B) Perioperative complications occurred in 6 patients, 2/6 lead to residual neurological deficit.
- C) Efficacy on clinical symptoms: at last follow up the symptoms resolved completely in 10/22 patients (8 ptosis, 14 n. III., 1 n. IV., 12 n. VI. plegia, 6 trigeminal neuralgia); improved partially in 8/22, remained stable in 4/22 and deteriorated in 1/22 patient. One asymptomatic patient with incidentally detected aneurysm remained asymptomatic after treatment.

Conclusions: Neurointerventional treatment of cavernous carotid aneurysms is demanding but associated with high technical success rate. Analysis of a large scale database collected by the international multicenter study may reveal the true value of invasive treatment in this subgroup of patients.

MULTIMODALITY IMAGING IN INFLAMMATORY BOWEL DISEASE

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Dr. Zsolt Tarjan was an Associate Professor in the Department of Radiology at Semmelweis University. He worked in the United Kingdom in the past 8 years and returned to Hungary recently to lead a new project in Bajcsy-Zsillinszky Hospital.

Aim: The aim of this presentation is to demonstrate the diagnostic armamentarium of various radiological modalities in IBD.

Methods: Comparative examinations have been performed in the past 15 years for different aspects of IBD including small bowel ultrasound, transrectal, transvaginal, perineal ultrasound, perineal MRI, contrast enhanced ultrasound, oral contrast ultrasound, Leucocyte scintigraphy, PET-CT, small bowel enteroclysis, CT enteroclysis, CT enterography, MR enterography, CT colonography, virtual colonography and virtual enterography.

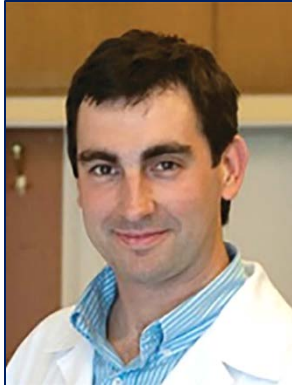
Results: The radiological imaging in CD is needed for lesions not reachable by the endoscope, for categorizing, for follow-up and detecting complications. Different modalities fit best for these different tasks. The goal of imaging in UC is rather to help differential diagnosis and detection of complications. While in UC there are good correlation between laboratory and endoscopic signs of activity and severity so there is not much need for radiological activity indices, in CD the clinical activity does not correlate with the histological changes. Although CDAI is widely used for clinical studies, it includes several subjective factors, thus radiological activity indices may be of help. The results of multiple prior studies of our research group in this field are summarized together with review of evidences from the current literature and personal experiences will be shown.

Conclusions: Although published evidences are available, there are substantial differences in the practice in the diagnostic workup and follow up of IBD based on access of the methods and local experience. Personal suggestions are going to be shown with emphasis on the differences in the US, GB and EU practice.

COMPREHENSIVE ULTRASONOGRAPHIC EVALUATION OF THE BACKGROUND OF THE DEVELOPMENT OF CAROTID AND FEMORAL ATHEROSCLEROTIC PLAQUES IN TWINS

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Dr. Adam Tarnoki graduated from Semmelweis University in 2008 and completed a residency in radiology at that institution. He is currently an Assistant Professor at the Department of Radiology at Semmelweis University and serves as Vice President of the Hungary Chapter of the HMAA.

Aim: Development of carotid and femoral atherosclerotic plaques proved to be heritable in previous studies. However, no comprehensive ultrasonographic evaluation of the volume and types of plaque has been performed, which affects the treatment of different plaque types.

Methods: Comprehensive carotid and femoral 3D ultrasound examination (Samsung RS85, arterial analysis, 15MHz probe) was performed in 92 Hungarian twins (54 monozygotic, MZ and 38 dizygotic, DZ twin pairs, mean age 54 ± 13 years). The volume of plaques was automatically measured and the plaque type was grouped according to echogenicity. Raw heritability was evaluated using the Falconer formula.

Results: The heritability of the total number of carotid and femoral plaques ($C = 0.633$, $E = 0.525$) and total plaque volume ($C = 1.049$, $E = 0.585$) was not detected. Although the number of carotid plaques themselves has been found to be hereditary ($A = 0.492$), the volume of carotid and femoral plaques as well as the number of femoral plaques were not heritable. More MZ twin pairs were discordant in the presence of soft plaques in the carotid artery as DZ twin pairs, but greater similarity in femoral plaques was not detected between MZ twins, which does not indicate a genetic background. The presence of calcified and mixed echogenic carotid plaques in the MZ twins was more concordant as in DZ twins, indicating inheritance.

Conclusion: The total number and volume of carotid and femoral plaques are influenced by the environment. Different plaque types have different backgrounds: while calcified and mixed echogenic carotid plaques are more affected by genetics, soft carotid and femoral plaques are more affected by the environment.

IMAGING EPIGENETICS: THE NEW WORLD OF RADIOGENOMICS AND THE ROLE OF MICROBIOME IN TRANSLATION RESEARCH

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Aim: Imaging technology has developed rapidly over the past decade by providing emerging new imaging techniques, especially advances in MR, ultrasound and CT technique to investigate radiological phenotypes more comprehensively. Involving identical twins, who share the same genetic background, but different unique environment can help to understand how genes and the environment, including gut microbiome contribute to the development of complex diseases, combined with imaging.

Methods: We summarized the current knowledge on twin studies combined with imaging including studies dealing with epigenetics and microbiome.

Results: Combination of epigenetics with imaging can answer questions whether various imaging phenotypes can predict epigenetic modification, that are related to organ (such as brain) structure, function and metabolism, which impacts disease risk and progression. Modern ultrasound, mammography, MR, CT and molecular imaging techniques can be used to define disease endophenotypes more comprehensively. The integration of genetic imaging methods with epigenetic markers in humans appears promising, especially in neuroimaging. Noninvasive imaging tools visualize changes in disease phenotypes in vivo. This evolving development led to a new research discipline, imaging epigenetics, that will provide deeper insight into the causative pathogenetic and pathophysiological pathways through which genes and environment interrelate during life and impact physiology, pathophysiology, aging and disease, especially in monozygotic twins discordant for a chronic disease. One of the most important epigenetic markers, the gut microbiome has been also linked to various diseases, including obesity, atherosclerosis and neurodegenerative diseases. Large twin samples allow the assessment of the relationship between host genetic variation and the diversity of gut microbiomes in various diseases.

Conclusions: The knowledge on imaging epigenetics and on the role of microbiome may open doors for the development of novel biomarkers and preventive and disease-modifying treatments.

DIGITAL BREAST TOMOSYNTHESIS (DBT): AN OVERVIEW

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Aim: An overview of the theory, operation, and regulatory requirements. Comparison of Digital Breast Tomosynthesis (3D) to Full Field Digital Mammography (2D).

Methods: The physics behind Digital Breast Tomosynthesis and image reconstruction. Comparison of different vendors methods of acquisition, and to regular mammography. Dose considerations, quality assurance, and regulatory requirements.

Results: Digital Breast Tomosynthesis can reduce or eliminate the tissue overlap effect. 3D mammography can detect 41% more invasive breast cancers and reduces false positives by up to 40%.

Conclusions: Digital Breast Tomosynthesis has the potential to be used in place of Full Field Digital Mammography.

EXPANDING THE INDICATIONS FOR THE ENDOVASCULAR MANAGEMENT OF ACUTE ISCHEMIC STROKE

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Aim: Stroke is the leading cause of disability in the United States. Ischemic stroke due to occlusion of major intracranial blood vessels represents a significant proportion of acute strokes and is associated with elevated morbidity and mortality. Large trials have shown that endovascular stroke therapy (EST) is highly efficacious and safe in patients with severe symptoms presenting early after symptoms onset. Evidence has been emerging that EST may also be feasible in a broader patient population, outside previously established therapeutic indications.

Methods: We review the evolution of endovascular technology, and available scientific evidence for the treatment of acute ischemic stroke. We discuss the results of several recently published trials along with our own research data.

Results: Large randomized controlled trials published in 2014-15 included patients with severe neurological deficits due to large vessel occlusion in the brain. Target treatment times were less than 6-8 hours in most cases. The endovascular arm had higher recanalization rates and better clinical outcomes than the control population receiving conservative medical management. Additional trials in 2017 and 2018 showed successful utilization of EST for patients selected with advanced imaging outside the 6-hour window. Recent studies, including our own research, also suggest a potential benefit of EST for patients presenting with mild symptoms despite the presence of a large vessel occlusion.

Conclusions: Several recent trials have demonstrated significant benefit of EST, which has changed the landscape of acute stroke management. Emerging evidence also suggests that EST may benefit a broader patient population than previously thought.

SPREADING DEPOLARIZATION ASSOCIATED POTASSIUM WAVE INITIATES VASOCONSTRICTION IN THE MOUSE CEREBRAL CORTEX

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Reka Toth is a 5th year medical student at the Faculty of Medicine, University of Szeged, working in the Group of Cerebral Blood Flow and Metabolism for 4 years. Our main interests are focusing on secondary cellular injuries after stroke, especially the pathomechanism of cortical spreading depolarizations.

Aim: Recurrent spreading depolarizations (SD) are pathophysiological phenomena, which appear spontaneously in the injured brain. SDs exacerbate the primary injury in cerebral ischemia by augmenting the metabolic crisis. The typical hyperemic response to SD is failing and superseded by hypoperfusion under severe ischemic conditions, but the underlying mechanisms are yet unclear. Here we set out to gather evidence that the elevation of extracellular potassium concentration ($[K^+]_e$) associated with SD plays a central role in the SD coupled vasoconstrictive signaling.

Methods: Mice were anesthetized with 1% Avertin (20 μ L/g) or 1.5–2% Isoflurane. SDs were elicited in a caudal craniotomy over the parietal cortex by topical application of 1M KCl, while the DC potential signature of propagating SD events, together with the associated changes in $[K^+]_e$ and cerebral blood flow (CBF) were recorded from a rostral cranial window (n=15). In other mice (n=8), potassium imaging was achieved with two-photon microscopy, relying on a fluorescent potassium indicator dye, Asante Potassium Green 2 (APG 2).

Results: The SDs triggered raised $[K^+]_e$ over the vasoconstrictive threshold (35.5 ± 5.3 mM), which corresponded with a profound elevation of APG-2 fluorescence intensity (0.14 ± 0.03 μ F/F). Significant initial vasoconstriction was found in the pial and penetrating arterioles (penetrating a. from 16.4 ± 3.2 to 6.7 ± 5.1 μ m) synchronous with the peak of the fluorescent signal, with concomitant decrease in CBF (from 100.0 ± 0.8 to 74.0 ± 9.1 %).

Conclusions: Our results prove that remarkable increase in $[K^+]_e$ during SDs coincides in space and time with the constriction of cortical arterioles, therefore $[K^+]_e$ significantly contributes to hypoperfusion in the ischemic nervous tissue.

ELEVATED PENTRAXIN-3 IS ASSOCIATED WITH COMPLEMENT CONSUMPTION IN THE ACUTE PHASE OF THROMBOTIC MICROANGIOPATHIES

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Eszter Trojnár is a 2nd year PhD candidate of Semmelweis University, where she conducts experimental work with focus on complement mediated glomerular diseases, such as thrombotic microangiopathies (TMA). Her thesis project is to analyze the role of anti-factor H antibodies in hemolytic uremic syndrome. In addition to that she participates in multiple laboratory based investigations that explore the pathogenesis of TMA.

Aim: Pentraxin-3 (PTX-3) and C-reactive protein (CRP) have both been shown to regulate complement activation in vitro. While CRP is produced by the liver, prompt PTX-3 release is mediated by neutrophil granulocytes at local sites of activation. Thrombotic microangiopathies (TMA) are life-threatening diseases that are often accompanied by complement dysregulation and consumption. Since neither the role of PTX-3 nor that of CRP has been investigated in complement consumption in vivo, our aim was to determine the systemic pentraxin levels in acute phase TMA and to analyze their relation to the complement profile, laboratory parameters and clinical improvement of patients.

Methods: We enrolled 171 patients in this study with the diagnosis of typical hemolytic uremic syndrome (N=34), atypical HUS (N=44), secondary TMA (N=63), thrombotic thrombocytopenic purpura (TTP) (N=30) and 69 age-matched healthy individuals. PTX-3 and CRP levels, complement factors and activation parameters were determined from acute phase blood samples, while the clinical data, blood count and chemistry were collected retrospectively from patient files. Sheep red blood cell based hemolytic assay and alternative pathway (AP) activity ELISA were used to determine the in vitro effect of PTX-3 on AP activation.

Results: Pentraxin-3 levels were elevated in acute phase TMA, with the maximal PTX-3 levels observed in secondary forms associated with a higher acute phase mortality in this subgroup. PTX-3 elevation in TTP was exceptional, however the majority of these patients had high CRP. PTX-3 displayed correlation to classical laboratory parameters of TMA and we found that PTX-3, but not CRP was associated with signs of complement consumption in vivo, while PTX-3 significantly decreased the AP hemolytic activity in vitro.

Conclusions: Our results provide a detailed description of acute phase TMA patients' complement profile linked to changes in the systemic pentraxin levels. Both our in vitro and in vivo observations highlight the potential regulatory role of PTX-3 in complement-mediated tissue damage in TMA that may fuel further molecular studies on the function of PTX-3 in the pathogenesis of complement driven diseases.

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HEMATURIA, HEMOTYSIS AND HAMSTERS: A CASE STUDY

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Dr. Ujlaki is currently applying for medical residency in the US, working in the meantime as a plasma center physician in Hungary. He is an avid reader of Mesopotamian archeology, natural history, and science fiction, and enjoys scuba diving, running, and cooking.

A 48 year old male presents to his primary care physician complaining of fever, fatigue, myalgia, and headaches lasting 6 days. 2 days later, the patient develops hematuria and hemoptysis and is referred to Szent Imre Hospital for evaluation of possible Goodpasture syndrome or granulomatosis with polyangiitis. The disease is progressing rapidly and both anti-glomerular basement membrane antibody and C-ANCA ELISA are negative.

STRUCTURE AND SPECIFIC AIMS OF THE NATIONAL ONCOGENOMIC AND PERSONALIZED MEDICINE PROGRAM IN HUNGARY

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Dr. Istvan Valyi-Nagy is a specialist in hematology and oncology and the CEO of the Central Hospital of Southern Pest and National Institute of Hematology and Infectious Diseases. He is also the Primary Investigator of the National Program for Oncogenomics and Personalized Medicine.

Aim: In January 2017, the Hungarian National Oncogenomic and Personalized Medicine Program was initiated as a scientific and R&D consortial project of the Central Hospital of Southern Pest-National Institute of Hematology and Infectious Diseases (CHSP-NIHID), the National Institute of Oncology (NIO), the Oncompass Medicine, Inc. (OCM) and the 4iG Information Technology Company, Inc. (4iG). Specific aims of the first of its kind nationwide program in Eastern Europe include: 1. Development of well structured clinical, clinico-pathological, and genomic databases of selected forms of hemato-oncological diseases and solid tumors. 2. Development of computerized decision supporting tools for molecular oncoteams and the pharmaceutical reimbursement practice of the Hungarian National Health Insurance Company, 3. Easy access provision for patients to detailed molecular diagnosis and clinical trials. As an initial step, a state funding of approximately \$11,5 Mn was provided for a period of 3 years.

Methods: CHSP-NIHID and NIO are national centers for hemato-oncology, stem cell transplantation and solid tumor treatment in Hungary. Driver gene molecular targets for innovative drugs will be identified by next generation sequencing (NGS). The list of potentially effective drugs and drug combinations will be provided using computerized decision supporting tools already developed for analysis. We will employ in vitro systems for testing the effect of drug combinations using cell lines and surviving cultures from tumors of patients. Targeted kits for identifying molecular targets for specific tumor types will be developed. BigData analytical methods will be applied for the management of nationwide patient registers.

Results: The basic structure of a computerized patient database containing clinical and oncogenomic data of individual patients is under development. In the last months of 2017 a cloud-based information technological (IT) tool, the National Electronic Health Information Space (NEHIS), will start its operation and our oncological patient database will be connected to the NEHIS network. It is intended that patient data could be obtained and information distributed via NEHIS all across Hungary. Individual patients already enjoy the advantages of the advanced decision making procedures developed by partners in the consortium.

Conclusions: Hungary has a population about 10 Mn and has a „single payer” health insurance system. The gradual development of nationwide oncological patient databases connected to NEHIS will provide an optimal engine for directing patients to HiTech oncological centers, extensive use e-health applications, and interconnection of providers and payers. Personalized medicine centers will produce and obtain all the necessary information for advanced patient care. The development of a One Country, One Payer, One IT System is a unique possibility to integrate individual patient care, up to date translational science, e-health methods, and computerized decision supporting tools to increase the quality of cancer treatment.

3D TECHNOLOGIES IN THE SUPPORT OF SURGICAL PLANNING

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Peter Varga graduated from the University of Pecs Medical School in 2015. He is one of the founding members of the 3D Printing Center of the University of Pecs. His research focuses on 3D technologies in personalized medicine.

Aim: Additive manufacturing solutions become more and more widely used in surgical planning. Several applications are well described in the literature like personalized surgical guides, endo- and exoprosthesis, software-based planning, patient education tools, etc. As a research group report, this talk intends to present our so far completed cases that profited from 3D printing and 3D software technologies.

Methods: We compared the feasibility of three life-sized 3D printed models in different orthopedic, cardiac surgery and pediatric surgery cases. We have created patient-specific heart models that were not only involved in pre-surgical planning but in designing a patch cutting guide as well. A software-based method (finite element analysis) was also involved in our studies to achieve the most advantageous functional outcome.

Results: We found that life-sized 3D printed models can be beneficially applied in perioperative planning. When combined with software-based planning methods of finite element analysis (FEA) or computational fluid dynamics (CFD) it is a more powerful tool in the hands of a surgeon. Our interdisciplinary team of doctors and engineers provided state-of-the-art solutions for numerous complicated cases.

Conclusions: 3D technologies - 3D printing, virtual planning, FEA, CFD used on patient-specific radiological data - can provide a great benefit in complicated cases.

DEIMINATED FIBRINOGEN REFINES FIBRIN STRUCTURE AND INCREASES CHEMICAL RESISTANCE OF THROMBI

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Imre Varju earned his MD, summa cum laude, at Semmelweis University in 2011. Ever since then, his research interest has focused on the intersection of inflammation and thrombosis. He earned his PhD with a Doctoral Student Excellence Award in 2015 by Semmelweis University. During his postdoctoral experience, he won an EMBO fellowship to the National Institute for Biological Standards, UK, a Fellowship by the Hungarian Academy of Sciences, and a Fulbright Scholarship to Harvard. Besides, he also taught medical students for 8 years in 3 languages. His dual passion for science and health education brought him to the Health Communication Program of Columbia University, where he currently serves as a Lead Teaching Assistant and a full-time student supported by the University's Merit Award. He spent his summer practicum at FCB Health, a top-4 healthcare advertising firm. Currently, he also serves as a medical consultant for the Public Good Projects, focusing on social-media-mediated health interventions.

Aim: Fibrinogen is the circulating precursor protein of fibrin, the major building block of vital haemostatic clots as well as life-threatening thrombi. Peptidyl-arginyl-deiminase (PAD) enzymes recognize fibrinogen as substrate and catalyze its deimination at specific arginyl residues. The presence of deiminated forms of fibrinogen (DFg) is well-known in atherosclerotic plaques as well as in the synovia of patients with rheumatoid arthritis. At the same time, the abundance and the function of DFg in thrombi has remained unknown. However, neutrophil-released PAD enzymes are known to be critical for thrombus formation in in vivo models. As this constellation allows for the colocalization of fibrinogen and PAD enzymes, we hypothesized that DFg are present in venous thrombosis, and shape the mechanical and chemical resistance of the forming thrombus.

Methods: We employed a range of in vivo and in vitro methods to test our hypothesis. In vivo venous thrombosis was induced by incomplete ligation of inferior vena cava in anesthetized C57BL/6J mice. At various timepoints after the induction, thrombi were extracted and processed, and the presence of DFg was tested by western blot using specific anti-DFg antibodies. For the in vitro assays, model thrombi were generated from human fibrinogen previously deiminated by human PAD4. The effects of fibrinogen deimination on the structure of model thrombi was tested using scanning electron microscopy (SEM), laser scanning microscopy (LSM), turbidimetry, and permeability measurements. The effects of DFg on the mechanical properties of model thrombi were examined using atomic force microscopy (AFM) and rheometry. The effects of DFg on the chemical resistance of the model thrombi were evaluated using turbidimetry and IBIDI-plate-based lysis assays.

Results: DFg were widely present in venous thrombi formed in vivo with no significant variation in intensity over time elapsed after induction (1-24 hours). Incorporation of DFg in model thrombi decreased median fibrin fiber diameters as evidenced by SEM (122 [interquartile range: 93-135] nm for control vs. 90 [interquartile range: 72-123] nm for model thrombi containing DFg). SEM and LSM confirmed a 50% increase in fibrin fiber density in DFg-containing clots supported by a reduction of the permeability coefficient (1.45x10⁻⁸ cm² for control vs. 5.1x10⁻⁹ cm² for DFg-containing model thrombi). These structural changes were in line with an increased resistance of DFg-rich model thrombi against tissue-

type-plasminogen activator (tPA)-induced chemical degradation as evidenced by a 40% increase in time until 50% degradation in turbidimetric assays and a 18% decrease in degradation front run distance over 40 min in IBIDI-assays. At the same time, the presence of DFg decreased the mechanical stability of model thrombi based on results of rheometry and AFM-based nano-thromboelastography (20-40% decrease in maximum force amplitude).

Conclusions: Our study is the first to describe the presence of deiminated forms of fibrinogen in in vivo venous thrombosis. Our results obtained from a range of in vitro and in vivo investigations suggest that the presence of deiminated fibrinogen fine-tunes structural properties of thrombi, leading to increased chemical resistance (less sensitivity of therapeutic degrading agents such as tPA) and decreased mechanical stability (more susceptibility to embolus formation in vivo).

INTRODUCTION TO HMA-UK, YOUNGER SISTER OF HMAA. REVIEW OF DOCTORS' MIGRATION OF HUNGARIAN AND EASTERN-EUROPEAN ORIGIN SINCE EU ACCESSION

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Dr. Attila Vegh is CEO of Capio AB, one of Europe's leading healthcare companies. Prior to his current role, he was Chairman and CEO of Penta Hospitals International (PHI), the largest and fastest growing network of hospitals and clinics in Central and Eastern Europe. He also served as CEO at some of the UK's largest academic medical centres in London, Cambridge and Manchester. He delivered the fastest ever hospital turnaround in the UK. Prior to his CEO roles, he was leading large commercial transformation programs in blue-chip global companies in over 15 countries with McKinsey's, the world's leading strategy consultancy. He started his career as a doctor and has years of experience as an academic

researcher and professor. Dr. Vegh has been the founding President of the Hungarian Medical Association of United Kingdom since its start in 2014.

Aim: Introduction of the Hungarian Medical Association of UK (HMA-UK) and overview of migration of Hungarian medical professionals.

Methods: We present the changing tendencies of medical migration in the EU and the background of these changes.

Results: The HMA-UK serves approx. 1,700 doctors of Hungarian origin practicing and living in the United Kingdom. Since Hungary joined the European Union in 2004, doctors' migration from the East and South of Europe towards the West has seen unprecedented scale, the East training a significant portion of Western clinical workforce. During the first 10 years of EU membership, close to 50% of fresh graduates considered leaving their homeland in several Eastern-European countries, with approximately 15-20% leaving every year. These trends have been slowing down since 2012/14, once CEE economies started dramatically improving, translating to higher salaries. Although scale of migration is reducing, given aging medical workforce with one third above 55 years of age, these positive trends need further improvements and reverting.

Conclusions: The HMA-UK focuses on two objectives:

1. To create a strong support network for its members for cooperation, mutual support, networking and professional development.
2. To create links between Hungary and UK, foster opportunities for return to practice in home country, and invite students and residents for organized study trips in the UK.

MANAGEMENT OF CONGESTIVE HEART FAILURE FOCUSING ON NON-PHARMACOLOGICAL TREATMENT

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Prof Dr Gabor Veress is the Director of State Heart Hospital in Balatonfüred. He is an active cardiologist and cardiac rehabilitation specialist. During his leadership in the last 20 years the Heart Hospital of Balatonfüred evolved into an invasive cardiology center of Veszprem county.

Aim: Heart failure (HF) is considered an epidemic disease in the modern world affecting approximately 1% to 2% of adult population and 3% to 4% of adults aged over 65 years. At present, approximately 26 million people worldwide are living with HF. The outlook for such patients is poor, with survival rates worse than those for bowel, breast or prostate cancer together. Currently, HF is the main reason of hospitalization for patients aged over 65 and it imposes a significant economic burden on health care systems. HF occurs, usually as a consequence of coronary artery disease or hypertension, and causes breathlessness, effort intolerance, fluid retention, and increased mortality. The 5-year mortality in people with systolic HF ranges from 25% to 75%, often owing to sudden death following ventricular arrhythmias. The aim of our work was to study the effectivity of non-pharmacological treatment options in patients with congestive HF.

Methods: Besides optimal drug treatment, under special clinical circumstances, we implanted modern pacemakers, automatic defibrillators (ICD) and biventricular pacemakers (resynchronisation PM-therapy) into our patients.

Results: Growing evidence demonstrates reduced morbidity and mortality when patients with HF with reduced ejection fraction (HFrEF) are treated with an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB), a beta-blocker (BB), and a mineralocorticoid/aldosterone receptor antagonist (MRA) in appropriate doses. Besides optimal drug treatment non-pharmacological treatment, such as open heart surgery, coronary interventions, TAVI, ICD, PM, CRT and mechanical therapies including VADS are useful particularly in the management of HF patients with refractory symptoms.

Conclusions: According to our observations, these non-pharmacological treatments improve the life expectancy and quality of life of patients with congestive HF.

AUTOIMMUNE CYTOPENIAS IN PRIMARY IMMUNODEFICIENCIES WITH RECOMBINATION ACTIVATING GENE DEFECTS

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Dr. Walter's early training was at the University of Pecs in Hungary, where she received her MD in 1996 and PhD in virology in 2002. She was a research fellow in infectious diseases at the Center for Pediatric Research at the East Virginia Medical School in Norfolk, VA, completed her pediatric residency at Children's Hospital of the King's Daughters, EVMS, and her fellowship in pediatric allergy and immunology at Boston Children's Hospital, Harvard Medical School. She served as a Research Assistant Professor at EVMS, and more recently as an Instructor and Assistant Professor at Harvard Medical School. Prior to joining

University of South Florida (USF), Dr. Walter was the Director of the Pediatric Immunodeficiency Program and Principal Investigator for the Center for Immunology and Inflammatory Diseases at the Massachusetts General Hospital and remains affiliated as an Immunologist Consultant with the hospital. Currently Dr. Walter is the Robert A. Good Chair and Division Chief in Pediatric Allergy/Immunology at University of South Florida and Johns Hopkins All Children's Hospital. She continues with translational research in Immunology through human studies and animal models. Her focus is mechanistic understanding of combined immunodeficiencies and immune dysregulation. She also collaborates nationally and internationally in genetic evaluation of patients with primary immunodeficiencies and advocates for targeted therapies based on the underlying disorder of the immune system.

Aim: Hypomorphic mutations of recombination activating genes 1 and 2 (RAG1/2) results in partial RAG activity and causes a wide spectrum of clinical disease with phenotypes consistent with leaky severe combined immunodeficiency (SCID), Omenn Syndrome (OS), and combined immunodeficiency with granuloma and/or autoimmunity (CID-G/AI). Within patients displaying these phenotypes, we have identified the presence of autoantibodies targeting a wide variety of self-antigens, including multiple cytokines, red blood cells and platelets. While autoimmunity secondary to RAG deficiency has been associated with delayed diagnosis, multiple systemic complications, and even death, our current understanding is limited primarily to case series. It is also unclear if abnormal T cells and/or intrinsic early B cell defect contributes to this phenomenon. Throughout our study, we reviewed the literature and our own database for clinical presentation and treatment outcome of patients with RAG deficiency and autoimmunity. In addition, we also examined T and B cell development, behavior and tolerance checkpoints that may contribute to autoreactive phenotype and autoantibody production in partial RAG deficiency.

Methods: In reviewing the literature and our own database, we identified 85 patients with confirmed RAG deficiency and further compiled the largest cohort to date of 63 patients with prominent autoimmune and/or hyperinflammatory pathology. In this cohort, diagnosis of RAG deficiency was delayed a median of 5 years from the first clinical signs of immune dysregulation. The majority of patients (52.4%) presented with more than one complication indicative of immune dysregulation, with the most common etiologies being cytopenias (85.7%), granulomas (23.8.6%), and inflammatory skin disorders (20.6%). Infections, including live viral vaccinations, were an inciting trigger for autoimmunity in 36.5% of cases. Burden of autoimmune disease management was substantial and included transplantation in 19 cases (42.2% of total HSCT). Cytopenias had early onset (median 1.9, 2.1, and 2.6 years for autoimmune hemolytic anemia (AIHA), immune thrombocytopenia (ITP) and autoimmune neutropenia (AN) respectively), and were refractory to IVIG, steroids, and rituximab in the majority of cases (64.7%, 73.7%, and 71.4% for AIHA, ITP, and AN, respectively). Evans syndrome in particular was associated with lack of response to first-line treatment.

Results: In the patients (n=10), a significant reduction in the transitional and mature naive B cell compartment are observed with an expansion of CD38- "activated" naive B cells. Mature naive B cell compartment are enriched in polyreactive clones when compared to the healthy controls. The memory B cell compartment was skewed towards non-

switched and marginal zone subsets. In vitro activation assay revealed increased tendency of mature naïve B cells isolated from patients to develop into both memory B cells and plasma cells. Tfh cells are expanded and display an activated phenotype compared to healthy donors. In vitro functional assay revealed that Tfh cells from RAG deficient patients provide stronger stimulus to naive B cells for activation, class-switching and maturation to antibody-secreting plasma cells. Accordingly, patient Tfh cells express costimulatory molecules and produce more IL-21 cytokine at a higher level compared to healthy donor Tfh cells.

Conclusions: In summary, autoimmunity can be a presenting sign of RAG deficiency and should prompt further evaluation. Multi-lineage cytopenias in particular are often refractory to immunosuppressive treatment and may require hematopoietic cell transplantation. Immune dysregulation includes both B and T cell tolerance checkpoints.

COVERED ENDOVASCULAR RECONSTRUCTION OF AORTIC BIFURCATION (CERAB) AN ALTERNATIVE TO TRADITIONAL REVASCULARIZATION IN AORTO-ILIAC OCCLUSIVE DISEASE

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Dr. Winkler was born in Budapest and attended Arany Janos Gimnazium (1982-1986). He attended medical school in Frankfurt am Main, Johann Wolfgang Goethe Universitat. He has been living in the US since 1995. He completed a surgical residency at Temple University and vascular fellowship at Pennsylvania Hospital, Philadelphia, PA.

Aim: Aorto-iliac revascularization for occlusive arterial disease has evolved over the years. More and more minimally invasive treatment options are available. We present our experience with a newer alternative to aorto-bifemoral bypass surgery and bilateral aorto-iliac stenting by using a bifurcated covered stent graft for the reconstruction of the aorto-iliac segment.

Methods: We reviewed the available literature with regard to CERAB and conducted a retrospective review of patients' charts treated with this procedure at our institution.

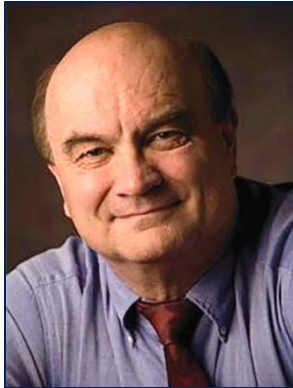
Results: A total of 19 patients were treated at our institution with CERAB over the last 5 years. Primary patency rate was 89% (17/19) and secondary patency rate was 100% (19/19). This was comparable to reported data.

Conclusions: CERAB is an excellent alternative treatment for aorto-iliac revascularization with very good primary and secondary patency rates. CERAB also allowed for subsequent distal endovascular revascularization procedures which is often needed in this patient population.

DISEASE OF THE CENTURY: DEMENTIAS

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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.

Cognition is that operation of the mind process by which we become aware of objects of thought and perception, including all aspects of perceiving, thinking and remembering. The dementias are a progressive, debilitating and presently incurable set of conditions characterized by neurodegeneration with a severe decline in cognitive functioning, including memory and communication. It is a permanent and progressive disease that eventually renders people unable to care for themselves. 5.7 million Americans are living with Alzheimer's. By 2050, this number is projected to rise to nearly 14 million.

Under the umbrella of dementia a lot of different types of dementias exist. During the presentation the author will detail the characteristic features of the different types of dementias. He will also present the pathologic changes in the brain in dementias, the diagnostic stools, and the limited treatment options for the dementias. The current research's result will be discussed also.

In our ageing, society tackling dementia is one of the biggest challenges facing the WHO and care system in the 21st century. There is a need for large-scale, prospective international, community-based study of dementia, to explore more closely the risk factors to plan preventive strategies. Talking to scientists, it became clear that probable a new way of researching the disease is needed. Future research may be helpful in fostering the development of effective treatments or cure for patient with dementias. "By bringing together the best scientific minds to discover the causes of these terrible diseases, we can and will beat them."

TRENDS IN ACUTE STROKE MANAGEMENT: OUR EXPERIENCE

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Aim: To review and give an overview of acute stroke care, stroke chain highlights and data from our institution.

Methods: TPA is administered to appropriate patients who meet the NIHSS score and inclusion criteria guidelines. In case of TPA induced ICH, no current evidence-based guidelines are available to guide medical management of TPA reversal, however there are empirical protocols with some physiological rationale that are in use, such as thrombectomy. All candidates for possible mechanical thrombectomy (as per CT Angiography findings) are transferred to the area tertiary comprehensive stroke center.

Results: Our Recent Experience at University of Maryland Capital Region Health Center (PGHC): Our hospital is a Level II trauma center, with annual patient volume of over 55,000. There are 421 inpatient beds, 23 ER beds, 24 ICU beds, 10 CCU/Acute stroke beds. Our stroke volume per representative year:

2014: Total Stroke: 270: (229 completed strokes 41 TIA); 7 received TPA; Endovascular transfer: 0

2015: Total Strokes :313: (257 strokes; 56 TIA); 11 received TPA; Endovascular transfer: 0

2016: Total Strokes :668: (636 strokes; 32 TIA); 25 received TPA; Endovascular transfer: 0

2017: Total Strokes: 768: (681 strokes: 87 TIA): 33 received TPA; Endovascular transfer: 6

2018: (Jan to June): in progress but total TPA = 17; Endovascular transfer: 10

Conclusions: Acute stroke care continues to evolve with new evidence based therapeutic modalities being added over time. Our data show that with greater public awareness of stroke symptoms, earlier presentation for treatment as well as better streamlining of the GWTG-S protocol and more efficient interplay of all emergency and medical staff personnel within the stroke care chain, better outcomes and lesser disability are possible post stroke in the general population.

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