ACE2 drives dendritic cell function and neuroantigen specific immune responses

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The renin-angiotensin system (RAS) is known for its role as a regulator of blood pressure and sodium homeostasis. Its key hormone, Angiotensin II (AngII) also modulates immune function, thereby promoting end organ damage in cardiovascular disease and autoimmune inflammation. Angiotensin converting enzyme 2 (ACE2) is a novel entity within the RAS which antagonizes actions of AngII by cleaving it into Ang1-7. We studied the role of ACE2 in murine experimental autoimmune encephalomyelitis (EAE) a disease model characterized by activation of myelin-reactive T cells that approximates key features of human multiple sclerosis. Unexpectedly, mice that lack ACE2 (ACE2ko) showed ameliorated clinical symptoms of EAE (n = 30 ACE2ko vs 33 ctrl). This was not associated with altered frequencies of splenic CD4+ and CD8+ T cell subsets, NK cells or B cells, but with a slight reduction of CD11c+ dendritic cells (DC; n = 4, p <0.05). We then tested the capacity of DC lacking ACE2 to induce myelin antigen specific T cell responses in vitro. ACE2 deficiency in DC had no effect on their ability to drive T cell proliferation but reduced their ability to induce FoxP3+ (n = 4, p <0.001) and IL-17A+ effector T cell subsets from naive CD4+ T cells by 50% (n = 4, p <0.001). In summary, ACE2 may constitute a new player in DC function with a pivotal role in driving neuroantigen specific immune responses.


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Anatomical variations in branching of the celiac trunk. Practical value in surgery

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Methods. Investigation of the medical literature resources on normal human anatomy, clinical anatomy and operative surgery.

Results. Systematical classification and description of the branches of celiac trunk, including several nonstandard cases. Variations of origin and course of the arteries of celiac trunk are not only of the anatomical interest, but also of practical and clinical importance. Knowledge on the alternative branching of the celiac trunk is important for operations such as liver transplantation, for vascular ligation and for surgical and radiological procedures around the head of the pancreas.

One of the factors exponentiating a risk of the intraoperative iatrogenic complications is the difficulty of differentiation of aberrant and additional branches of celiac trunk through the laparoscopic and laparotomic access. The surgeons see a strong reason of the intraoperative complications in atypical blood supply of organs of the abdominal cavity, which often challenges a surgeon and leads to severe complications, the frequency of which is still increasing. Undoubtedly the vascular patterns are influential in planning and performance of all the abdominal surgeries.

The ovary anatomy. Follicular cycle. Ovulation.

Supervisor(s): Normal Human, professor Anatomy Department of Voronezh N.N. Burdenko State Medical Academy
Can the anatomy of the heart be taught using 3D reconstructed CT images? A Pilot-study

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Purpose. The utility of theoretical versus practical teaching methods is still debated. Evolution of the multi-detector computed tomography (MDCT) technology has allowed for high resolution imaging and 3D reconstruction of the heart. We sought to investigate the feasibility and effectiveness of a practical approach using volume rendered CT images to teach the anatomy of the heart to first year medical students.

Methods and materials. 27 first year medical students who achieved at least 80% on their first midterm exam took part in the study. Students were randomized into three groups: theoretical lecture (TL, n=6), practical dissection (PD, n=10) and practical radiology (PR, n=11) group. All groups took part in a 1 hour course focusing on the macroscopic features of the heart using the group-specific teaching method. Effectiveness of the teaching techniques was tested by a written exam, where 25 theoretical questions were asked, and 25 features were questioned on anatomical specimens. Statistica 10 software was used for statistical analysis

Results. The PD and the PR groups scored significantly higher (p<0.05) on the theoretical exam compared to the TL group. No significant differences were seen in the practical question scores between the three groups.

Conclusions. The results show that practical methods may be more effective in teaching anatomy as compared to theoretical methods. State of the art radiological images can provide valuable help for medical students to understand complex 3D structures.

Supervisor(s): Pál Maurovich-Horvat MD, assistant lecturer Heart Center Semmelweis University, Károly Altdorfer associate professor Department of Anatomy, Histology and Embryology Semmelweis University

Characterisation of Streptococcus pneumoniae isolates from ophthalmic infections

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Introduction. Conjunctivitis can have both bacterial and viral origin, but in children S. pneumoniae is the leading pathogen. According the literature, mostly non-typeable strains are responsible for outbreaks, whereas both capsulated and non-typeable strains are involved in sporadic infections. Our aim was to examine pneumococci isolated at the Semmelweis University, during a 4-year period.

Materials and methods. Fifty-five Streptococcus pneumoniae strains were isolated from conjunctiva of patients (mean age 13,6 years) at the Semmelweis University and Debrecen, between 2009-2012. In addition to the routine laboratory methods, identity of the strains was confirmed by lytA PCR. Antibiotic susceptibility was determined by Etest for penicillin, erythromycin, clindamycin and ciprofloxacin, and by disc diffusion for cefotaxime, imipenem and linezolide. Serotyping was performed by combining conventional agglutination (Pneumotest Latex Kit and MAST antisera) and PCR.

Results. Out of the 55 strains, we could determine the serotypes in 48 cases. Great diversity was observed among the serotypes, 12 different types were identified. Serotype 19F was most frequent (n=7), followed by types H (n=6), 3 (n=5), 6A (n=4),15B (n=4), 11A (n=4), G (n=4), and types 6B, 8, 9, 10, 15A, 19A, 28F and D with (n<3). The remaining 7 isolates are either non-typable or have a very rare type which we have no means to determine. Regarding penicillin, 75% of the isolates were fully sensitive and 25% fell into the intermediate category (highest MIC was 2 mg/L). Higher resistance rates were obtained for the macrolides: 10 strains (18,5%) were resistant; 4 of these were serotype 19 and 3 non-typeables. All strains fell into the intermediate category for ciprofloxacin (MIC: 0,125-1,5), but were fully sensitive to linezolide.

Conclusions. Most of our strains (87%) were capsulated, therefore, as our results suggest, the presence of a capsule is indeed important for ocular colonisation. The great serotype diversity and variable antibiotic susceptibility patterns suggest that these were non-outbreak cases. The vaccine coverage of PCV-7 and PCV-13 would be 20,0% and 41,8%, respectively, which is higher than usually reported in the literature, due to the higher proportion of capsulated strains in this study.

Supervisor(s): Orsolya Dobay MD assistant lecturer Medical Microbiology, Adrienn Tóthpál MD research fellow Medical Microbiology, Semmelweis University
Functions of cardiovascular system fluctuate in the dependence on circadian timing. The blood pressure, Heart rate and electrophysiological properties of myocardium are affected by light-dark cycle. It is necessary to choose the right anaesthesia for making an experimental chronobiological models under in vivo conditions. Effects of Pentobarbital and Ketamine-xylazine anaesthesia on changes of ECG parameters in dependence on Light and dark cycle were compared. Adapted female Wistar rats (age 3-4 months, weight 330 ± 40 g) were used for experiments performed in two phases. (Light and Dark phase of animals day regime). ECG output was recorded and evaluated during each experiment. The results have shown that Pentobarbital anaesthesia can eliminate Light-Dark differences in individual parameters of ECG. Therefore Pentobarbital is not suitable anaesthesia for making experimental models under in vivo conditions unlike Ketamine-xylazine anaesthesia.

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Changes in PQ and QT intervals during apnoic episode and reoxygenation in rat model. Chronobiological study / I. Bačová ... [et al.]. In: Physiological Research. - ISSN 0862-8408. - Vol. 60, no. 4 (2011), s. 25P.

Chronobiological changes of ECG parameters during apnoe and reoxygenation in Wistar rats /Ivana Bačová, Pavol Švorc Jr., Imola Bračoková. - Č. projektu: VEGA 1/4303/07. In: Physiological Research. - ISSN 0862-8408. - Vol. 56, iss. 3 (2007), s. 3P.


The liposomal INH are effective against TB

Conclusion. The liposomal INH are effective against TB

Introduction. Liposomes are phospholipid vesicles with bilayer membrane structure. They can be applied to targeted and more effective drug delivery. The tuberculosis (TB) is caused by M. tuberculosis. These bacteria are able to survive in macrophages. The therapy against tuberculosis takes minimum 6 months so it can be highly toxic.

Aim. The aim of our study was to develop liposomal isoniazid against TB

Methods. We have made liposomes from dipalmitoylethanolamine-0-phosphorylcholine (DPPC), or from dioleoyl-phosphatidyl-ethanolamine (DOPE), cholesteryl hemisuccinate (CHEMS) and polyethylene-glycol related distearoylphosphatidyl-ethanolamine (DSPE-PEG). Both types were treated with ultrasound to get small unilamellar liposomes. We have used isoniazid (INH) as antituberculotics. We have measured the size of liposomes with dynamic light scattering measurements on the formulation day, than 2 and 7 days later. We have stored the samples at 4 and 20 °C. The changes of the diameter show the rate of aggregation. We have measured the drug – liposomes interaction with isotherm titration calorimetry. The liposomal drugs’ in vitro activity against TB was determined on M. tuberculosis H37Rv culture and on M. tuberculosis H37Rv infected MonoMac6 human macrophage culture. To make some in vivo study, we tried to label the liposomes with 99mTc.

Results. The radius of the DPPC vesicles has changed from 20-30 nm to 40-60 nm. The DOPE:CHEMS:DSPE-PEG liposomes did not aggregate in 7 days (Radius: 90 nm). There are more INH binding sites in the DOPE:CHEMS:DSPE-PEG liposomes than in the DPPC liposomes (3,1±0,3/1000 lipids vs. 1,7±1,6/1000 lipids). Also the binding constant is higher in the DOPE:CHEMS:DSPE-PEG liposomes (222±93/µmol vs. 44,9±23/µmol). Both liposomal drugs were effective against M. tuberculosis in vitro. On the bacterial culture the DOPE:CHEMS:DSPE-PEG liposomes have killed all of the bacteria, while there were 3 colonies after the treatment with the DPPC liposomal INH. Treating the infected macrophage culture with DOPE:CHEMS:DSPE-PEG liposomal INH was not any colony forming unit, while five times more free INH could not kill all TB bacteria. The DPPC liposomes are able to be labelled with 99mTc.

Conclusion. The liposomal INH are effective against TB bacteria in vitro. It can be a new alternative treatment against TB to decrease the therapeutic side effects and toxicity.


Developing liposomal isoniazid

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Influence of nucleogenic amino acids on the Warburg effect in primary and metastatic colon cancer cell lines under different oxygen conditions

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Introduction. The common feature of cancer cells is the Warburg effect – synthesis of abundant amounts of lactate, even in the presence of oxygen. In rapidly proliferating cells glycolysis also delivers L-serine, an essential substrate for nucleic acid and lipid biosynthesis. The another source of lactate is glutaminolysis - the pathway in which L-glutamine is also converted to L-aspartate, the substrate for nucleotide synthesis. Oxygen availability may influence lactate synthesis in relation to synthesis of L-serine from glycolysis and/or L-aspartate from glutaminolysis.

Aim. The aim of the study was to compare the effect of L-serine and L-aspartate on proliferation rate, glucose utilization and lactate synthesis (the Warburg effect) in the primary and metastatic colon cancer cells at atmospheric and tissue normoxia.

Materials and methods. The study was carried out on the primary (SW 480) and metastatic (SW 620) colon cancer cell lines. Cells were cultured at 10 and 21% oxygen in hypoxic chamber with oxygen controller. L-aspartate and/or L-serine were added to medium at physiologically relevant concentrations. Cell proliferation was determined by trypan blue exclusion assay with the use of automatic counter, glucose and lactate level with Randox kits. The Warburg effect was assessed as the lactate-glucose ratio.

Results. The proliferation rate was the most intensive for the metastatic cells cultured at 21% oxygen tension and the presence of both L-aspartate and L-serine. L-aspartate had no effect on glucose uptake neither in the primary nor in the metastatic cell lines. The most intensive glucose utilization was at the atmospheric oxygen tension in the metastatic cell line in the presence of L-serine. Lactate synthesis was increased by the L-serine and/or L-aspartate in all settings and it was the highest in the metastatic cells at 10% oxygen tension. The highest lactate-glucose ratio (5.42) was observed for L-aspartate at 10% oxygen, whereas the lowest (1.56) for L-serine at 21% oxygen tension.

Conclusions. Nucleogenic amino acids enhance the Warburg effect both in metastatic and primary colon cancer cells. The effect is more pronounced under tissue normoxia compared to atmospheric normoxia. Increased lactate-glucose ratio (≥2:1) indicates an important contribution of glutaminolysis in lactate synthesis in colon cancer cells.


Protective effect of dipeptiven solution on multiorgan injury after mesenteric ischemia

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Ischemia-reperfusion (IR) injury of small intestine is a serious complication of several surgical procedures with devastating injury to small intestine and distant organs. Aim of this experiment is to determine the impact of Dipeptiven solution pretreatment on histopathological changes in jejunum and lung tissue after IR of small intestine. Male Wistar rats (n=30) were divided into 3 groups: ischemia-reperfusion group (IR, n=12), group with Dipeptiven (con inf., 0.75 mg/kg) pretreatment, performed prior to ischemia-reperfusion (D+IR, n=12) and control group without ischemic insult (C, n=6). In both experimental groups ischemia of cranial mesenteric artery was performed in duration of 60 minutes and after 1 and 24 hours reperfusion period followed (IR1, IR24,D+IR1,D+IR24). Histopathological damage of small intestine was determined by evaluation of histopathological injury (Park-Chiu score), population of Goblet and Paneth cells (alcian blue, floxine-tartrazine), immunohistochemical (anti-Ki-67, anti-PCNA, anti-MPO). Lung injury was determined by morphometry of interalveolar septum thickness (HE), immunohistochemistry (anti-PCNA, anti-MPO, anti-CDC163). In small intestine increased MPO+ was noticed after 1 and also 24 hours of reperfusion in IR groups in comparison with pretreated groups (IR24 vs. D+IR24, p<0.001). Proliferation assessed through Ki67 and PCNA antibodies showed in both cases increased proliferation in D+IR groups after 1 and 24 hours of reperfusion in comparison with untreated groups (PCNA, IR1 vs. D+IR1, p≤0.001). Goblet cells were diminished massively in IR1, whereas in D+IR1 group their population was increased. After 24 hours of reperfusion in both group numbers were similar. Lungs morphometry of septa showed increased thickness in both reperfusion period in IR groups in comparison with dipeptiven pretreated group (IR1 vs. D+IR1, IR24 vs. D+IR24, p<0.001). Proliferation/reparation capacity of lung tissue showed increased proliferatory rate in both IR groups, whereas in D+IR groups proliferatory rate was decreased (D+IR24 vs. IR24, p<0.001). Assessment of inflammation via MPO and CDD163 resulted in their increase in IR periods (IR24 vs. D+IR24, p<0.001). Supported by APVV-0252-07, and CEMIO-ITMS-26220120058.


Supervisor(s): Štefan Tóth senior lecturer Chair and Department of Biochemistry, MD, Medical University of Warsaw
Restoration of spermatogenesis with highly differentiated sertoli cells in bilateral abdominal cryptorchidism in animal model

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Introduction. There is a growing interest among the medical community worldwide to address the issue of male infertility. One of the leading causes of male infertility is cryptorchidism. We propose specific measures as treatment for the complications of cryptorchidism and restoration of fertility. The goal of our investigation is to assess the histological changes in the testicular tissue of the animals after allogeneic transplantation of cultures, enriched with differentiated Sertoli cells.

Methods. The experiment was conducted at the laboratory of PFUR. A total of 26 out bred juvenile male rats aged between 15 and 26 days were sacrificed. All written consents were obtained from the ethics committee of PFUR. The animals were divided into four groups, with seven animals in the first three groups and five in the last group. The first stage of the study comprised of creating a model of bilateral abdominal cryptorchidism by retracting the testicles into the abdominal cavity attaching them to the anterior abdominal wall. The gonads were reduced after 90-95 days. The rats from the first group were injected with a MEM/F12 solution, enriched with highly differentiated Sertoli cells (1.2 × 10^6 K-K/100 micro liter in each testicle) and tryptophan blue dye. The second group was injected with MEM/F12 with only tryptophan blue dye. The testicles from the third group were exposed without further manipulation. The forth group was the control group, the testicles exposed after 28 days of cryptorchism. Testicles from the first three groups were analyzed for histological changes after 28 days of descent.

Results. The first group showed morphological changes in the testes with presence of regenerative processes, and recovery of spermatogenesis in convoluted the tubules, as well as the number of spermatogenous epithelium.

Conclusion. We have identified pattern of recovery and regeneration of spermatogenesis leading towards a feasible treatment for infertility due to cryptorchidism.

Supervisor(s): Vladimir A. Bychkov, Professor, DSc, PhD, MD, Department of Hospital Surgery, The Faculty of Medicine, Peoples' Friendship University Russia

The role of enhancers in semisolid preparations

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Enhancers may help absorption and/or penetration after administration in to the body. Some compounds have poor ability to pass through biological membranes, or in the case of preparations applied on the surface of the skin has no power to cross the layers.

In such cases we can elevate the property applying enhancers for both purposes. Generally chemical enhancers are small molecules help the transport of other materials in different way. E.g. they can reversibly change the structure of the skin, or by physical actions (applying current, or UV radiation) they can help the cross of the layers.

The skin has a protective function to prevent the penetration of foreign compounds, therefore the aim is to assure the entrance of the molecules through the Stratum corneum. This may be achieved by using penetration enhancers, or methods to enhance the absorption.

Among the chemical enhancers often used surface active agents, such as Span or Tween derivatives, because with lowering the surface tension between wateric and lipophilic phase the penetration is enhanced. The enhancement is studied generally with the aid of artificial membranes, Franz cell or cadaver skin in vitro.

In my work I studied the effect of surface active agents and a special group of materials, the sugar esters on the transport of metoprolol as a model drug. The results were compared in the case of ointment preparation with active compound and active material in combination of enhancer. First the liberation was tested and after the absorption in vitro was determined. The apparatuses applied were ointment cell for liberation test and Sartorius Absorption Tester for Ointments in the case of absorption studies.

The results show that among the surface active agents the lipophilic type (Span 80) enhancer in a greater extent helps the liberation than the hydrophilic one (Tween 20). In the case of sugar esters the same situation may be observed, the lipophilic type (S-370) has greater impact on liberation than the hydrophilic one (L-1695).

When the penetration (absorption) was tested, the enhancer effect of surface active type excipient was no significant, but applying sugar ester the lipophilic type doubled the penetrated amount.

It can be stated that the application of sugar ester in TTS may elevate the penetration of metoprolol through the skin.

Supervisor(s): Sylvia Marton, professor Department of Pharmacy, Semmelweis University
Adaptation of the cerebrocortical microcirculation to unilateral carotid artery occlusion: a laser-speckle study in mice
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Introduction. The cerebral circulation is capable of compensating for severe reduction in blood supply, as evidenced by the lack of neurological symptoms in most patients having unilateral internal carotid artery stenosis or occlusion. The goal of the current study was to determine the potential contribution of endothelial nitric oxide synthase (eNOS) – an essential component of circulatory homeostasis – to the acute and subacute adaptation of the cerebrocortical microcirculation after unilateral carotid artery occlusion (CAO).

Methods. Wild type (WT) and eNOS deficient (eNOS-KO) adult male mice were anesthetized using isoflurane during femoral artery cannulation, and ketamine-xylazine for the rest of the experiment. Cerebral blood flow (CBF) was measured using the laser-speckle method in the microcirculation of three cortical regions (frontal, parietal and temporal) of both hemispheres. After determination of baseline blood pressure and cerebrocortical perfusion, the left common carotid artery was ligated and acute changes in the CBF were recorded. A period of 10 minutes was allowed to observe subacute changes. Arterial blood gas and acid-base parameters were determined before the termination of the experiments and were found to be within the physiological range.

Results. CBF dropped promptly on the side of CAO in both WT and KO mice; the changes were most pronounced in the temporal region. Although there was a tendency for enhanced CBF reduction in eNOS-KO animals (-20–30% in the different regions) as compared to WTs (-15–25%), the differences didn’t reach the level of statistical significance. In the subacute phase, CBF remained reduced with most severe changes in the temporal region in both groups. The CBF reduction was significantly more marked in eNOS-KOs (-7–14%) as compared to WTs (-3–7%).

Conclusion. Unilateral CAO induces a strong acute and mild subacute CBF reduction in the ipsilateral hemisphere, which effects are most pronounced in the temporal cortex, i.e. the territory of the middle cerebral artery. The eNOS system plays an important role in the adaptation of the cerebrocortical circulation to CAO, at least in the subacute phase. Our results indicate that supporting this compensation by improving the bioavailability of NO may improve cerebrocortical perfusion after CAO in patients with impaired endothelial function.

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Our workgroup has no prior publication with these results.

Biochemical investigation of ventricular myocardial cell apoptosis in experimental arterial hypertension
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The development of chronic heart failure can be the result of the programmed death of cardiomyocytes, which are mostly deterministic cells. Thereupon this work is aimed to study animals with renovascular arterial hypertension the activity of caspase 3 and caspase 8, which are the apoptotic enzymes.

Materials and Methods. The experiment was performed on 25 male chinchilla rabbits weighing 2.4–2.7 kg. The animals were divided into 4 groups. In rabbits of the experimental group was modeled on renovascular arterial hypertension by Harry Goldblatt. In the corresponding period of research animals were dissected the hysterectomy of the hearts was made. Ventricular myocardial tissue of rabbits were ground in a homogenizer, and the resulting supernatant was used to evaluate the activity of caspase-3 and -8, which was determined by using colorimetric sets “Caspase 3 and Caspase 8 Assay Kit, Colorimetric”.

Results. Significant increase in the activity of caspase 3 in the myocardium of the left ventricle compared with the control group was observed only after 4 weeks after modeling hypertension. Later on this term the activity of caspase 8 was defined and the strong trend towards its growth was found, but the difference from the control was doubtful. Our results suggest significant increase in the intensity of apoptotic processes in the cells of left ventricular in renovascular hypertension. Unreliability of the differences in the activity of caspase 8 in the control and experimental groups of animals confirms the prevalence of mitochondrial mechanism for the initiation of cell death. In the right ventricular myocardial caspase 3 significantly increased at 2 weeks after the modeling of hypertension. With a certain activity of caspase 8 in the right ventricular myocardium in rabbits with 4-week hypertension significant differences from control values were not found. Consequently, chronic overload of the left ventricle of the heart confirmed in the published data on the early involvement of the right ventricle to the disease process.

Findings. In experimental renovascular hypertension the increase of activity of caspase 3 in the ventricular myocardium indicates the increased apoptotic processes with the myocardium with chronic heart overload. The absence of significant increase in the activity of caspase 8 indicates the initiation of the caspase cascade of mitochondrial pathway.

(Supervisor(s): Madina M. Azova, Associate Professor, PhD, MSc (Biology), Department of Biology and General Genetics, The Faculty of Medicine, Peoples’ Friendship University of Russia)
Glutathione and glutathione detoxification system in the liver of animals with streptozotocin induced diabetes

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Methods. Role of this work is to investigate the levels of reduced glutathione and activity of glutathione detoxification system (glutathione S-transferase, glutathione peroxidase) in liver of animals with streptozotocin induced diabetes. In order to achieve this, we used model of experimental streptozotocin induced diabetes in new born rats (6 control group and 6 study group) by administration of streptozotocin in the 2nd and 9th day of their life, in dose of 45 mg/kg of body mass intraperitoneally. The animals were sacrificed at the 12th week. From the liver of experimental animal we prepared 10% (w/v) homogenate in 0.25 mol/l of sucrose. We determined the reduced glutathione (GSH) by the method of Van Doorna et al (1980) using Ellmanov reagent. Activity of glutathione S-transferase were determined by the method of Habig and Jakoby (1981) using 1-chlor-2,4-dinitrobenzene as the substrate and activity of glutathione peroxidase by spectrophotometric UV-method Paglia and Valentine(1967).

Results. Amount of reduced glutathione (GSH) in the liver of diabetic animals was significantly decreased, compared to the control group (8.8 µmol/g of tissue versus 7.78 µmol/g of tissue). Activity of glutathione S-transferase (0.52 µkat/g of tissue versus 0.61 µkat/g of tissue) and also glutathione peroxidase (0.62 µkat/g of tissue versus 1.03 µkat/g of tissue) were significantly elevated compared to the control group.

Discussion. Decreased level of reduced glutathione (GSH) in the liver of diabetic animals is in agreement with the idea of increased oxidative stress in the liver of the experimental animals. Decreased levels of this important metabolite reflects its enhanced utilization and indicates the increased activity of GSH-dependent enzymes and also the decreased regeneration of the reduced form of glutathione.


Microstructure modifications of surfaces affect endothelialisation: importance for stent design

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Background. Coronary artery disease (CAD) is the leading cause of death in the developed countries. Stent implantation, combined with dilatation of stenosed arteries, is currently one of the most performed interventions in CAD, but it requires a long-term dual anti-platelet therapy (DAPT) to prevent thrombosis on extrinsic stent material and subsequent vessel occlusion. By accelerating the growth of endothelial cells on the stent surface to provide a barrier between the implant and the circulating blood, the duration of DAPT could be reduced. We analysed the effects of different microstructured surfaces on stent endothelialisation in vitro.

Methods. Differently designed, 2-5 µm high elevations or hollows were lithographically etched on silicon plates, subsequently coated with silicon carbide. As controls, smooth silicon plates, bare metal substrates, and cell culture plastic were used. Endothelialisation was assessed using human umbilical vein endothelial cells (HUVECs). The experiments in static conditions were performed using 8-well Ibidi slides (n=17), and cell attachment under arterial flow conditions was analysed using a programmed pump (n=10). To measure cell spreading and growth, actin cytoskeleton was visualised with green phallolidin. For cell counting, nuclei were stained with Hoechst 33258 stain. Images were taken with incident-light fluorescent microscope used for studies of non-transparent objects.

Results: Compared to smooth surface, 4-5 µm structures improve endothelial cell attachment and growth, whereas smaller, spiky structures (2 µm) influence endothelialisation negatively. Moreover, cell spreading is induced by larger structures (4-5 µm), whereas smaller structures (2 µm) and bare metal substrate induce cell rounding. The silicon carbide coating does not affect cell-surface interactions and shows advantages over bare metal substrate. The results obtained with silicon carbide-coated substrates were confirmed in uncoated substrates with the same structure patterns. Flow experiments were performed to simulate in vivo flow in the arteries, which positively verified the results of experiments under static conditions.

Conclusion. Microscale modifications of stent surface which accelerate endothelialisation might prove clinically beneficial by improvement of the safety profile following stent implantation.
Pattern of Use and Safety of Dietary Supplements Taken by Patients with Diabetes Mellitus Type 2 in Târgu Mures - Survey

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Although diabetic patients in Romania get an efficient treatment for free, media and public opinion favours the use of supplementary products.

Purpose. To study the patterns of dietary supplement usage and their characteristics in patients with diabetes mellitus type 2 in Mures county, Transylvania.

Materials and methods. A thorough review of supplements available in pharmacies and herb stores of Targu Mures was carried out. We analyzed the evidence-based nature of the compounds, the reported effects, side-effects, price and the quality of the leaflet. Each supplement got a mark. We have interviewed 200 patients with DM2 (mean age: 60.07 years). The questionnaire recorded the name, the cost/month, the length of the use of the supplement(s), the effect and possibly side-effects detected by patients and all the data they knew about the supplementary products used.

Results. 54.5% of the patients used some kind of dietary supplement; 22.94% used more than one. 38.5% of the patients didn’t know the mechanism of action of the dietary supplements they took. 41.3% couldn’t detect any effect after taking them. The dietary supplements recommended by doctors or books were cheaper, than those suggested by pharmacists or the media (p=0.03). Altogether, we found 69 products with 311 components. 72.46% of the products reduces blood-sugar levels, 63.76% influences the cardio-vascular risk and 15.94% helps avoiding polyneuropathy. 27.7% of the component’s claimed effects cannot be found in the scientific literature and 56% of the products may produce side-effects. Only 50% of the leaflets were adequate. The two most frequent components were the common Vaccinium extractum (bilberry extract) and Gymnema sylvestre.

Conclusion. Diabetic patients use frequently dietary supplements. Those recommended by the media, were expensive, ineffective and 8.3% even toxic. As side-effects can be found in the majority of the cases, it is advisable to take these supplements with precaution. There should be more information provided to the patients.


Supervisor(s): Dr. Mónika Szabó senior lecturer, Department of Internal Medicine, University of Medicine and Pharmacy Targu Mures, Dr. Fazakas Zita adjunct professor, Department of Internal Medicine, University of Medicine and Pharmacy Targu Mures

Reduced thrombogenicity and improved endothelial cell migration by microstructure modifications of stent surface

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Introduction. Atherosclerosis and resulting cardiovascular disease are currently the most common cause of death and illness in the world. Dilatation of stenosed arteries combined with stent implantation to keep narrowed arteries open is currently one of the most performed cardiovascular interventions, but requires a long-term therapy with anti-platelet agents to prevent stent thrombosis. Stents with microstructured surfaces should improve stent vascularisation, reduce thrombotic events and consequently shorten the length of anti-thrombotic therapy.

Methods. Differently designed, 2-5 µm high elevations or hollows were lithographically etched on silicon plates, subsequently coated with silicon carbide. As controls, smooth silicon plates, bare metal substrates, and cell culture plastic were used. The migration of human umbilical vein endothelial cell (HUVECs) was assessed in a modified barrier assay using cell culture inserts (n=10). Actin cytoskeleton was visualised with green phalloidin. Platelet concentrate and native blood were incubated on the different surfaces in static and flow conditions to investigate surface thrombogenicity (n=10). For cell counting, P-selectin antibody conjugated with fluorescein was used. Images were taken with an incident light fluorescent microscope used for studies of non-transparent objects.

Results. Comparing different types of structured surfaces, improved endothelial cell migration over 72h was observed for 4-5 µm pillow-like structures, whereas smaller spiky structures (2 µm) hollows and smooth surfaces had a negative effect on endothelial migration. Moreover, substrate specific interactions between the tested endothelial cells and the structure relief could be detected.

The thrombogenicity assays under static and flow conditions performed using whole blood and platelet concentrate showed that the platelet adhesion was reduced on larger structures as compared to smaller sharp-edged structures, hollows, or the smooth surfaces.

Conclusions. Different microstructured surfaces have strong influence on endothelial cell migration and platelet adhesion. These results will open new possibilities to design stents with improved adherence and migration of endothelial cells, and with reduced surface thrombogenicity.

“Microstructured surfaces for improved hemocompatibility and functionality of stents” Matthias Nothhaft, Christoph Lutter, Iwona Cicha, Alexander Rzany, Werner G. Daniel, Christoph D. Garlich

Supervisor(s): Christoph Garlich professor Department of Cardiology and Angiology, University Hospital Erlangen, University of Erlangen-Nuremberg, Iwona Cicha professor Department of Cardiology and Angiology, University Hospital Erlangen, University of Erlangen-Nuremberg
Remodelling of the aorta in experimental models of L-NAME- and 24-hour illumination-induced hypertension

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Introduction. Chronic blood pressure rise results in remodelling of the vascular wall. Competitive inhibition of nitric oxide synthase (NOS) by N(G)-nitro-L-arginine methyl ester (L-NAME) results in the reduced NO production and arterial hypertension development – NO-deficient hypertension. Inhibition of circadian increase of melatonin by 24-hour illumination also leads to the blood pressure increase – melatonin-deficient hypertension.

Aim. The aim was to show, whether continuous light exposure or L-NAME treatment modifies the size of aorta and expression of aortic collagen type I and type III.

Material and methods. Three groups of 3-month-old Wistar rats (eleven per group) were treated for six weeks:
- Controls, L-NAME-group and Continuous light exposure-group. Systolic blood pressure (SBP) was measured by a plethysmography each week. The thickness of tunica media of the aortic wall and inner circumference of aortic lumen were investigated and the expression of collagen type I and type III in the interstitial tissue space of tunica media was detected. The cross-sectional area of the aorta, diameter of the internal lumen, as well as the ratio of inner lumen and thickness of tunica media of the aortic wall were calculated.

Results. SBP was increased in both L-NAME and continuous light-treated groups. The thickness of tunica media of the aortic wall was increased in L-NAME-hypertension but not in continuous light-hypertension. The total collagen (collagen type I + III) volume was significantly decreased in melatonin-deficient hypertension but not in NO-deficient hypertension.

Conclusions. While L-NAME-hypertension is associated with the increased thickness of aorta, continuous light-hypertension results in a significant decrease of the total collagen volume. The results indicate that the type of the aortic remodelling depends on the pathogenetic factor inducing chronic hemodynamic overload.

Keywords. Aorta, collagen, morphometry, continuous light exposure

Simko F, Paulis L. Melatonin as a potential antihypertensive treatment. J Pineal Res

The impact of different anesthetic agents on electrical stability of the heart

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Most experiments performed on laboratory animals under in vivo conditions require using general anesthesia. Three different types of general anesthetic agents (Pentobarbital, ketamine-xylazine, Zoletil) were compared according to their ability to affect ECG parameters. Animals were divided into three groups where each anesthetic agent was applied on one group. The experiments were performed on female Wistar rats (age 3-4 months, weight 320±40 g.), previously adapted under constant conditions (light-dark regime, 12:12 hours for 4 weeks), during their active phase. ECG output was recorded and evaluated during each experiment. Significant differences were observed among the individual groups in RR, PQ, QT, QTC intervals as well as between amplitudes of P wave. Interindividual differences have revealed that the smallest variability of the middle values of the measured parameters appeared after administration of Zoletil anesthaesthesia.

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Changes in PQ and QT intervals during apnoic episode and reoxygenation in rat model. Chronobiological study / I. Baèová ... [et al.]. In: Physiological Research. - ISSN 0862-8408. - Vol. 60, no. 4 (2011), s. 25P.
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The role of the leucine-rich repeat kinase 2 (LRRK2) in development and severity of inflammatory bowel disease (IBD)

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Background. Genome Wide Association Studies (GWAS) identified the gene encoding Leucine-Rich Repeat Kinase 2 (LRRK2) as high susceptibility gene for Inflammatory Bowel Disease (IBD). As a central node in immune regulation, LRRK2 negatively regulates the expression of NFAT-depending cytokines by constraining its transfer to the nucleus. An enhanced susceptibility for IBD and increased disease severity in mice deficient in LRRK2 in an acute Dextran Sodium Sulfate (DSS) colitis model has been described. We investigated the role of LRRK2 in chronic DSS colitis in mice that is closer to human IBD.

Methods. Chronic DSS colitis was induced in LRRK2 -/- mice (KO) and wildtype mice (WT) (n=10 each) by administration of four 7-day cycles of 3 % DSS in drinking water with 10 days of recovery between the cycles. Animals were sacrificed for sample collection four weeks after the last DSS cycle. Control mice (n= 10 KO; n=10 WT) were given regular drinking water. Colitis severity was evaluated by monitoring of weight, colon length, spleen weight, myeloperoxidase (MPO) activity, colonoscopy score (murine endoscopic score of colitis, MEICS), and histological score (both performed by two independent investigators blinded to the genotype). Expression of IL-6, IL-10, IL-18, TNF, INF, iNOS, and MCP1 was determined in RNA isolated from colonic tissue and mesenterial lymph nodes by real-timePCR.

Results. None of the assessed parameters of colitis severity revealed any difference between LRKK2 -/- and WT mice. However, colon length, spleen weight, MPO activity, MEICS and histoscore showed significant differences between experimental and control group indicating successful induction of the chronic DSS colitis.

The determined mRNA levels did not disclose any significant difference from WT mice in colonic tissue or in mesenterial lymph nodes.

Conclusions. Our data show that a deficiency in LRRK2 is not accompanied by significantly higher susceptibility or disease severity in mice suffering from chronic DSS induced colitis which stands in contrast to results regarding an acute DSS induced colitis model. This leads to the hypothesis, that LRRK2 deficiency may play a major role in acute colitis which is mainly perpetuated by a hyperactive innate immune response in contrast to chronic colitis that is in turn perpetuated mostly by an overshooting adaptive immune response.


Supervisor(s): Carsten Alexander Wagner professor Institute of Physiology, University of Zurich
Acute cellular changes and histopathological injury of jejunal mucosa to intestinal heterotopic allotransplantation in rats

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Small bowel transplantation (SBTx) is sometimes only chance of solving problems concerning life threatening conditions of small intestine. Acute tissue response of small intestine graft undergoes histological alternation in course of histopathological damage, proliferatory and inflammatory response as well. The aim of presented experimental study was to analyse the histopathological changes in jejunal graft tissue in first hours after hetrotopic allotransplantation in rats. In experiment adult Wistar rats (male, 250-350 g, 12 donors – TxD, 12 recipients – TxR, 6 controls) were used. The rats were assigned into following groups: recipient group with 1 and 6 hours survival (Tx1/R, Tx6/R) and donor groups with 1 and 6 hours survival (Tx1/D, Tx6/D) and control group (C, n=6). In biopie sample following parameters were evaluated: histopathological injury index (HII), Goblet and Paneth cell population, morphometry of jejunum (HE), proliferatory activity of jejunum (anti-PCNA) and myeloperoxidase expression (anti-MPO). Determination of HII pointed out on low degree of damage in recipient samples after one and six hour of reperfusion (Tx1/B, Tx6/B) and its significant increase after one hour of reperfusion in jejunal graft samples – Tx1/D (p<0.05). The injury of jejunal graft wall was confirmed by significant reduction of the villous high and the thickness of the jejunal wall (p<0.001, resp. p<0.01). The higher PCNA expression was found in jejunal grafts 6 hours after transplantation – Tx6/D. In epithelial layer PCNA expression increased significantly (p<0.001; Tx6/D vs. Tx1/D) and were similar to those found in recipient samples and control group. Evaluation of MPO expression pointed out on significant (p<0.001) increase of MPO+ cells in Tx1/D and after 6 hours after implantation decreased value of MPO+ was marked in Tx6/D and comparable to recipient values (p<0.01) and control groups. Goblet cell determination pointed out on decreased number of both cell populations in Tx1/R and Tx6/R in comparison with donor and control group. Our experiment concerning heterotopical small intestine allotransplantation pointed out on acute tissue injury and increased of proliferatory, inflammatory and histopathological changes in jejunum in postimplantant period.

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Arsenic contamination of drinking water in Bangladesh

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Access to safe water supply is one of the most important detriment of health and socio-economic development. At present about 7-8 million tubewells to tap better quality water. These tubewell installation initiatives have contributed significantly to the halving of infant mortality over 36 years from 161 per 1000 in 1960 to 83 per 1000 in 1996. The detection of arsenic in the ground water was first made in West Bengal in 1983 and in Bangladesh in 1987. About 24.5 million people are currently chronically exposed to high levels of arsenic in drinking water derived from ground water supplied by millions of hand pump tubewells. Present experiment to identify the arsenic cases are by external manifestations especially with the presentation on the skin called melanosis and keratosis with the history of consuming arsenic contaminated water for a prolonged period.

Materials and Methods. A list of 244 patients was made. Thus in each group there were 50 patients and the groups were as follows Gp I: Drinking water from green-marked tube wells (safe water) and receiving antioxidant treatment, Gp II: Drinking water from green-marked tube wells but were not receiving antioxidant treatment, Gp III: Drinking water from red-marked tube wells (high arsenic contaminated water) and receiving antioxidant treatment, Gp IV: Drinking water from red-marked tube wells (high arsenic contaminated water) but were not receiving antioxidant treatment, Gp V: Drinking water from both red and green-marked tube wells.

Results. 95.6% of the respondents of all the groups used tube well water for drinking and cooking purposes. The respondents of group V and group I used pond water less than that of other groups. The perception of all the respondents of group I felt that they are improving from the illness by taking safe water and antioxidants regularly. The majority of respondents of group I also felt that they are improving by green arsenic safe water only. On the other hand, a few respondents of group III felt that they are improving but all other respondents felt that they are not improving at all. It was observed that the respondents who took arsenic-safe drinking water from green-marked tube well and antioxidants regularly melanosis improved. The respondents who were using red-marked tube well water and antioxidants only 2 of them improved; all other respondents either deteriorated or didn’t improve.

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Assessment of Culprit Lesions in NSTEMI versus Unstable Angina using 64 Multi-slice Computed Tomography

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Background. While several CT plaque features such as positive remodeling (PR), adjacent spotty calcification (SP) or the presence of low-density plaque (LDP) have been demonstrated to be associated with unstable plaques, it is still unknown whether their severity and extent present any differences between different types of ACS. We studied the characteristics of low density plaque (LDP) burden in patients with different types of acute coronary syndrome (ACS), using 64-slice computed tomographic (CT) assessment.

Material and Method. In 45 subjects with ACS (22 UA and 23 NSTEMI), 118 coronary plaques were evaluated using a CT multi-slice 64 acquisition including the burden with low-density atheroma, remodeling index (RI) and SP. Receiver operator characteristic (ROC) analysis was performed to calculate the cut-off points for the predictivity of plaque characteristics and transform to binominal variable. The sensitivity, specificity, positive and negative predictive values of variables was calculated. Multivariate logistic regression analysis was performed to evaluate the significant predictors for NSTEMI or UA.

Results. The presence of a plaque more than 20 mm³ in volume with a CT density <30 HU (p=0.0009) and the presence of all 3 markers of plaque vulnerability (LDP, SC or PR) (p=0.01) significantly correlated with the presence of an NSTEMI versus UA. ROC analysis of plaque features associated with NSTEMI indicated that the burden with LDP <30 HU, was a good indicator for differentiating between lesions in NSTEMI or in UA (area under the curve 0.85).

Conclusions. Culprit lesions associated with NSTEMI showed a higher burden with lower density cores than those associated with UA.


Comorbidity of anorexia nervosa

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Clinical feature of anorexia nervosa is a combination of mental and severe endocrine disorders and dissimulation of patients theirs health condition, that is why the disease is diagnosed late. Difficulties in diagnostics of anorexia nervosa are possible because of comorbidity of anorexia nervosa and other mental disorders, which often comes to the foreground in the diagnosis. The concept of comorbidity and its types in respect of anorexia nervosa is particularly difficult to describe, considering different views on its nosology.

Bulimia nervosa most authors consider as a stage version of the syndrome of anorexia nervosa, combining them into a single disease. During catamnestic research of 26 patients were identified following eating disorders: anorexia nervosa 6 (22%), bulimia nervosa 18 (71%), psychogenic vomiting 2 (7%), which evolved in the background of already existing concurrent psychopathology: organic brain damage 4 (16%), personality disorders 5 (17%). Alcoholism in 2 (7%) patients developed after the diagnosis of anorexia nervosa and bulimia nervosa. It is often replaced uncontrolled craving for food. Panic, mixed, anxiety and depression, obsessive-compulsive, hypochondriacal disorders, somatoform autonomic dysfunction occurred in 3 (13%) patients. They could mark before and after the development of eating disorders, and obsessive-compulsive disorder and hypochondriacal symptoms were part of anorexia nervosa syndrome. It should be noted that in the patients examined only 8% of cases, there is one psychiatric diagnosis. In 92% of patients there were 2 or 3 of psychiatric diagnosis. In this case, eating disorders occurs against a background other psychopathology in 45% of patients. In 44% of patients except discontent about imaginary or exaggerated obesity there were other types of dismorphism-dismorphphobia syndrom: 12% resorted to cosmetic surgery on different parts of the body and organs for the purpose of correction. As a result of of these operations occurred comorbid iatrogenic diseases. Combination with comorbid somatic and neurological disorders prior to, or complicate eating disorders was noted in 99% of cases. In 6 (22%) of the patients were noted stigmas of dys-embryogenesis. The selection of types of comorbidity in the long-term study of anorexia nervosa would show its nosologic nature and prognostic criteria for it.
Computer-assisted liver punctures with electromagnetic tracking – experiments under avoidance of disturbing effects

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Today complex punctures in the liver are being performed via CT guidance. Previous studies showed a high benefit of computer-assisting systems, working with optical tracking. Nevertheless, such systems failed to become widely accepted in the daily hospital routine, one of the reasons being the need of a direct line of sight throughout the whole procedure.

We performed five punctures with electromagnetic tracking to analyze if precise liver punctures are feasible. Five agar nodules in an explanted porcine liver in a motion simulator represented our targets.

Control CT-scans showed good positioning of the needles with a mean error of 6.1±1.8 mm. We are planning further experiments with a new field generator that protects the electromagnetic field from distortions caused by the patient stretcher.

Multimodal visibility of a modified polyzene-F-coated spherical embolic agent for liver embolization: feasibility study in a porcine model; Portal vein embolization using a Histoacryl/Lipiodol mixture before right liver resection; Superselective embolization for the management of postpancreatectomy hemorrhage: a single-center experience in 25 patient; The use of balloon-expandable stent grafts for the management of acute arterial bleeding;

Supervisor(s): Nadine Bellemann M.D. Diagnostic and Interventional Raiiology of the University-Hospital Heidelberg

CT-based attenuation corrected myocardial perfusion spect in women: preliminary results

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Background. Myocardial Perfusion Scintigraphy (MPS) is a well-established non-invasive method for the assessment of coronary artery disease (CAD). Recently published data show that MPS has a pooled sensitivity of 88% and specificity of 61%. The main limitations of the study are soft-tissue attenuation artefacts (most commonly the diaphragm in men and the breast in women) which result in the reported lower specificity.

Aim. The purpose of the study was to evaluate the performance of CT-based attenuation correction (AC) MPS in women.

Materials and methods. We studied a group of 55 consecutive female patients (mean age: 65.71±12.1) who were referred for MPS on suspicion of myocardial ischaemia, 8 of them with known CAD.

All patients underwent a 2-day Tc-99m-tetrofosmin stress/rest imaging with dipyridamole stress. Images were acquired by a Siemens Symbia T2 SPECT/CT using low-dose 2-slice CT for AC. Both corrected and uncorrected studies were evaluated with Corridor 4DM software, using 17-segments model, 5-point segmental scoring scale from 0 (normal) to 4 (absent). We determined and compared corrected and uncorrected summed stress score (SSS), summed rest score (SRS), summed difference score (SDS) of the anterior left ventricle wall (anterior, anterolateral, anteroseptal and anteroapical segments).

Results. SSS, SRS, and SDS for AC versus non-AC were 3.04±4.51 vs 2±4.03; 3±3.93 vs 1.58 vs 2.93; and 1.53±2.74 vs 1±2.18, respectively. There were statistically significant differences for SSS and SRS (p<0.005) while difference for SDS was nonsignificant (p=0.07).

Discussion. SDS values were similar, thus the quantitative assessment of ischaemia was unaffected by AC. SSS and SRS values were consistently higher with AC than without AC which might mislead the interpreting physician to describe nonexistent defects. In the background of these higher values we suspect overcorrection in several cases. However, the quality of the images acquired with AC was better than without AC making qualitative analysis easier.

Conclusion. In our patient population of 55 women, AC did not prove to provide incremental advantage in quantitative analysis, but by improving the quality of the images, it allowed a more confident qualitative analysis.


Supervisor(s): István Szilvási professor Semmelweis University Department of Nuclear Medicine, Dr. Radácsi Andrea specialist Euromedic Kft. Péterfy Hospital
Long-term complications of type 2 diabetes, depending on the body weight from birth to adulthood

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Background. The occurrence of type 2 diabetes around the world is growing increasingly higher. The low or high birth weight (SGA, LGA), depending on the gestation period, is linked to the subsequent onset of obesity. In turn, prolonged obesity is a major risk factor for diabetes.


Method and materials. During the survey, 114 diabetic patients living in and around Marosvásárhely have been examined, out of which 104 patients (53.8% women, 46.1% men) met the inclusion criteria. A detailed questionnaire was filled out with each patient. The development of their birth, childhood, adolescent, young adult, and adult weight was recorded. The use of pharmacological treatment was recorded, as well as the appearance of chronic complications of the disease (nephropathy, retinopathy, polyneuropathy and angina pectoris), by taking into consideration the moment of the disease’s onset.

Results. The patients from group LGA are all overweight and 91% of them have developed certain long term complications of diabetes. In SGA the obesity rate is the highest, in the course of different stages of life. At the same time, 73% of the overweight patients have developed long term complications of diabetes.

Conclusion. Based on the results, we found that the LGA group is highly susceptible to complications of diabetes. The SGA group presents a risk factor to childhood obesity. In the case of overweight patients, the complications develop earlier and much more quickly.

Therefore, it should be important to carefully monitor pregnancy and to raise awareness, among children and adolescents, of the negative consequences of obesity, through information campaigns.

Predictors of mortality in mechanically ventilated patients out of the ICU

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Background. All over the word, the demands for intensive care beds far exceed their availability. In Israel this shortage has lead to an unbearable situation of mechanical ventilation of patients, out of the ICU, in the internal medical wards. These patients are often rejected from being admitted into the ICU due to their advanced age and poor functional status. Being mechanically ventilated in the internal medical wards increases their morbidity and in hospital mortality.

Objectives. To define a group of patients that have the best chance to survive the mechanical ventilation in the medical wards. This information would provide essential tools for better triaging of mechanically ventilated patients from internal medical departments towards the ICU.

Methods. This is a retrospective study, reviewing charts of patients who were mechanically ventilated for the entire period in the internal medical wards, from January 1st 2009 to December 31st 2010, in Assaf Haroeh Medical Center, Israel.

Results. A total of 437 mechanically ventilated patients were included, the mean age of which were 81 and in hospital mortality of 72.3%. According to a stepwise logistic regression analysis the factors that independently predicted outcome were: respiratory indications for mechanical ventilation (OR=0.23, P<0.001), tracheostomy usage (OR=0.08, P<0.001), cardiac indication for mechanical ventilation (OR=0.17, P<0.001) creatinine level (OR=0.23, P<1.71), re-intubation (OR=5.34, P=0.01), duration of hospital stay before intubation (OR=1.14, P=0.006), age (OR=1.04, P=0.005) and had undergone CPR (OR=4.7, P=0.003).

Conclusions. The study suggests that the indication of mechanical ventilation is one of the most important factors in consideration of in hospital mortality. Respiratory and cardiac indications for mechanical ventilation as a favorite outcome whereas undergoing CPR as the worst prognosis. Other variables that have a negative affect are higher creatinine in the first day of admission, longer hospital duration stay before intubation, re-intubation and older age. These findings can serve as more objective tools for a triage of mechanically ventilated patients from the internal medical wards to the ICU. This study is especially relevant in the era of a tremendous surge in the ICU facilities demands, as the population becomes old and suffers from chronic and complex diseases, which lead to constantly searching for cheaper, yet effective solutions.

Supervisor(s): Semmelweis University Department of Pulmonology

Orvostudományi értesítő, 85. kötet, 1. különszám, the 19th Students’Scientific Conference-2012, Marosvásárhely

CLINICAL SCIENCES I.


Semmelweis International Students’ Conference-2013 — ORVOSKÉPZÉS
The economic burden of benign prostatic hyperplasia in Hungary

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Background. In Hungary the number of patients with benign prostatic hyperplasia (BPH) has been triplicated in the recent decade. The guideline on the treatment of BPH 2012 reports 140,000 patients treated with drugs and 8,000 patients treated with TURP for the year 2011. It also assumes that there are total 350,000 patients in Hungary. According to the demographic forecasts the number of patients will have been raising significantly by 2020. The question arises as to whether our health care service and its financing system are prepared for handling the higher number of patients.

Objective. To determine the disease burden of BPH in Hungary.

Methods. Using demographic statistics by age group of the Hungarian Central Statistical Office (KSH) and the results of international BPH prevalence surveys we estimated the number of BPH patients in 2011 and the expected number for the year 2020. Then a direct cost calculation of BPH was performed including the costs of drugs, outpatient care and inpatient care. Average daily medication costs were derived from the Public Drug Master Database of National Health Insurance Fund Administration (OEP). Outpatient care costs were counted from International Classification of Procedures in Medicine (ICPM, in Hungary: OENO) and the inpatient care costs were assigned from the Diagnosis Related Groups (DRG, in Hungary: HBCs).

Results. Depending on the prevalence applied for the estimation of the total number of BPH patients, we found 265,838–562,324 patients for the year 2011, that signifies 12,08–25,26% of the affected age group (40+). By 2020, 24,215–51,203 new patients are expected, the rate of increase is 10,53% in all age groups. Yearly societal disease burden of BPH: TURP 1554,6MFt, alpha-blockers 990,1 MFt, PSA test 206,4 MFt, urologist visits 157,5 MFt, finasteride 114,67 MFt prostate ultrasound 74,5 MFt. Total out-of-pocket medication costs of BPH per year are about 2764,72 MFt: alpha-blockers 389,54 MFt.

Conclusion. This study proves that the economic burden of BPH in Hungary is underestimated. There are lack of data to calculate the not health-related direct costs and the indirect costs. By performing the first BPH quality of life and cost-of-illness survey in Hungary it would become possible to make sustainable decisions in health care financing.

Supervisor(s): Attila Majoros, MD, PhD senior lecturer
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Weekly rhythm in the South African (Namibia) undergraduates or graduates students

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Weekly rhythms have no visible geophysical counterpart. Many researchers believe their socially determined and tied to the length of the working week. In favor of the biological rhythms of nature weekly rhythm say many observations, although these rhythms are much less studied than circadian or annual. The seven-day rhythm of the electrocardiogram is stored in the primary patients with angina. The seven-day periodicity of reactivity and adaptation processes revealed by the example of people taking mud treatments, treated with pharmacotherapy and physiotherapy courses. Currently, there is evidence of a possible external pacemaker for these rhythms by establishing that the interplanetary magnetic field changes its parameters with a period of about 7 days. Changes in light and magnetic field of the Earth support the existence of an oscillating circuit, while solar activity and weather factors simulate their appearance, causing a phase shift in the structure of biorhythms. There is much evidence that it is in the weekly cycle will change human performance. The literature is almost no information on chronoadaptation to 7-days rhythms students. We studied the laws of formation biorhythmic ecological and physiological mechanisms of adaptation undergraduates or graduates in chronoadaptation to studying and living at the University of Namibia. Analysis of the weekly dynamics functional reserves of students was made on Stress Index (SI). It has been shown that the average value of this index for the week was significantly higher among younger students in relation to a similar magnitude in senior students. For undergraduates SI equaled 164 ± 3.7, while the seniors it was 137 ± 2.9 units. Period with low level functional reserves of an organism in the two groups were from Wednesday until Friday and Sunday. The average value of SI in those days was significantly higher in younger student’s courses - 151 ± 3.8, while the senior students - 127 ± 3.6 units. One of mechanisms of this phenomenon can be reorganization with chronostructure weekly biorhythms of students in the course of training Thus, the understanding of 7-day biorhythms gives the chance to predict the period’s student’s chronoadaptation younger and senior a course from Namibia and is timely by an anticipation principle to take necessary measures for preventive maintenance chronoadaptation disturbance.

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Acute rheumatic fever in the new millennium

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Purpose. To study the structure and special features of modern clinical manifestations of ARF in children. Materials and Methods: A total of 44 children, aged from 4.5 to 17 years, 16 boys and 28 girls, with anacute (82%) or chronic (18%), rheumatic fever, hospitalized in Morozov Children’s Hospital between 2001 and 2011. We used standard clinical-anamnestic, laboratory and instrumental methods.

Results. Only 40% of children were admitted with a defined diagnosis of acute rheumatic fever. The most common symptom of ARF was heart disease. Carditis was diagnosed in 91% of children. Isolated carditis in 15.9%. Carditis in conjunction with arthritis and/or chorea in 72.7%. Along with this a very high frequency of extracardiac lesion (84.1%) and the growth of rheumatic chorea (40.9%) have been noted. Half of patients were admitted in severe and moderate condition. Degree of severity of the condition is defined by circulatory failure and severe inflammatory changes. Endomycarditis prevails in the structure of rheumatic heart disease (70%). Isolated endocarditis or myocarditis was diagnosed in 14% of the children. 9% of patients had severe cardiac disturbances with the development of pancarditis and circulatory deficiency (grade: IIAB, functional class: II-III). 13.6% of children affected with ARF developed combined mitral and aortic valvular disease with valvulitis of both valves, in recurrent cases 25% of patients developed above-mentioned signs, which in turn indicates the significant increase of risk of valvular impairment if recurrent ARF occurs. Combined valvular disease is more common in males than in females (3:1).

Conclusions. 1) Presumably due to decreased awareness of medical personnel, primary underdiagnosis of ARF is revealed. 2) Cardiovascular system remains the most affected system in patients with ARF. While there is a tendency to less severe cardiac impairment, 20% of patients still develop severe cardiac impairment associated with pancarditis and/or combined valvulitis of mitral and aortic valves. 3) There is a growing tendency to the development of neurorheumatism.

Supervisor(s): Valeriya A. Artamonova, Associate Professor, PhD, MD, Department of Pediatrics; Marina G. Kantemirova, Associate Professor, PhD, MD, Department of Pediatrics, The Faculty of Medicine, Peoples' Friendship University Russia

Arterial blood supply of the pancreas – a surgical anatomical study

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Introduction. Data on the blood supply of the pancreaticoduodenal anatomical-surgical unit from different countries and races are variable, therefore we aimed to investigate and analyze those arterial variations in the Hungarian population. Furthermore, we intended to correlate the variations with embryology of the pancreatic vascular bed.

Materials and methods. We examined 48 corrosion casts of human abdominal organ complexes. The resin was injected into the abdominal aorta, and the parenchyma was corroded. Thereafter, using the most widely accepted nomenclature we analyzed the casts macroscopically. Digital photographs and 3D CT images were taken.

Results. The anterior superior pancreaticoduodenal artery (ASPDa) arose from the gastroduodenal artery (GaDa) in 44 casts, in the remaining cases we found atypical origin, from the coeliac trunk (TC) (1 case) and the common hepatic artery (CHa) (1 case), from the proper hepatic artery (PHA) in 2 cases. The posterior superior pancreaticoduodenal artery (PSPDa) arose from the CHa in 3 casts, from the PHa in 2 casts and from the TC in 1 cast. The inferior pancreaticoduodenal artery (IPDa) originated from the superior mesenteric artery (SMA) with a short common trunk in 7 cases. About 50 % (25 casts) of cases displayed the variation described in the literature as the dominant one in which both an upper jejunal artery and the superior mesenteric artery contribute to the formation of IPDa. The anterior and posterior IPDa arose separately from the SMA in 16 casts. The body of the pancreas was supplied exclusively by the transverse pancreatic artery (TPa) in 3 casts and this branch arose from the SMA or the GaDa in 10 cases.

Conclusions. We described rare variants of the ASPDa, and PSPDa. The incidence of variations concerning the origin of the inferior anterior/posterior pancreaticoduodenal arteries greatly differed from the data available in the literature. The rate of TPa arising from the SMA or the GaDa was higher than those recorded in the literature. Our results stress on the importance of the detailed preoperative radiological analysis of the upper abdominal vascular structures to reduce the postoperative complications. The apparent discrepancies of published data underline the importance of the present survey in which we have begun to accumulate data relevant to Hungarian population.

The research group did not publish (without –ed) any publication about that topic previously.

Supervisor(s): László Harsányi MD professor 1st Department of Surgery, Ágnes Neméskéri MD associate professor Department of Human Morphology and Developmental Biology, Semmelweis University
Childhood pneumococcal sepsis

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Introduction. Sepsis is management a challenge to the medical community especially those caring for infants and children; however, early recognition and intervention improves the outcome for infants and children. Mortality from pediatric sepsis ranges from 9% to 35%. In the event of late recognition the mortality rate is significantly higher. Case description: A 14 month child with 10 day history of febrile fever, productive cough and convulsions presented with dyspnea, greyish skin, peripheral cyanosis, nasolabial triangle cyanosis, anuria and general adynamia at the emergency department on 16.10.11. Physical examination revealed systolic murmur, enlarged liver palpated at 3 cm. Lab diagnosis showed anemia 65 g/l, coagulopathy. Blood culture revealed pneumococcal infection. A chest CT revealed left sided polysegmental pneumonia, left sided pneumothorax, hypopericardium and 100 ml of fluid in pericardial space without any significant cardiac dysfunction. Antibiotic therapy commenced with infusion of Claforanam 1g per day. Tienam 60 mg/kg (2 weeks), Vancomycin, 3 doses of Pentaglobin totaling 7.5 g. Voltaren, Veroshpiron, Furosemide and Asparcam. On 21.11.11 the status of the child was satisfactory. No fever and catarhal symptoms. All lung fields clear without wheezing. Heart sounds moderate level and rhythmic. The abdomen was soft and painless. Decrease in size of liver (2.5 cm), with normal diuresis. The child was discharged without further complications.

Discussion. This case illustrates that an intensive and concerted antimicrobial therapy with aggressive fluid resuscitation has a favorable outcome even in significantly late admissions.

Supervisor(s): Marina G. Kantemirova, Associate Professor, PhD, MD, Department of Pediatrics, Mustafa Khaled, Department of Pediatrics, PhD candidate, MD, The Faculty of Medicine, Peoples’ Friendship University Russia

Combined method of trigeminal neuralgia surgical treatment evaluation

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Background. One of the most difficult pain syndromes known to humanity is trigeminal neuralgia. This syndrome is characterized by shooting pain in ipsilateral face that is accompanied by a filling of an electric discharges, which is amplified upon sensation of cold air, at conversation, chewing and tooth brushing. Pain never goes to another part of the face, doesn’t irradiate to the neck or ear. American neurosurgeon P. Jannetta demonstrated that if the pulsing vessel near nerve is found and taken away by teflon, neuralgia will disappear immediately (Jannetta P. et al., 1977). This method became the basis of modern surgical treatment of trigeminal neuralgia and is known as microvascular decompression of trigeminal nerve (MVD). The way of evaluating of the MVD results that was offered by the author in the 70s of XX century may require some revisions. Recently, a new scoring system for obtaining objective surgical results from MVD for trigeminal neuralgia was proposed to document treatment results using consistent criteria in a standardized manner (Kondo A. et al., 2012).

Purpose. Evaluate the results of trigeminal neuralgia MVD by combined method scale.

Materials and methods. We examined 82 patients that had undergone MVD of trigeminal nerve in Uzhhorod Regional Center of Neurosurgery and Neurology from 1997 to 2012. Patients include 39 males (48%) and 43 females (52%). Patients’ age ranged from 35 to 80 years old. The average duration of presurgical period was 7 years. We questioned patients by combined method scale and we took into account postoperative pain rate described by the following scale: completely pain-free; occasional slight pain, self-controlled, without medication; moderate pain, controllable by medication; persistent pain, not controllable by medication, not cured. The second criterion in our questionnaire was rate of surgical complications (no complications; slight cranial nerve or cerebellar dysfunction, not bothersome for daily life; both subjective and objective cranial nerve or cerebellar dysfunction, problematic for daily life). The total results of MVD for trigeminal neuralgia was evaluated and analyzed by combining the postoperative pain rate together with the complication rate.

Results. The MVD was successful in 88% of patients that were operated. The percentage of excellent scores was 37%, good-36%, fair – 15% and poor score 12%.

Conclusion. Research results showed us the high effectiveness of MVD in patients with trigeminal neuralgia. The use of combined method scale allowed us more objectively judge the results of surgical treatment and rate of surgical complications.

Supervisor(s): Volodymyr Smolanka, MD, PhD, Professor of Neurosurgery and Chairman, Department of Neurology, Psychiatry and Neurosurgery; Yuriy Chomolyak, MD, PhD, Associate Professor of Neurosurgery, Department of Neurology, Psychiatry and Neurosurgery, Uzhhorod National Universit
Evaluation of the efficacy of complex treatment of pulmonary hypertension in infants with bronchopulmonary dysplasia

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Background: Pulmonary hypertension (PH) complicates the course of bronchopulmonary dysplasia (BPD) in newborns and leads to late mortality and morbidity during infancy. It has been shown that infants with BPD in association with late PH have a mortality rate of 52% within 2 years after diagnosis. Despite recent advances in understanding the pathogenesis of PH with subsequent improvement of therapeutic strategies, few studies have been conducted to investigate the efficacy of these strategies for infants with BPD.

Objective. Evaluate efficacy and long-term results of complex therapy of severe pulmonary hypertension (PH) in infants with bronchopulmonary dysplasia (BPD). Inclusion criteria: echocardiographic features of PH (mean pulmonary artery pressure ≥35 mHg) according to the measurement of tricuspid regurgitant jet velocity (TRJV). Exclusion criteria: presence of hemodynamically significant congenital heart disease (except of patent ductus arteriosus, atrial septal defect and persistent foramen ovale).

Methods. In this study we have reviewed medical records of 10 infants with classic form of BPD who were under thorough care from 2009 through 2012. Gestational age: 25-41 weeks. All infants received mechanical ventilation (8-99 days). In 100% of cases severe form of BPD was diagnosed. The course of BPD was complicated by the development of chronic respiratory failure. Hemodynamically significant improvement was defined by ≥20% decrease in the ratio of systolic pulmonary artery pressure (sPAP) to systemic systolic blood pressure (ssBP).

Results. A median duration of sildenafil treatment was 5.5 months (2-9 months). In 9 infants (90%) hemodynamically significant improvement was achieved which was confirmed by echocardiography (p<0.005). After conducted treatment significant reduction of sBP (84±36 vs. 36±12 mmHg, p=0.005) and sPAP/ssBP were observed. Oxygen saturation: improvement was established (82±12 vs 93±4, p=0.005) and sPAP/ssBP were observed. Oxygen saturation: improvement was established (82±12 vs 93±4, p<0.005).

Conclusion. Results of the study suggest that complex therapy is effective for treatment of PH in infants with BPD.

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Genetics of infantile steroid-resistant nephrotic syndrome in the Hungarian cohort

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Steroid-resistant nephrotic syndrome (SRNS) represents a common cause of chronic renal failure in childhood. Based on its etiology, two major forms are distinguished, an immune and a genetic form. As their treatment is different, the selection of the genetic form is important, but only possible by mutational screening.

Our aim was to introduce the mutational screening of the causative genes in the Hungarian cohort of infants with SRNS. Out of a cohort of 58 patients with SRNS or nephrotic range proteinuria (>40 mg/m²/h), 10 children were diagnosed with SRNS below 1 year of age. The SRNS was isolated in all but 1 case, that of a boy with associated hypospadias giving the clinical picture of Denys-Drash syndrome. Renal biopsy, performed in 8 cases, showed diffuse mesangial sclerosis in 1, minimal change disease in 2 and focal segmental glomerulosclerosis in 5 cases. All cases were sporadic and issue of a non-consanguineous marriage. The coding exons and the adjacent intronic junctions of NPHS2, NPHS1, and PLCe1 genes and exons 8 and 9 of the WT1 gene were directly sequenced in 8, 5, 1 and 2 patients, respectively.

Five patients were found to carry a mutation in either the NPHS2 (n=2), NPHS1 (n=1) or WT1 (n=2) genes. Nephrotic syndrome was congenital in the boy with compound heterozygous NPHS1 mutations (c.468C>G, p.Y156* and c.1048T>C, p.S350P). He is currently 2 years old with a normal renal function. The two children carrying either a homozygous (c.413G>A, p.R138Q) or a heterozygous NPHS2 mutation (c.948delT, p.A317Lfs*31) presented with SRNS at the age of 3 and 8 months and progressed to end-stage renal disease (ESRD) at the age of 6 and 2.5 years, respectively. No mutation was found in the 2nd allele of the child the heterozygous NPHS2 mutation, thus its causative role in this case is not certain. The two children carrying with WT1 mutations, a boy with Denys-Drash syndrome (c.1180C>T, het., p.A394W) and a girl (c.1187A>G, het., p.D396G) presented with SRNS at the age of 2 and 3 months, respectively. Their renal function rapidly progressed to ESRD within a month. No mutation was found in PLCe1.

In accordance with the literature, at least half of the cases with infantile SRNS has a genetic origin. Their identification is clinically important in order to establish appropriate treatment, to assess the rate of progression and for genetic counseling.


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Introduction. Fabry disease (α-galactosidase A deficiency) is an X-linked lysosomal storage disorder, which causes accumulation of globotriaosylceramid in different organs. The newest and most effective treatment is enzyme replacement therapy (ERT), which decreases progression of organ damage and stabilizes the condition of the patient. Pulmonary involvement leads to obstructive ventilatory disorder and airway inflammation, however data on frequency and severity, as well as the effect of ERT on lung involvement are missing.

Methods. Eleven patients (n=5) and carriers (n=6) with known genetic mutation were screened for pulmonary manifestations including physical examination, chest x-ray, lung function test, diffusion measurement and blood gas analysis. Repetitive measurements were performed on 6 patients on ERT (average follow-up 3 years).

Results. Lung involvement was present in all patients and one carrier, all of them having also other organ involvement and required ERT (age: 34.4±13.0 years). Symptoms suggestive for lung disease were scarce, however in all patients on ERT non reversible obstructive ventilatory disorder was present (forced vital capacity (FVC) 3.5±1.1 L (87.2±16.5 %ref), forced expiratory volume in 1 second (FEV1): 2.1±0.9 L (63.3±24.7 %ref)). Blood gases, diffusion of CO, chest x-ray were normal. ERT resulted in stabilization of lung function in all treated patients (AFVC: 0.14±0.42 L (7.5±10%); FEV1: 0.13±0.31 L (7.4±14.0%)).

Conclusion. Fabry disease in affected patients and carriers results mainly in asymptomatic lung involvement, characterized by non reversible obstructive ventilatory disorder. ERT resulted in stabilization of airway obstruction during follow-up, emphasizing the importance of regular pulmonary assessment and effective therapy.

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Is it necessary to perform x-ray absorptiometry in young IBD patients to predict the risk of fracture?

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Background. Inflammatory bowel disease (IBD) patients have an increased risk of osteoporosis related fractures. Necessity of bone density measurement in IBD patients is not clearly defined, however, the risk of fracture increases among them. Fracture Risk Assessment Tool (FRAX) score computes the 10-years probability of the major osteoporotic fractures and particularly hip fracture. Clinical FRAX (c-FRAX) does not include the bone mineral density (BMD) measurement. We aimed to compare the value the c-FRAX to FRAX enhanced with dual x-ray absorptiometry (DEXA) (bmd-FRAX) in IBD patients.

Methods. 169 consecutive IBD patients (128 Crohn’s disease (CD) and 41 ulcerative colitis (UC); female/male: 88/81) were included into the study. Mean age of the patients was 35.9±11.7 years, 7.6% of them was postmenopausal women. FRAX-scores were calculated with the online tool using a Hungarian algorithm. Bone mineral density measurements were performed by DEXA. Calculations were performed using SPSS statistics 15.0 software.

Results. In patients under 40 the c-FRAX score regarding major osteoporotic fracture risk was significantly higher compared to bmd-FRAX (1.9±1.1 vs. 1.4±0.8, p<0.01). The same difference was observed computing the probability of hip fractures (c-FRAX: 0.4±0.7 vs. bmd-FRAX: 0.3±0.5; p<0.05). In a subgroup analysis the fracture risks have not differed in CD vs. UC patients. Major fracture risk c-FRAX and bmd-FRAX were 3.0±3.4% és 2.5±2.7% in CD and 3.4±3.4% and 2.5±2.4% in UC patients (non-significant (NS)). Clinical FRAX and bmd-FRAX showing hip fractures (c-FRAX: 0.4±0.7 vs. bmd-FRAX: 0.3±0.5; p<0.05). In a subgroup analysis the fracture risks have not differed in CD vs. UC patients. Major fracture risk c-FRAX and bmd-FRAX were 3.0±3.4% és 2.5±2.7% in CD and 3.4±3.4% and 2.5±2.4% in UC patients (non-significant (NS)). Clinical FRAX and bmd-FRAX showing hip fracture risk were 0.8±1.5% and 0.6±1.4% in CD and 0.8±1.3% and 0.4±0.7% in UC, respectively (NS). We did not observe any correlation between FRAX scores and calcium intake, physical activity, severity, extent- and duration of the disease. Subgroup analysis regarding steroid use and body mass index has not been performed due to the FRAX system included in these parameters.

Conclusion. Guidelines regarding IBD associated osteoporosis advise to perform the DEXA measurements in patients with some special risk factors for bone loss. In our study the fracture risk according to FRAX scores completed with DEXA were lower than clinical FRAX - especially in patients younger than 40 years. Our results suggest that DEXA enhanced FRAX may have an advantageous role in preventing over medicating young IBD patients.

About FRAX (Fracture Risk Assessment Tool): none, about osteoporosis:

Low bone mass in microscopic colitis. (2011, BMC Gastroenterol)
Clinical relevance of changes in bone metabolism in inflammatory bowel disease. (2010, World J Gastroenterol)
Comparison of the effects of 1,25 dihydroxyvitamin D and 25 hydroxyvitamin D on bone pathology and disease activity in Crohn’s disease patients (2009, Inf Bow Dis)
Osteoporosis associated with inflammatory bowel diseases (2004, Orv H)

Supervisor(s): Pál Miheller MD senior lecturer II, Department of Internal Medicine, Katalin Lőrinczy MD research fellow II, Department of Internal Medicine, Semmelweis University
Monocyte chemoattractant protein-1 (MCP-1) as a proinflammatory marker in children and adolescents with hyperuricemia.

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Introduction. Hyperuricemia is strongly associated with obesity and metabolic syndrome. It was found that uric acid induced in vitro an increase in the production (mRNA and secreted protein) of monocyte chemoattractant protein-1 (MCP-1), an adipokine playing an essential role in inducing the proinflammatory state in adipocytes in obesity.

Aim. The purpose of the study was to check:
1. the serum concentration of monocyte chemoattractant protein-1 (MCP-1) in children and adolescents with hyperuricemia,
2. the influence of obesity on MCP-1 level in hyperuricemic patients.

Patients and methods. The study involved 52 hyperuricemic patients aged mean 15.53 ± 1.7 yrs. Twenty seven healthy individuals with normal serum uric acid (SUA) level were selected as healthy controls (C). Serum MCP-1 (sMCP-1) was measured in all the participants by enzyme-linked immunosorbant assay (ELISA).

Results. The age and sex of studied children did not differ from healthy controls (p>0.05). Almost 58% of teenagers were obese. Hyperuricemic patients showed increased sMCP-1 (median: 69.58 pg/mL) vs. controls (48.39 pg/mL; p< 0.01). MCP-1 showed an inverse association with BMI Z-score (r= -0.42, p< 0.01). The obese children presented significantly higher levels of sMCP-1 (median: 81.69 pg/mL) in comparison with non-obese (median: 59.62 pg/mL; p< 0.01). The positive correlation was observed between SUA and BMI Z-score (r= 0.42, p< 0.01). MCP-1 showed an inverse association with age (p<0.05).

Conclusion. Hyperuricemia might be responsible for the increase in serum MCP-1 concentration. The obesity is an additional factor influencing the production of proinflammatory chemokine MCP-1, however the potential causal role of hyperuricemia and/or obesity in systemic inflammation needs further investigation.


The diagnostic performance of a novel lesion specific coronary artery calcium score for predicting obstructive coronary artery disease

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Introduction. Coronary Artery Calcium Scoring (CACS) is used as an independent predictor of adverse cardiac events. Use of CACS to predict obstructive coronary artery disease has also been described. Our aim was to compare the diagnostic performance of a novel Lesion Specific CACS (LS-CACS) with conventional Agatston CACS (A-CACS).

Methods. We examined 218 patients (120 male, 56±12 years) who underwent a cardiac CT scan during in the months from September to November 2012. Scans were performed with a 256-slice CT scanner (100–120 kV, 200–300 mAs/rot, 0.27s rotation time, 128×0.625mm collimation, Philips Brilliance iCT) using prospective ECG triggering – “Step-and-shoot” – mode. The CACS assessment was performed with a dedicated software developed at the Piedmont Heart institute (Atlanta, Georgia). The LS-CACS of the 4 major coronaries (left main, left anterior descending, right coronary and left circumflex artery) was quantified on the non-contrast scans. The presence of severe stenosis was defined by a diameter stenosis of ≥70% based on the coronary CT angiography images. We used CACS cutoff values that were described in prior research as giving maximal predictive ability for severe coronary stenosis: A-CACS = 790 and LS-CACS = 182. We determined the diagnostic performance of different CACS by calculating sensitivity and specificity values and area under curve (AUC) of the receiver-operating characteristic (ROC).

Results. 30 patients had ≥1 stenosed coronary. The median and IQR (interquartile range) for A-CACS was 110 (28–284) and for LS-CACS 55 (21–124). Median CACS for stenosed and non-stenosed vessels were 323 (135-625) versus 67 (21-190) for A-CACS and 110 (62-308) versus 49 (17-75) for LS-CACS (all p<0.001). Sensitivity and specificity were 20% and 98% for A-CACS, and 40% and 94% for LS-CACS, respectively. AUC values were A-CACS = 0.88, and LS-CACS = 0.87. Comparison between the ROC’s showed no significant difference (p=0.34).

Conclusion. With the predetermined cutoff values both A-CACS and LS-CACS had high specificity, which is an important test characteristic to identify patients with severe coronary artery disease. However, the relatively low sensitivity values preclude the safe rule out of severe coronary stenosis in patients with low CACS.


Supervisor(s): Pál Maurovich-Horvát MD, PhD, MPH assistant lecturer The department of Cardiovascular Imaging in the Heart and Vascular Centre, Mihály Károlyi MDPHD student The department of Cardiovascular Imaging in the Heart and Vascular Centre, Semmelweis University
Activation of soluble guanylate cyclase ameliorates renal extracellular matrix overproduction in experimental diabetes

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Introduction. The pathogenesis of diabetic nephropathy is associated with abnormalities of the NO-cGMP axis and functional imbalance of matrix metalloproteinases (MMPs) and their inhibitors (TIMPs). The PDE-5 inhibitor sildenafil has been reported to reduce extracellular matrix (ECM) production in type-2 diabetic rats. We investigated whether restoring cGMP levels by soluble guanylate cyclase (sGC) activator cinaciguat may attenuate renal ECM overproduction in type-1 diabetic rats.

Methods. Diabetes was induced in male Sprague-Dawley rats with single dose of streptozotocin (60 mg/kg). Experimental groups were (n=8/group): 1) Non-treated diabetic (DM); 2) Diabetic + cinaciguat (treated with 10 mg/kg/day per os for 8 weeks, DM-Cin); 3) Non diabetic controls (Co). Kidneys were analyzed after 8 weeks of treatment for histology and mRNA expression levels.

Results. In diabetic rats, cinaciguat treatment elevated serum cGMP levels (Co: 18±2, DM: 15±3, DM-Cin: 36±19 pmol/ml, p<0.05), reduced glomerulosclerosis (score: Co: 0.1±0.1, DM: 0.6±0.2, DM-Cin: 0.2±0.1, p<0.05) and collagen-IV expression (score: Co: 2.0±0.3, DM: 3.6±0.2, DM-Cin: 2.6±0.2, p<0.05). CTGF mRNA expression was also reduced in DM-Cin rats (relative expression, Co: 0.9±0.1, DM: 1.9±0.5, DM-Cin: 0.8±0.3, p<0.05). MMP2 expression was reduced in DM rats but restored in DM-Cin rats (Co: 0.7±0.2, DM: 0.3±0.1, DM-Cin: 0.8±0.4, p<0.05). TIMP-1 was markedly elevated in DM rats but almost normalized in DM-Cin rats (Co: 1.0±0.1, DM: 4.6±2.4, DM-Cin: 1.4±0.6, p<0.05). In contrast, MMP9 expression was reduced in both diabetic (DM and in DM-Cin) rats, regardless of treatment (Co: 1.0±0.1, DM: 0.2±0.1, DM-Cin: 0.2±0.2, p<0.05).

Conclusion. We conclude that NO-independent activation of sGC might attenuate the progression of renal ECM accumulation in type-1 diabetic rats by direct effects on MMP2 and TIMP-1 expression, indicating the potential clinical use of cinaciguat in diabetic nephropathy.


Anti-TNF-alpha treatment improves carbohydrate metabolism in patients with IBD

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Background. TNF-alpha has an important role in metabolic profile and insulin resistance. Adipose tissue has been recognized as an immune organ, secretes numerous immunomodulatory factors and seems to be a significant source of inflammatory signals known to cause insulin resistance. Although, the regulation of carbohydrate metabolism by TNF-alpha in inflammatory bowel disease (IBD) is poorly understood. Previous studies have shown increase endogenous ghrelin production among patients suffering from IBD. The aim of our study was to assess the changes of serum ghrelin levels and carbohydrate metabolism during anti-TNF-alpha therapy in IBD.

Methods. 17 IBD patients (4 with Ulcerative Colitis (UC), 13 with Crohn’s disease (CD)) were treated with biological therapy (5 mg infliximab per kg at week 0, 2, 6 and then in every 8 weeks; or adalimumab 160/80 as an induction and 40 mg/2 weeks as a maintenance therapy). Mean age of the patients was 34.2±9 years. Oral glucose tolerance test (75 gr) was performed and HbA1c, insulin levels, inflammatory and routine parameters were measured at the first visit than 3 and 12 month later. Insulin resistance calculated by homeostatic model assessment (HOMA-IR). Ghrelin levels were measured by radioimmunoassay using polyclonal rabbit-antibody. Calculations were performed using SPSS statistics 15.0 software.

Results. The insulin resistance significantly differed to the 3th and 12nd month of the therapy (HOMA-IR at week 0.: 1.40±1.02 vs. week 12.: 0.27±0.24, and month 12.: 0.20±0.38, respectively; p<0.01). Oral glucose tolerance improved at the end of the study. We observed decreasing trend in ghrelin concentrations (at week 0.: 1044.60±427.95 vs. week 12.: 957.77±170.33 vs. month 12.: 944.03±260.50; NS). There was strong correlation between ghrelin levels and hemoglobin-A1c levels (r=0.74). Ghrelin concentration did not correlate neither to clinical activity indexes (partial Mayo score: r=0.391; Crohn’s disease activity index: r=0.120457), nor inflammatory parameters (C-reactive protein: r=0.01).

Conclusion. Anti-TNF-alpha therapy improve carbohydrate metabolism in IBD patients. Improving metabolic parameters of patients treated with anti-TNF agents is an additional benefit of this kind of medications in IBD.

There was no other publication of the topic that was published by the research group.
Characterization of cell-derived microvesicles (MVs) in joint diseases

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Introduction. Microvesicles (MVs) are cell-derived membranous structures limited by a phospholipid bilayer. The assessment of MVs may give insight into the pathomechanism of various disorders and may serve as potential novel biomarkers in diseases. However, there are numerous pitfalls that may confound the correct assessment of MVs, including the presence of non-vesicular particles (protein aggregates, immune complexes) in biological fluids.

Aim. To analyze synovial fluid (SF) derived MVs from patients with osteoarthritis (OA, n=10), rheumatoid arthritis (RA, n=9) and juvenile idiopathic arthritis (JIA, n=10) by flow cytometry.

Materials and methods. MVs were identified by fluorescent membrane markers, including annexin V (a common MV marker) as well as cell-type specific surface markers by flow cytometry. Using our novel differential detergent lysis method, we differentiated MVs from protein aggregates based on their distinct detergent sensitivity.

Results. We successfully differentiated MVs from protein aggregates and immune complexes and confirmed the presence of IgM and IgG immune complexes in SF samples from patients with JIA. Using the differential detergent lysis method, we differentiated MVs from protein aggregates based on their distinct detergent sensitivity.

Conclusions. Our data suggest that joint diseases are characterized by unique MV signatures, and MVs might be used as future biomarkers.


I was actively participated in the research leading to one of the above publications.

Supervisor(s): Edit Buzás professor, Bence György assistant research fellow, Department of Genetics, Cell- and Immunobiology, Semmelweis University

Effects of Pharmacological Activation of the Soluble Guanylate Cyclase in Diabetic Cardiomyopathy

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Introduction. Cardiovascular (CV) function in diabetes is severely impaired, which involves decreased nitric oxide (NO) production of the vascular wall. The second messenger of NO signaling is cyclic guanosine monophosphate (cGMP), which is generated via the activation of soluble guanylate cyclase (sGC). Elevated intracellular cGMP-levels have been reported to exert cytoprotective effects in oxidative stress. Recently, activators of sGC such as cinaciguat have been developed. We investigated the effects of chronic activation of sGC by cinaciguat in diabetic cardiomyopathy in a rat model of Type 1 diabetes.

Methods. Type 1 diabetes was induced by a single intraperitoneal injection of streptozotocin in Sprague-Dawley rats. Diabetic rats of the treatment group were treated with 10 mg/kg/day cinaciguat via oral gavage for 8 weeks, whereas control animals received placebo. We performed left ventricular (LV) pressure-volume analysis with a Millar conductance microcatheter to assess cardiac function, and calculated sensitive contractility parameters such as preload recruitable stroke work (PRSW). In addition to our functional experiments, we also performed immunohistochemical measurements, and myocardial gene expressions were investigated with quantitative real time polymerase chain reaction (qRT-PCR).

Results. We found significantly changed myocardial expression of atrial natriuretic factor (ANF), endothelial nitric oxide synthase (eNOS) and matrix metalloproteinases (MMPs), and also observed elevated myocardial transforming growth factor-β (TGFβ) immunoreactivity in our diabetic rats compared to healthy controls. We also found decreased LV contractility (PRSW: 49.5±3.3 vs. 83.0±5.5 mmHg; p<0.05) and diastolic function (time constant of LV pressure decay, τ: 17.3±0.8 vs. 10.3±0.3 msec, p<0.05) in the untreated diabetic animals. The cinaciguat-treated diabetic rats showed improved expression of ANF, MMP-9 and TGFβ, and significantly better systolic (PRSW: 66.8±3.6 vs. 49.5±3.3 mmHg, p<0.05) and diastolic (τ: 14.9±0.6 vs. 17.3±0.8 msec, p<0.05) function compared to untreated diabetics.

Conclusions. Our results demonstrate that cinaciguat prevents diabetes-associated deleterious myocardial changes and improves diabetic cardiac dysfunction in our rat model. Pharmacological activation of sGC might represent a novel therapy approach for diabetic cardiomyopathy.


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European IPF Network: a new international database and first registry of Hungarian patients with idiopathic pulmonary fibrosis

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Introduction. Idiopathic pulmonary fibrosis (IPF) is a rare and life-threatening disease. IPF is defined as a specific form of chronic, progressive fibrosing usual interstitial pneumonia (UIP) of unknown origin, occurring primarily in older adults and limited to the lung. As in Hungary no studies about IPF exists, the Department of Pulmonology of the Semmelweis University joined a new international Program – the European IPF Network (eurIPFnet) to register patients with IPF in an online database, collect data and get an overview about our Patients with IPF.

Methods. Patients completed a detailed questionnaire about exposure to different inhalative noxa at home, work and leisure activity, symptoms and progression of their disease. Examination results preceding diagnosis of IPF were collected including blood and blood gas analysis, auto-antibody screening, six minute walk test (6MWT), detailed pulmonary function test, high resolution computer tomography (HRCT) and lung biopsies.

Results. Since March 2012 nine patients (male:female = 4:5, age 64.0 ± 12.6 years) where enrolled. Mean duration of the disease was 4.4 ± 3.9 years, most patients suffered from cough and dyspnea (both 78%). Lung function confirmed restrictive ventilatory disorder of different severity with decreased diffusion capacity of CO (FVC: 2.44 ± 1.26L, FVC%: 62.7 ± 24.1, FEV1: 1.99 ± 1.02L, FEV1%: 65.5 ± 24.8, TLC: 3.77 ± 2.34L, TLC%: 57.3 ± 25.0, DLCO%: 50.1 ± 24.5). 6MWT was variable (distance walked 407 ± 141m, saturation changed from 90 to 75%). HRCT showed in 6 cases pattern consistent or possible with UIP. Since registry started one patient died, one got lung transplanted and two patients are on the waiting list.

Conclusion. Using IPF registry a well characterized Hungarian IPF population was identified. Young Patients where all listed for lung transplantation. All patients had a significantly longer duration of the disease as compared to international mean survival time (3 to 5 years). Treatment options of older patients are not solved.

Supervisor(s): Dr. Veronika Müller associate professor, Department of Pulmonology, Semmelweis University

The effects of Kv1.3 and IKCa1 potassium channel inhibition on calcium influx of human peripheral T lymphocytes in rheumatoid arthritis

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Introduction. The transient increase of the cytoplasmic free calcium level plays a key role in the process of lymphocyte activation. Kv1.3 and IKCa1 potassium channels are important regulators of the maintenance of calcium influx during lymphocyte activation and present a possible target for selective immunomodulation.

Methods. Peripheral blood samples were drawn from 10 healthy individuals and 9 recently diagnosed RA patients. We registered the calcium influx kinetics of CD4, Th1, Th2 and CD8 cells following activation, applying a novel flow cytometry approach. We also assessed the sensitivity of the above subsets to specific inhibition of the Kv1.3 and IKCa1 potassium channels. Recordings were evaluated with our specific software. We measured the expression of Kv1.3 channel in the investigated lymphocyte subsets.

Results. The peak of calcium influx in lymphocytes isolated from RA patients is reached more rapidly, indicating that they respond more quickly to stimulation compared to controls. In healthy individuals, the inhibition of the IKCa1 channel decreased calcium influx in Th2 and CD4 cells to a lower extent than in Th1 and CD8 cells. On the contrary, the inhibition of Kv1.3 channels resulted in a larger decrease of calcium entry in Th2 and CD4 than in Th1 and CD8 cells. No difference was detected between the lymphocyte subsets in the sensitivity to IKCa1 channel inhibition among RA patients. However, specific inhibition of the Kv1.3 channel acts differentially on calcium influx kinetics in RA lymphocyte subsets. CD8 cells, which are mainly cytotoxic T lymphocytes are inhibited the most dominantly. Furthermore Th2 cells are also affected to a noteworthy extent.

Conclusion. The specific inhibitors of Kv1.3 channels seem to be unrelated to its altered expression hence functional alterations must also play a role in the detected differences.


Supervisor(s): Gergely Toldi MD PhD, First Department of Pediatrics Semmelweis University
The relationship between free radicals and pathogenesis of multiple sclerosis

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Recent studies have revealed the important role of oxidative and nitrative stress in pathogenesis of multiple sclerosis (MS). Selected markers of oxidative and nitrative damage, their mutual correlations and correlations with the state of the blood-brain barrier (BBB) in MS patients were analyzed in our study.

58 blood plasma samples of MS patients (test group) and 43 ones of healthy people (control group) were analyzed. The function of BBB in tested group was evaluated using the QA index. Total antioxidant plasma status (TAS), lipoperoxides, protein carbonyls, 3-nitrotyrosine and uric acid concentrations were measured. Student T-test and Pearson correlation coefficient were used for evaluation of statistical significance. Results are presented as average value ± SD.

Our study confirms earlier findings of decreased TAS in MS patients (1.41±0.47 mmol/l vs. 1.91±0.74 mmol/l, p<0.001) and increased lipoperoxidation (79.17±50.7 nmol/ml vs. 46.62±27.36 nmol/ml; p<0.001), which positively correlates with the state of BBB (r=0.289, n=58, p<0.05). It indicates the role of lipid peroxidation by deterioration of BBB. Elevated protein carbonyls confirmed oxidative damage of plasma proteins (0.44±0.08 nmol/mg P vs. 0.31±0.01 nmol/mg P, p<0.001), which are also attacked by nitrative stress, as proved by increased level of 3-nitrotyrosine (104.51±38.43 nmol/l vs. 21.57±3.67 nmol/l, p<0.001). Positive correlation between 3-nitrotyrosine and protein carbonyls (r=0.436, n=58, p<0.001) was also recorded. Uric acid concentration, which was physiological, negatively correlated with protein carbonyls’ level (r=0.328, n=58, p<0.05). This result suggests its role in proteins protection against oxidative stress, confirmed by positive correlation with TAS (r=0.328, n=58, p<0.05).

It can be concluded that oxidative and nitrative stress in MS patients affect a wide range of substances. It can change their properties and induce an autoimmune response. Also, it is necessary to reduce them in the therapeutic process.

Publications about free radicals in diseases

**Supervisor(s):** assoc. prof. RNDr. Jana Muchová, PhD, associate professor Institute of Medical Chemistry, Biochemistry and Clinical Biochemistry, RNDr. Terežia Kalnovičová, PhD, research fellow 1st Neurological Clinic, Medical Faculty, Comenius University in Bratislava

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Vitamin D level doesn’t correlate with disease extent and severity in Hungarian patients with inflammatory bowel diseases

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**Background.** Recent studies have shown that vitamin D has an important role in the immune regulation. Vitamin D is essential for innate and adaptive immune system, it plays an important role in the formation of immune tolerance, as well. Vitamin D deficiency has been observed in several western IBD (inflammatory bowel diseases) populations, but there is no data available about IBD patients from Eastern Europe.

**Methods.** We included 161 IBD patients (46 with UC (Ulcerative Colitis), 115 with CD (Crohn’s disease); female/male: 82/79) into the study. Mean age of the patients 35.9±11.7 years. Disease extent of UC and CD was defined based on the Montreal Classification (E1-3 and L1-3, respectively). Vitamin D insufficiency was defined as a level below 15 and 30 ng/ml, deficiency was defined as a level under 15 ng/ml. Calculations were performed using SPSS statistics 15.0 software. Paired and independent sample Student’s t-tests, Pearson correlations were applied.

**Results.** Fifty two percent of IBD patients had vitamin D insufficiency (CD: 53%, UC: 48%), 28% of them (CD: 25%, UC: 33%) had severe vitamin D deficiency. Only 20% of the IBD patients (CD: 22%, UC: 19%) had adequate vitamin D level (>30 ng/ml). The median vitamin D level was 22.74±10.61 ng/ml. Vitamin D levels did not differ regarding the type of the IBD (23.65±11.19 ng/ml vs. 19.89±7.66 in CD vs. UC; NS). There were no significant difference in vitamin D levels considering disease extent (CD-L1: 23.94±7.99 ng/ml, CD-L2: 23.79±8.62 ng/ml, CD-L3: 22.23±12.67 ng/ml; NS and UC-E1: 19.27±6.68 ng/ml, UC-E2: 19.06±6.54 ng/ml, UC-E3: 18.93±8.49 ng/ml; NS). Vitamin D concentration did not correlated neither to clinical activity indexes (partial Mayo score: r=-0.143; Crohn’s disease activity index: r=0.253) nor inflammatory parameters (C-reactive protein: r=0.008; erythrocyte sedimentation rate: r=0.012).

**Conclusion.** Vitamin D deficiency is common in Hungarian patients with IBD. In contrast with results of previously performed studies, our results show that Vitamin D concentration is independent from disease extent or severity in IBD patients. However, methodological differences of Vitamin D determination, seasonal variation of blood sample taking and other important factors need to be considered while evaluating the different results.

Nutritional influences in selected gastrointestinal diseases. (2011 Dig. Dis.)
Comparison of the effects of 1,25 dihydroxyvitamin D and 25 hydroxyvitamin D on bone pathology and disease activity in Crohn’s disease patients. (2009 Inflamm Bowel Dis.)
Osteoporosis associated with inflammatory bowel diseases. (2004 Orv Hetil.)

**Supervisor(s):** Pál Mihellér MD senior lecturer, II. Department of Internal Medicine, Kata tin Lőrinci MD research fellow II. Department of Internal Medicine, Semmelweis University

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Impacts of aligner material characteristics on aligner retention

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Aim. Nearly invisible thermoplastic appliances have become a common treatment option in orthodontics. Besides being popular for patients due to the aligners’ esthetic advantages compared to brackets, they also provide clinically significant amenities for example facilitated dental hygiene.

Aligner retention to the dental arch is critical for a successful treatment. Not only does retention allow adequate phonetics and esthetics, it defines an aligner’s functionality.

This study’s intention is to determine how certain material characteristics like elasticity, thickness and many more influence aligner retention.

Materials and methods. An upper jaw dental cast made of non-abrasive hard plastic was used to thermoform three different types of aligners (Clear-Aligner® soft (0,5 mm), Clear Aligner® medium (0,625 mm) and Clear-Aligner® hard (0,75 mm)). With Qualimeter (Emplexor® 100N) force (F stat) according to time (sec) was measured during aligner removal from the cast.

Each testing cycle was repeated four times.

Results. Clear-Aligner® soft (0,5 mm) presented the lowest force (12,18 N) for removal. The highest force (19,6 N) was measured during Clear-Aligner® hard (0,75mm) removal.

Conclusion. Less elasticity due to material thickness provides more retention. However, aligners made of thick, less elastic material may limit aligner esthetics and wearing comfort, as well as impede speech. Whereas soft, thin aligners may be more comfortable but less effective due to low retention.

1. Prevalence and distribution of permanent canine agenesis in dental paediatric and orthodontic patients in Hungary
2. Retention of Ultra Seal XT third generation fissure sealant in systematic pedodontic care
3. Prevalence of impacted permanent upper canine and its treatment in 11-18-year-old orthodontic patients

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Impacts of different Attachment shapes on aligner retention

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Aim. Attachments have expanded treatment possibilities of orthodontic aligners. By facilitating an aligners retention to the physiologically round surface of a tooth, attachments provide additional anchorage for the appliance. As a consequence of attachment invention and further development precise movements like rotation, torque and many more have become accomplishable in aligner treatment.

The purpose of this study is to evaluate aligner retention in accordance to different attachment shapes.

Materials and methods. Two upper jaw dental casts made of non-abrasive hard plastic were fabricated, each containing different attachments on all premolars (bevelled or ellipsoid – corresponding to Invisalign® attachment shapes). In order to maintain the exact attachment shape during the experimental cycle, the premolars were made of metal. Qualimeter (Emplexor® 100N) performed measurements of static force (F stat) referring to time (sec) during aligner removal from the casts. Three different types of aligners were tested on both casts in four cycles: (Clear-Aligner® soft (0,5 mm), Clear-Aligner® medium (0,625 mm) and Clear-Aligner® hard (0,75 mm)).

Results. The highest force (34,78 N) was measured during Clear-Aligner® hard (0,75mm) removal from the cast containing bevelled attachments. The ellipsoid attachments allowed aligner removal at the lowest force (14,7 N) with the Clear-Aligner® soft (0,5 mm) appliance.

Conclusion. Attachments allow appropriate retention of aligners, however, an aligner being too retentive due to the number, size and shape of attachments may create difficulties for the patient during aligner removal.

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Supervisor(s): Noémi Rózsa MD, associate professor
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Implant prosthodontics – modern imaging and data processing

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Currently, in the era of prosthodontics development, dental implants are becoming increasingly popular. With the introduction of Cone-Beam Computed Tomography, placing implants became positively safer, accurate, aesthetic and equally significant – much easier. Although besides highly accurate imaging techniques and equipment, dentists require precise programs, that would enable them to fully analyze received images. Thorough analysis of obtained data is extremely important, as it provides indispensable information which makes implant placing decisively more convenient and safer. The subject of this article is to present current imaging techniques widely used in dentistry, with particular emphasis on the possibilities of modern CBCT scanners. It contains major pros and cons of Cone-Beam CT and its comparison to the Computed Tomography. This article pays special attention to indispensably important software cooperating with the progressive CBCT scanners. The essay presents comparison of two such programs – SimPlant (Materialise) and CS 3D (Carestream Health). The purpose of it, is to facilitate to the reader dominant advantages and disadvantages of particular software, bring closer each additional capabilities of them and helps choosing the most adequate for one’s needs.

The paper has not yet been published.

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Is the use of products containing caffeine a threat to dental health of the nation?

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Clinical survey of 34 students from medical faculty at the age from 18 to 20 was conducted. After the analysis of the results patients were divided into two groups: both groups in comparison of 100% the cases of rational individual hygiene of an oral cavity, absence use of such subjects and means of hygiene as tooth flosses and a tooth conditioner is revealed. Nevertheless patients of the first group of 19 people (55.89 %) showed the satisfactory hygienic condition of oral cavity IH=1.5±0.1, in 26.4% (9 patients) was revealed a small amount of a soft tooth raid in cervical area after which removal smooth brilliant enamel is defined. In 47.6% (14 patients) cases the compensated course of carious process CFE=3.2±0.8, and in 100% of cases the constant F – a seal that testifies to stabilization of carious process prevailed. Patients of the second group have comparisons – in 44.11% (15 people from 34) cases according to the anamnesis were revealed to regular use of drinks and products (chocolate, Coca-Cola) containing caffeine, and amount of caffeine, exceeded recommended daily norm more than twice – on the average 200–250 mg of caffeine per day (admissible norm is – 100 mg), and during examinations and stressful situations consumption of drinks and the products containing caffeine – increased twice and lead more to the daily use of caffeine up to 600 mg per day. Based on dental research results it was concluded as unsatisfactory hygienic condition of oral cavity IH=3,1±0,1, plentiful soft tooth raid in cervical area after removal by means of a method of vital coloring showed caries in a spot stage; the mineralized tooth deposits in the field of cutters of the bottom jaw; catarrhal gingivitis PMA=29±2.3; the active subcompensated course of carious process CFE=7.3±0.7, and in 100% of cases the constant C – caries prevailed. In 6% (2 patients) the enamel erosion was revealed, in 17.6% (6 patients) vertical pathological erasability of forward group of teeth was revealed.

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The aim of this article is to show the differences between Cone Beam Computer Tomography (CBCT), which is increasingly more often used in dentistry and laryngology, and spiral tomography. Because of the growing application of 3D imaging, it was decided to present the advantages and disadvantages of both types of tomography. For inventing tomography, its creators, Hounsfield and Cormark, received the Nobel prize in 1979. Spiral tomography uses a panoply of rays which turn in a spiral around the patient and which directs itself onto a detector.

In the spiral tomography, the sharpness of the image is lower and the dosage of radiation absorbed by the patient is much higher in comparison with CBCT, which reduces its application.

Cone beam tomography is the newest method. CBCT uses beams of radiation in the shape of a cone and scans the space, not the surface, as is the case in spiral tomography.

The reconstruction of a high quality 3D picture is based on the cross-sections made during one rotation of the lamp around the patient’s head. Examinations are with many fields of viewing. Such examinations involve, from a couple of teeth to the whole part of the facial skeleton. The total time of exposure takes about 6 seconds, but the total scan lasts about 20 seconds. About 300 images are generated during this time.

The computer program enables viewing of any of the cross-section slices, the sagittal and transverse cross-sections, the frontal plane, or all at once. It is also possible to show the so called “broken” cross-section (different layers of individual teeth). The individual slices are made with the quality of 0.09–0.3 mm. Thanks to the low doses of radiation, the variations in the field of imaging, and the regulated resolution, the application of CBCT is growing. This examination is used in craniofacial surgery as well as implantology, and in planning implantoprosthetic treatment involving planning future prosthetic replenishments, also in periodontology, endodontology and orthodontics.

Cone beam tomography increasingly more often is chosen over spiral tomography because of the many disadvantages and the invasive nature of the latter.

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Objective. Our group developed a protocol for neural differentiation of human dental pulp stem cells, but it is not completely applicable for rat dental pulp stem cells (rDPSC). Our aim was to optimize it for differentiation of rDPSC cultures.

Methods. Cells were isolated from rat’s lower incisors, and cultivated under standard conditions. As neural differentiation first we activated the PKA-PKC system and induced the cells with growth factors. Cells were maintained for two more weeks with bFGF and retinoic-acid containing media. Differentiation was performed on fetal calf serum (FCS), laminin (LA), poly-L-lysine (PLL), poly-L-lysine/laminin (LYLA), ornithin/laminin (ORLA) and on untreated surface (NTC). Marker expression was studied with Q-PCR, and proliferation with WST-1 test.

Results. Within 24 hours, cells attached to the surface displaying similar morphologies. We observed three different cell types: fibroblast-like cells, epitheloid cells and large flat cells. In the first differentiation step the cells formed ridges on FCS coating, but spread out on other surfaces. During the induction the proportion of cells with neural morphology increased but during the first maturation stage it decreased. To the second maturation stage neuronal-like cells were visible on LYLA, ORLA and PLL surfaces. At the end of the differentiation the expression of neural markers such as NFM and NSE increased six times and twice on LYLA and ORLA surfaces in compare to NTC. The rate of the proliferation decreased during the differentiation. The highest proliferation was found on ORLA surface.

Conclusion. Neural morphology was more evident and neural markers elevated while rat pulp cells were cultured on a combination of lysine-laminin and ornithin-laminin. During the differentiation the proliferation decreased, the cells formed neural-like morphology and some cells decayed.

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