

CROATIAN INTERNATIONAL PUBLICATIONS

by Dunja Gorup

dunja.gorup@gmail.com



Šegota D¹, Diklic A¹, Jurkovic S^{1,2}. **Implementation of quality assurance program in radiography-2-year experience of collaboration with public health institutions in west region of Croatia.** *Radiat Prot Dosimetry*. 2018 Dec 1;182(3):329-334. doi: 10.1093/rpd/ncy069

¹Medical Physics Department, Clinical Hospital Centre Rijeka, Krešimirova 42, Rijeka, Croatia; ²Department of Physics, Faculty of Medicine, University of Rijeka, Braće Branchetta 20, Rijeka, Croatia

Quality Assurance program on using ionizing radiation is mandatory in all EU member states but this is still not implemented in most facilities in Croatia mostly because of a lack of medical physicists in diagnostic radiology. Since public health institutions in Croatia do not employ medical physicists in diagnostic radiology, collaboration between these institutions in west region of Croatia with Clinical Hospital Center Rijeka (CHC) was initiated during the year 2015. Physicists from CHC Rijeka performed periodical Quality Control (QC) tests and were included in optimization process. Results of QC tests during the period of 2 years showed a lot of improvements-equipment is maintained more frequently, some old units were replaced with new ones and all institutions acquired QC equipment so radiographers could perform daily and monthly QC tests. All these activities showed that medical physics support in radiology departments is necessary and can improve clinical practice.

Blaslov K¹, Naranda FS², Kruljac I³, Renar IP². **Treatment approach to type 2 diabetes: Past, present and future.** *World J Diabetes*. 2018 Dec 15;9(12):209-219. doi: 10.4239/wjcd.v9.i12.209.

¹Department of Endocrinology, Diabetes and Metabolic Diseases Mladen Sekso, University, Hospital

Center Sestre Milosrdnice, Zagreb 10000, Croatia; ²School of Medicine, University of Zagreb, Zagreb 10000, Croatia; ³Department of Endocrinology, Diabetes and Metabolic Diseases Mladen Sekso, University Hospital Center Sestre Milosrdnice, Zagreb 10000, Croatia.

Type 2 diabetes mellitus (DM) is a lifelong metabolic disease, characterized by hyperglycaemia which gradually leads to the development and progression of vascular complications. It is recognized as a global burden disease, with substantial consequences on human health (fatality) as well as on health-care system costs. This review focuses on the topic of historical discovery and understanding the complexity of the disease in the field of pathophysiology, as well as development of the pharmacotherapy beyond insulin. The complex interplay of insulin secretion and insulin resistance developed from previously known "ominous triumvirate" to "ominous octet" indicate the implication of multiple organs in glucose metabolism. The pharmacological approach has progressed from biguanides to a wide spectrum of medications that seem to provide a beneficial effect on the cardiovascular system. Despite this, we are still not achieving the target treatment goals. Thus, the future should bring novel antidiabetic drug classes capable of acting on several levels simultaneously. In conclusion, given the raising burden of type 2 DM, the best present strategy that could contribute the most to the reduction of morbidity and mortality should be focused on primary prevention.

Separovic Hanzevacki J¹, Gasparovic H², Reskovic Luksic V³, Ostojic Z³, Biocina B². **Staged management of a giant cardiac hydatid cyst: a case report.** *BMC Infect Dis*. 2018 Dec 27;18(1):694. doi: 10.1186/s12879-018-3599-2.

¹Department of Cardiovascular Diseases, School of Medicine, University Hospital Centre Zagreb, Kispaticeva 12, 10 000,

Zagreb, Croatia;²Department of Cardiac Surgery, School of Medicine, University Hospital Centre Zagreb, Zagreb, Croatia;³Department of Cardiovascular Diseases, School of Medicine, University Hospital Centre Zagreb, Kispaticeva 12, 10 000, Zagreb, Croatia.

BACKGROUND: We report on a 21-year-old patient with a giant symptomatic hydatid cyst of the interventricular septum, to whom a staged management approach was employed. Induction medical therapy led to a reduction in the size of the cyst, which was then completely removed via surgical excision. **CASE PRESENTATION:** A 21-year-old male Caucasian, with main complaints of fatigue and palpitations, was referred to our Centre due to a cystic formation in his left ventricle. The workup consisted of transthoracic echocardiography and cardiac magnetic resonance, which revealed a huge hydatid cyst in an active stage of disease, occupying the basal and mid part of the interventricular septum. Due to the size of the lesion and lack of viable myocardium in the affected area, the patient was declared inoperable and medical therapy was initiated. Serial echocardiography revealed a significant reduction in the size of the lesion and degradation to transitional and inactive stage, after which successful surgical excision of the cyst was performed. In the course of the medical treatment, the patient experienced sustained ventricular tachycardia causing loss of consciousness, which did not reoccur after surgical excision. **CONCLUSION:** Medical therapy can result in the degradation of a giant heart hydatid cyst, enabling surgical excision. Heart hydatid cyst can lead to potentially lethal arrhythmia irrespective of its size and stage, which does not reoccur after successful surgical excision.

Vugrinec Mamic M1, Hojsak I, Mišak Z, Kerman V, Kolaček S. Treatment in a Tertiary Intestinal Rehabilitation Center Improves Outcome for Children With Short Bowel Syndrome. Gastroenterol Nurs. 2018 Dec 20. doi: 10.1097/SGA.0000000000000324.

¹Referral Center for Pediatric Gastroenterology and Nutrition, Children's Hospital Zagreb, Zagreb, Croatia.

The aim of this study was to determine prognostic factors in pediatric patients with short bowel syndrome and very short bowel syndrome (defined as less than 25 cm of the bowel with or without colon). This was a retrospective, sin-

gle-center, observational study that included patients with intestinal failure. Thirty-eight children with short bowel syndrome were included in the study (mean age at diagnosis = 8.4 [range = 0-48] months; female/male = 20/18); 12 children (31.6%) had very short bowel syndrome. Weaning from parenteral nutrition was achieved in 29 (74.5%) of children with short bowel syndrome but only in 4 (33%) in the very short bowel syndrome group. Positive prognostic factors associated with successful weaning from parenteral nutrition were an absolute higher length of the residual intestine, a remnant of at least some part of the colon, and treatment in an experienced center from the diagnosis. Patients with short bowel syndrome and very short bowel syndrome should be treated in a center experienced in intestinal rehabilitation.

Sinković M¹, Towler L². Sexual Aging: A Systematic Review of Qualitative Research on the Sexuality and Sexual Health of Older Adults. Qual Health Res. 2018 Dec 25:1049732318819834. doi: 10.1177/1049732318819834.

¹University of Zagreb, Zagreb, Croatia;² University of Southampton, Southampton, United Kingdom.

Negative stereotypes regarding the sex lives of older adults persist, despite sexuality being an important factor that influences the quality of life. We conducted a systematic review of the qualitative literature on the sexuality and sexual health of older adults to address which topics have been researched and the quality of research within this field. We searched PsycINFO, SocINDEX, MEDLINE, and CINAHL for qualitative articles investigating the sexuality of adults aged 60+ years. We analyzed 69 articles using thematic analysis to synthesize their findings. We identified two overarching thematic categories: psychological and relational aspects of sexuality (personal meanings and understandings of sex, couplehood aspects, and sociocultural aspects) and health and sexuality (effects of illness and/or treatment on sexuality, and help-seeking behaviors). Research is needed into male sexual desire and pleasure, culture-specific and sexual/gender identities and their effect on outcomes such as help-seeking behavior and sexual satisfaction, and sexual risk-taking in older adults.

Kljajic Z¹, Roje Z², Becic K³, Capkun V⁴. Obstructive sleep apnea in children: How

it affects parental psychological status? *Int J Pediatr Otorhinolaryngol.* 2018 Nov 30;117:157-162. doi: 10.1016/j.ijporl.2018.11.032.

¹University Department of ENT, Head and Neck Surgery, University Hospital Center Split, Croatia; ²Private ENT Practice dr. Željka Roje, Split, Croatia; ³School of Medicine, University of Split, Croatia; ⁴Department of Nuclear Medicine, University Hospital Center Split, Croatia.

PURPOSE OF THE STUDY:The aim of this study was to evaluate the influence of obstructive sleep apnea (OSA) in children on maternal and paternal anxiety.**PATIENTS AND METHODS:** This prospective study was conducted from January 2013 until January 2016 in the Ear, Nose and Throat (ENT) Department at the University Hospital of Split, Croatia. The parents of 59 children with a median age of 5 years (range: 2-9) who were suffering from obstructive sleep apnea (OSA) due to adenotonsillar hypertrophy were enrolled into the study. All children were scheduled for adenoidectomy or adenotonsillectomy because of airway obstruction. In addition, their parents completed the 20-item State-Trait Anxiety Inventory-1 (STAI-1) and 20-item State-Trait Anxiety Inventory-2 (STAI-2) questionnaires before the operation and 30 days after the surgery when their children had considerable improvements in breathing during their sleep. The STAI is an instrument that quantifies both state (STAI-1) and trait (STAI-2) anxiety. State-Trait Anxiety Inventory-1 (state anxiety) is intended to measure transitory anxiety at a specific time (related to OSA symptoms in our study), whereas STAI-2 (trait anxiety) measures long-term anxiety. **RESULTS:**Overall, the study included 57 mothers and 53 fathers of 59 children diagnosed with OSA. The mean preoperative STAI-2 score of parents was 31.1 ± 7.5 ; for fathers it was 28.2 ± 6.3 , and for mothers it was 33.7 ± 7.6 . The STAI-1 and STAI-2 scores showed significant differences before and after the surgery according to gender. The mean score of mothers was 5.5 (95% CI: 2.8 to 8.1) higher than the mean score of fathers ($t = 4.1$, $p < 0.001$) on the STAI-2 scale. The mean score of mothers was 5.6 (95% CI: 0.48 to 0.7) higher than the mean score of fathers ($t = 2.2$; $p = 0.032$) on the preoperative STAI-1 scale. The mean score of mothers was 1.95 (95% CI: 0.35 to 3.6) higher than the mean score of fathers ($t = 2.4$; $p = 0.017$) on the postoperative STAI-1 scale. The mean score of mothers was 6.22 higher than the mean score of fathers ($p = 0.029$) on the preoperative STAI-1 scale, adjusted for the STAI-2 scale. The mean score of mothers

was 1.8 higher than the mean score of fathers ($p = 0.039$) on the postoperative STAI-1 scale, adjusted for the STAI-2 scale. These data suggest that differences between the preoperative and postoperative STAI-1 score for mothers was the highest (51 ± 7) in children with severe OSA and the lowest (28 ± 14) in children with mild OSA ($p < 0.001$). The difference between the preoperative and postoperative STAI-1 score for fathers was the highest (48 ± 6.6) in children with severe OSA and the lowest (25 ± 10) in children with mild OSA. **CONCLUSION:** The results of our study suggest that obstructive sleep apnea in children is a disturbing symptom for parents and is associated with a significant level of anxiety that depends on OSA severity. After the surgical treatment of the children (adenoidectomy or adenotonsillectomy), the anxiety level of both parents decreased. We suggest that preoperative psychological intervention should be considered in selected cases for mothers and fathers of children with severe OSA in order to diminish the symptoms of anxiety that can compromise normal postoperative recovery in operated children.

Petrovic A¹, Veeraraghavan P², Olivieri D², Nistri A², Jurcic N², Mladinic M³. Loss of inhibitory synapses causes locomotor network dysfunction of the rat spinal cord during prolonged maintenance in vitro. *Brain Res.* 2018 Dec 19. pii: S0006-8993(18)30647-4. doi: 10.1016/j.brainres.2018.12.029.

¹Neuroscience Department, International School for Advanced Studies (SISSA), Trieste, Italy; Department of Biotechnology, University of Rijeka, Rijeka, Croatia; ²Neuroscience Department, International School for Advanced Studies (SISSA), Trieste, Italy; ³Neuroscience Department, International School for Advanced Studies (SISSA), Trieste, Italy; Department of Biotechnology, University of Rijeka, Rijeka, Croatia.

The isolated spinal cord of the neonatal rat is widely employed to clarify the basic mechanisms of network development or the early phase of degeneration after injury. Nevertheless, this preparation survives in Krebs solution up to 24 h only, making it desirable to explore approaches to extend its survival for longitudinal studies. The present report shows that culturing the spinal cord in oxygenated enriched Basal Medium Eagle (BME) provided excellent preservation of neurons (including motoneurons), glia and primary afferents (including dorsal root ganglia) for up to

72 h. Using DMEM medium was unsuccessful. Novel characteristics of spinal networks emerged with strong spontaneous activity, and deficit in fictive locomotion patterns with stereotypically slow cycles. Staining with markers for synaptic proteins synapsin 1 and synaptophysin showed thoroughly weaker signal after 3 days in vitro. Immunohistochemical staining of markers for glutamatergic and glycinergic neurons indicated significant reduction of the latter. Likewise, there was lower expression of the GABA-synthesizing enzyme GAD65. Thus, malfunction of locomotor networks appeared related to loss of inhibitory synapses. This phenomenon did not occur in analogous opossum preparations of the spinal cord kept in vitro. In conclusion, despite histological data suggesting that cultured spinal cords were undamaged (except for inhibitory biomarkers), electrophysiological data revealed important functional impairment. Thus, the downregulation of inhibitory synapses may account for the progressive hyperexcitability of rat spinal networks despite apparently normal histological appearance. Our observations may help to understand the basis of certain delayed effects of spinal injury like chronic pain and spasticity.

Degoricija V¹, Potočnjak I², Gastrager M³, Pregartner G⁴, Berghold A⁴, Scharnagl H⁵, Stojakovic T⁵, Tiran B⁵, Marsche G⁶, Frank S⁷. HDL subclasses and mortality in acute heart failure patients. *Clin Chim Acta*. 2018 Dec 19. pii: S0009-8981(18)30650-8

¹University of Zagreb School of Medicine, Šalata 3, 10000 Zagreb, Croatia; University Hospital Centre Sisters of Charity, Department of Medicine, Vinogradska 29, 10000 Zagreb, Croatia; ²University Hospital Centre Sisters of Charity, Department of Medicine, Vinogradska 29, 10000 Zagreb, Croatia; ³Gottfried Schatz Research Center for Cell Signaling, Metabolism and Aging, Molecular Biology and Biochemistry, Medical University of Graz, Neue Stiftingtalstraße 6/6, 8010 Graz, Austria; ⁴Institute for Medical Informatics, Statistics und Documentation, Medical University of Graz, Auenbruggerplatz 2, 8036 Graz, Austria; ⁵Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medical University of Graz, Auenbruggerplatz 15, 8036 Graz, Austria; ⁶Otto Loewi Research Center, Medical University of Graz, Austria; ⁷BioTechMed-Graz, Mozartgasse 12/II, 8010 Graz, Austria. ⁷Gottfried Schatz Research Center for Cell Signaling, Metabolism and Aging, Molecular Biology and Biochemistry, Medical University of Graz, Neue Stiftingtalstraße 6/6, 8010 Graz, Austria; ⁷BioTechMed-Graz, Mozartgasse 12/II, 8010 Graz, Austria.

The link between HDL subclasses and the prognosis of cardiovascular diseases remains controversial. We thus evaluated the prognostic value of the HDL subclasses 3 and 2 cholesterol (HDL3-C, HDL2-C) as well as of total HDL-C for 3-month mortality in acute heart failure (AHF) patients. The serum levels of HDL3-C and total HDL-C were determined by detergent-based homogeneous assay. HDL2-C was computed by the difference between total HDL-C and HDL3-C. Out of the 132 analyzed patients, 35 (26.5%) died within three months after onset of AHF. Univariate logistic regression analyses revealed a significant inverse association of HDL3-C (odds ratio (OR) 0.46 per 1-SD increase, 95% confidence interval (CI) 0.27-0.72, $p = .001$) with 3-month mortality, whereas concentrations of total HDL-C and HDL2-C showed no significant association. After adjustment for various laboratory and clinical parameters known to be associated with mortality in heart failure patients, HDL3-C concentrations remained significantly associated with 3-month mortality (OR 0.34 per 1-SD increase, 95% CI 0.15-0.74, $p = .010$). We conclude that low admission serum levels of HDL3-C are associated with an increased 3-month mortality in AHF patients, whereas total HDL-C and HDL2-C showed no association. HDL3-C might thus be useful as a prognostic parameter in AHF.

Hojsak I^{1,2,3}. Probiotics in Functional Gastrointestinal Disorders. *Adv Exp Med Biol*. 2018 Dec 22.

¹Referral Center for Pediatric Gastroenterology and Nutrition, Children's Hospital Zagreb, Zagreb, Croatia; ²School of Medicine, University of Zagreb, Zagreb, Croatia; ³School of Medicine Osijek, University J.J. Strossmayer, Osijek.

Infantile colic, constipation, functional abdominal pain (FAP), and irritable bowel syndrome (IBS) are the most common functional gastrointestinal disorders (FGID). This chapter will review current evidence on the role of probiotics in the treatment of these FGID. The etiology of FGID is considered multifactorial, but the importance of intestinal microbiota in their development has been repeatedly emphasized. As a consequence, the potential role of probiotics in their treatment is being increasingly scrutinized. Presently, the strongest evidence of efficacy is for the use of *Lactobacillus reuteri* (L reuteri) DSM 17938 at the dose of 108 CFU/day for the treatment of infantile colic in breast-fed infants. Limited, yet encouraging, evidence exists for *Lactobacillus rhamnosus* GG (LGG) at the dose of 3×10^9 CFU and for a multi-strain preparation for the

treatment of IBS. In the treatment of FAP, there is some evidence for the use of *L reuteri* DSM 17938 at the dose of at least 108 CFU/day.

Ćelić T¹, Omrčen H², Španjol J³, Bobinac D¹. **Mechanisms of Bone Morphogenetic Protein-7 Protective Effects Against Cold Ischemia-Induced Renal Injury in Rats.** *Transplant Proc.* 2018 Dec;50(10):3822-3830. doi: 10.1016/j.transproceed.2018.08.035.

¹Department of Anatomy, Faculty of Medicine, University of Rijeka, Rijeka, Croatia; ²Department of Anatomy, Faculty of Medicine, University of Rijeka, Rijeka, Croatia; ³Clinic of Urology, University Hospital Rijeka, Rijeka, Croatia.

Deceased donor kidneys are exposed to cold ischemic insult which makes them particularly susceptible to the effects of cold ischemic injury during hypothermic preservation resulting in high rates of delayed graft function. Bone morphogenetic protein-7 (BMP-7) is a valuable reagent in the field of tissue regeneration and preservation under ischemic conditions. Following these insights, we investigated the effect of recombinant human BMP-7 (rhBMP-7) on graft preservation during cold ischemia. The study was conducted on an experimental model of kidney cold ischemia in rats. Kidneys were perfused with University of Wisconsin (UW) saline solution, rhBMP-7, or rhBMP-7 + UW, and exposed to cold ischemia for 6, 12, and 24 hours. In tubular epithelial cells of kidneys perfused with rhBMP-7 and rhBMP-7+UW solution, the expression of BMP-7 and E-cadherin was observed after 24 hours of cold ischemia. In kidneys not perfused with rhBMP-7, high expression of transforming growth factor- β and α -smooth muscle actin was found. Also, in kidneys perfused with rhBMP-7 solution, statistically higher levels of Smad1, Smad5, and Smad8 messenger RNA expressions were proven. BMP-7 maintains the morphology of kidney tissue better than UW solution during 24 hours of cold ischemia. BMP-7 prevents epithelial to mesenchymal transformation and consequently maintains epithelial phenotype of tubular cells.

Begovac J^{1,2}, Krznarić J¹, Bogdanić N¹, Močibob L¹, Zekan Š^{1,2}. **Successful treatment of genotype 3 hepatitis C infection in a noncirrhotic HIV infected patient on chronic dialysis with the combination of sofosbuvir and velpatasvir: A case report.**

Medicine (Baltimore). 2018 Dec;97(51):e13671. doi: 10.1097/MD.00000000000013671.

¹University Hospital for Infectious Diseases "Dr. Fran Mihaljević"; ²University of Zagreb School of Medicine, Zagreb, Croatia.

RATIONALE: Data on anti-HCV therapy in patients on dialysis is still evolving. Sofosbuvir is mainly eliminated through the renal route and there is controversy about its use in these patients. **PATIENT CONCERNS:** We describe a 53-year-old male patient with HCV genotype 3 and human immunodeficiency type 1 (HIV) infection on chronic dialysis. HIV infection was diagnosed in 1987 and since July 2007 the patient was compliant with his antiretroviral therapy (ART) and had an undetectable plasma HIV viral load on all follow-up measurements. The patient was known to have HCV infection since 1997 but has never been treated for chronic hepatitis C. Because of progressive renal impairment dialysis started in 2005. **DIAGNOSIS:** Before anti-HCV treatment commenced the patient liver transient elastography (FibroScan) indicated F3 fibrosis (stiffness, 11.6 kPa) and his HCV RNA viral load was 320,798 IU/mL (Abbott RealTime HCV assay). **INTERVENTION:** Fixed dose combination of sofosbuvir/velpatasvir (400mg/100mg) for 11 weeks. **OUTCOMES:** Twelve weeks after treatment cessation HCV RNA was undetectable, hence the patient achieved a sustained virologic response. The drugs were well tolerated and the patient did not report any side effects. **LESSONS:** Sofosbuvir/velpatasvir may be an option for HCV genotype 3 infection in patients coinfecting with HIV on long-term dialysis.

Kavazović I¹, Polić B¹, Wensveen FM^{1,2}. **Cheating the Hunger Games; Mechanisms Controlling Clonal Diversity of CD8 Effector and Memory Populations.** *Front Immunol.* 2018 Nov 29;9:2831. doi: 10.3389/fimmu.2018.02831

¹Department of Histology & Embryology University of Rijeka, Rijeka, Croatia; ²Department of Experimental Immunology, Amsterdam University Medical Center University of Amsterdam, Amsterdam, Netherlands.

Effector and memory CD8 T cells have an intrinsic difference in the way they must approach antigen; effector cells

need to address the pathogen at hand and therefore favor outgrowth of only high-affinity clones. In contrast, the memory pool benefits from greater clonal diversity to recognize and eliminate pathogens with mutations in their immunogenic epitopes. Effector and memory fates are ultimately the result of the same three signals that control T cell activation; T cell receptor (TCR) engagement together with co-stimulation and cytokines. Great progress has been made in our understanding of the transcriptional programs that drive effector or memory differentiation. However, how these two different programs result from the same initial cues is still a matter of debate. An emerging image is that not only the classical three signals determine T cell differentiation, but also the ability of cells to access these signals relative to that of other activated clones. Inter-clonal competition is therefore not only a selective force, but also a mediator of CD8 T cell fate. How this is regulated on a transcriptional level, especially in the context of a selective "hunger game" based on antigen-affinity in which only cells of high-affinity are supposed to survive, is still poorly defined. In this review, we discuss recent literature that illustrates how antigen-affinity dependent inter-clonal competition shapes effector and memory populations in an environment of antigen affinity-driven selection. We argue that fine-tuning of TCR signal intensity presents an attractive target for regulating the scope of CD8 T cell vaccines.

Kostović I^{1,2}, Išasegi IŽ^{1,2}, Krsnik Ž^{1,2}. Sublaminar organization of the human subplate: developmental changes in the distribution of neurons, glia, growing axons and extracellular matrix. *J Anat.* 2018 Dec 13. doi: 10.1111/joa.12920

¹Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Zagreb, Croatia; ²Centre of Excellence for Basic, Clinical and Translational Neuroscience, Zagreb, Croatia.

The objective of this paper was to collect normative data essential for analyzing the subplate (SP) role in pathogenesis of developmental disorders, characterized by abnormal circuitry, such as hypoxic-ischemic lesions, autism and schizophrenia. The main cytological features of the SP, such as low cell density, early differentiation of neurons and glia, plexiform arrangement of axons and dendrites, presence

of synapses and a large amount of extracellular matrix (ECM) distinguish this compartment from the cell-dense cortical plate (CP; towards pia) and large fiber bundles of external axonal strata of fetal white matter (towards ventricle). For SP delineation from these adjacent layers based on combined cytological criteria, we analyzed the sublaminar distribution of different microstructural elements and the associated maturational gradients throughout development, using immunocytochemical and histological techniques on postmortem brain material (Zagreb Neuroembryological Collection). The analysis revealed that the SP compartment of the lateral neocortex shows changes in laminar organization throughout fetal development: the monolayer in the early fetal period (presubplate) undergoes dramatic bilaminar transformation between 13 and 15 postconceptional weeks (PCW), followed by subtle sublamination in three 'floors' (deep, intermediate, superficial) of midgestation (15-21 PCW). During the stationary phase (22-28 PCW), SP persists as a trilaminar compartment, gradually losing its sublaminar organization towards the end of gestation and remains as a single layer of SP remnant in the newborn brain. Based on these sublaminar transformations, we have documented developmental changes in the distribution, maturational gradients and expression of molecular markers in SP synapses, transitional forms of astroglia, neurons and ECM, which occur concomitantly with the ingrowth of thalamo-cortical, basal forebrain and cortico-cortical axons in a deep to superficial fashion. The deep SP is the zone of ingrowing axons - 'entrance (ingrowth) zone'. The process of axonal ingrowth begins with thalamo-cortical fibers and basal forebrain afferents, indicating an oblique geometry. During the later fetal period, deep SP receives long cortico-cortical axons exhibiting a tangential geometry. Intermediate SP ('proper') is the navigation and 'nexus' sublamina consisting of a plexiform arrangement of cellular elements providing guidance and substrate for axonal growth, and also containing transient connectivity of dendrites and axons in a tangential plane without radial boundaries immersed in an ECM-rich continuum. Superficial SP is the axonal accumulation ('waiting compartment') and target selection zone, indicating a dense distribution of synaptic markers, accumulation of thalamo-cortical axons (around 20 PCW), overlapping with dendrites from layer VI neurons. In the late preterm brain period, superficial SP contains a chondroitin sulfate non-immunoreactive band. The developmental dynamics for the distribution of neuronal, glial and ECM markers comply with sequential ingrowth of afferents in three levels of SP: ECM and synaptic markers shift from deep to superficial SP, with transient forms of glia following this arrangement,

and calretinin neurons are concentrated in the SP during the formation phase. These results indicate developmental and morphogenetic roles in the SP cellular (transient glia, neurons and synapses) and ECM framework, enabling the spatial accommodation, navigation and establishment of numerous connections of cortical pathways in the expanded human brain. The original findings of early developmental dynamics of transitional subtypes of astroglia, calretinin neurons, ECM and synaptic markers presented in the SP are interesting in the light of recent concepts concerning its functional and morphogenetic role and an increasing interest in SP as a prospective substrate of abnormalities in cortical circuitry, leading to a cognitive deficit in different neurodevelopmental disorders.

Maslovara S^{1,2}, Butkovic-Soldo S^{3,4}, Pajic-Matic I², Sestak A¹. Vestibular atelectasis: Decoding pressure and sound-induced nystagmus with bilateral vestibulopathy. *Laryngoscope*. 2018 Dec 13. doi: 10.1002/lary.27724.

¹Department of Otorhinolaryngology, County General and Veterans Hospital Vukovar, Vukovar, Croatia; ²Department of Otorhinolaryngology and Maxillofacial Surgery, Department of Neurology, Medical Faculty, University of Osijek, Osijek, Croatia; ³Department of Neurology, Medical Faculty, University of Osijek, Osijek, Croatia; ⁴Department of Neurology Clinical Hospital Center Osijek, Osijek, Croatia.

We present the case of a 27-year-old male who presented with vertigo when pressing the entrance of his right auditory meatus and exposing his right ear to loud noise. A diagnostic procedure revealed bilateral labyrinth weakness, which was confirmed by caloric and rotational testing. The ocular vestibular evoked myogenic potentials investigation demonstrated a significant weakness of the right utriculus, whereas the cervical vestibular evoked myogenic potentials were normal, indicating preservation of the saccular response. Radiologic studies did not show evidence of labyrinthine dehiscence. We suspect the newly described association of this clinical syndrome with the previously described histopathology of vestibular atelectasis accounts for these findings.

Raos M¹, Zunec R¹, Mocibob M², Gojceta K¹, Lukic M¹, Golubic Cepulic B¹. Susceptible and protective HLA-DR and HLA-DQ alleles for Fya alloimmunization in the Croatian population. *Transfusion*. 2018 Dec 12. doi: 10.1111/trf.15087.

¹Clinical Department of Transfusion Medicine and Transplantation Biology, University Hospital Center Zagreb, Zagreb, Croatia; ²Department of Chemistry, Faculty of Science, University of Zagreb, Zagreb, Croatia.

BACKGROUND: Alloimmunization is a known risk of transfusion therapy caused by exposure to foreign RBC antigens. However, alloimmunization is not observed in all transfused patients. Human leukocyte antigen (HLA) molecules may contribute to the recognition and presentation of foreign antigens and to the potency of immune responses that result in the production of antibodies. The aim of this study was to determine the association of HLA-DR and HLA-DQ polymorphisms with alloimmunization to Fya antigen in Croatian patients. **STUDY DESIGN AND METHODS:** The study was conducted on 70 alloimmunized patients to Fya antigen and two control groups: 165 healthy Croatian individuals (Control 1) and 45 Fya antigen-negative non-immunized patients exposed to Fya antigen (Control 2). Phenotype frequencies for HLA-DRB1 and HLA-DQB1 alleles were compared between the cases and control groups. **RESULTS:** Statistically significant differences in phenotype frequencies between cases and controls were found for DRB1*04 (odds ratios [ORs], 10.5 and 18.7 for Control 1 and Control 2, respectively), DRB1*15 (ORs, 8.0 and 6.9), and DQB1*02 alleles (ORs, 0.2 and 0.03); and DRB1*04-DQB1*03:01 (ORs, 7.9 and 17.6), DRB1*04-DQB1*03:02 (ORs, 5.5 and 7.6), DRB1*15-DQB1*06:02 (ORs, 7.3 and 5.5), DRB1*03-DQB1*02:01 (OR, 0.1), and DRB1*07-DQB1*02:02 (OR, 0.3) haplotypes. **CONCLUSION:** Several HLA-DRB1 and HLA-DQB1 alleles and haplotypes were proved to contribute to and protect from alloimmunization to Fya antigens. Alleles DRB1*04 and DRB1*15, as well as haplotypes DRB1*04-DQB1*03:02 and DRB1*15-DQB1*06:02 can be considered as risk factors, while allele DQB1*02 and haplotype DRB1*03-DQB1*02:01 have a protective role in Fya alloimmunization.