

*Međunarodni Simpozijum I kategorije*

**Savremeni pristupi u primeni matičnih ćelija,  
transplantaciji organa i organizaciji  
službe hitne pomoći - saradnja lekara  
Beograda i lekara iz dijaspore**

*International Symposium of the 1<sup>st</sup> category*

**Current approaches for the application of stem cells,  
transplantation of organs and the organization of  
emergency services - cooperation between  
medical doctors from Belgrade and diaspora**

Beograd, Hyatt Regency, 12 – 13. maj 2016.  
Belgrade, Hyatt Regency, May 12 – 13<sup>th</sup>, 2016



**ZBORNİK SAŽETAKA  
BOOK OF ABSTRACTS**





**"Savremeni pristupi u primeni matičnih ćelija, transplantaciji organa i organizaciji službe hitne pomoći - iskustva lekara iz Beograda i dijaspore"**

**"Current approaches for the application of stem cells, transplantation of organs and the organization of emergency services - experience of doctors from Belgrade and the diaspora"**

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**SESIJA 1 – MATIČNE ĆELIJE I NJHOVA  
PRIMENA U TERAPIJI**

***SESSION 1 – STEM CELLS AND THEIR  
THERAPEUTIC APPLICATION***

## **MATIČNE ĆELIJE – PRIKUPLJANJE, EX VIVO MANIPULACIJA I KLINIČKA PRIMENA**

Prof. dr Bela Balint

*Dopisni član Srpske akademije nauka i umetnosti*

Ovaj skup ima za cilj da prikaže osnovna saznanja vezana za hemobiološke karakteristike i terapijsku primenu "nemanipuliranih" ili *ex vivo* tretiranih matičnih ćelija (MĆ) u oblasti transplantacijske (samoobnavljanje, diferencijacija i proliferacija) i/ili regenerativne medicine (plastičnost MĆ). Biće prikazani neki rezultati bazičnih istraživanja i kliničkih studija MĆ, uz kratak osvrt na dostignuća pri ispitivanjima kancerskih MĆ. U tom smislu, pokušaćemo da prikazemo sadašnje stanje u oblastima konceptualnih i metodoloških istraživanja MĆ – obuhvatajući različite pristupe u jednom "biološkom duelu/bitci", kao deo neprestane borbe lekara protiv bolesti.

Ukratko, sposobnost samoobnavljanja primitivnih hematopoeznih MĆ omogućava održavanje kontinuiteta njihove populacije u kostnoj srži – u uslovima fiziološke hematopoezne ravnoteže/balansa, ali i kada je ona delimično narušena. Manje primitivne populacije progenitora, potom, produkuju zrele krvne ćelije. Uopšteno, MĆ se mogu podeliti u embrionalne i "adultne". Embrionalne MĆ su sposobne da se diferencijuju u sve tipove ćelija organizma. Nedavno je ustanovljeno da slične osobine imaju i neke primitivne populacije adultnih MĆ sa potencijalom diferencijacije ne samo u sve vrste krvnih ćelija, nego i u neke somatske ćelije (transdiferencijacija). Tako, u određenim uslovima one mogu dati osteocite, hondrocite, hepatocite i druge ćelije. Zahvaljujući ovoj sposobnosti, slično mezenhimskim MĆ, hematopoezne MĆ su primenjive u regenerativnoj medicini.

MĆ mogu obezbediti repopulaciju koste srži u osoba sa delimično ili potpuno oštećenom hematopoezom – što je osnov za njihovu "konvencionalnu" transplantaciju. Izvođenjem ovih transplantacija obezbeđuje se kompletna i dugotrajna rekonstitucija hematopoeze, uz opšti oporavak u bolesnika posle visokodozne radio-hemioterapije. Zahvaljujući njihovom svojstvu plastičnosti, terapijska primena MĆ opravdana je u lečenju bolesnika sa oštećenjem miokarda, jetre, pankreasa, moždanog i drugih organa/tkiva. Kliničke studije pokazale su da primena/ubrizgavanje MĆ u neko oštećeno/ishemijsko područje rezultuje njihovim prihvatanjem i potencijalnom trans-diferencijacijom u ćelijsku liniju tog oštećenog tkiva (srca, arterijskog endotelijuma, itd.). Faktori rasta angiogeneze pospešuju formiranje kolaterala (kapilara i arteriola) u procesu poznatom kao "neoangiogeneza". Primena biomaterijala na bazi nanotehnologije i MĆ predstavlja novi pristup ili sledeću generaciju "alata" za tretman i zamenu oštećenih organa.

Ideja i koncept MĆ i njihova *ex vivo* ekspanzija u potpunosti su zasnovani na saznanjima i činjenicama koja potiču iz eksperimentalne hematologije. Tako, primena tretiranih hematopoeznih MĆ u kliničkim studijama pokazala se kao efikasna u smanjivanju post-transplantacijske agranulocitoze. Otkriće "adultne neurogeneze" je otvorilo novu eru u oblasti moderne neurobiologije – potvrđeno je da mozak ipak ima potencijal regenerisanja. Ovaj pristup bi mogao biti primenjen kod praćenja aktiviranih i/ili transplantovanih MĆ u ljudskom mozgu (moždani udar, multipla skleroza, itd.). Tretman primenom MĆ mogao bi biti takođe korišćen u



lečenju bolesti unutrašnjeg uha. Nedavno je nekoliko istraživača primenilo MĆ u lečenju poremećaja unutrašnjeg uha sa rezultatima koji obećavaju – ali ove studije zahtevaju dodatna istraživanja.

Na ovom skupu o MĆ će takođe biti prikazane ukratko neke karakteristike kancerskih MĆ (KMĆ), naročito njihova moguća uloga u dijagnozi i tretmanu bolesnika. Biće prodiskutovane tehnike i metodologije identifikacije markera kancerskih MĆ, neke specifičnosti njihovog metabolizma, zatim respiracije, genetskih i epigenetskih mehanizama, uključujući i DNK metilaciju, uz modeliranje ishoda samog kancera. Biće predstavljene neke od razlika između kancerskih i "normalnih" MĆ, zajedno sa konceptom ciljane ("target") terapije raka.

Na osnovu iznetog, moguće je reći da je konvencionalna transplantacija MĆ postala imperativna u lečenju bolesnika sa malignim i nekim benignim bolestima krvi, ali i drugim poremećajima (autoimunska oboljenja – npr. multipla skleroza). Koncept plastičnosti MĆ omogućava njihovu sve širu terapijsku primenu u oblastima regenerativne medicine (defekti unutar određenih organa/tkiva – ishemijska bolest srca, oštećenje jetre, zatim, gluvoća, osteogeneza imperfekta, retinopatija, itd.). Mehanizmi koji omogućavaju transdiferencijaciju i/ili "reprogramiranje" MĆ – posredstvom spoljašnjih ili unutrašnjih faktora – još su uvek samo delimično razjašnjeni. Međutim, postignuti povoljni klinički rezultati govore u prilog opravdanosti (uz stalno unapređenje postupaka) terapije pomoću MĆ u transplantacijskoj, ali i regenerativnoj medicini.

## **STEM CELLS – COLLECTION, EX VIVO MANIPULATION, AND CLINICAL APPLICATION**

Prof Bela Balint

*Corresponding member of the Serbian Academy of Sciences and Arts*

The basic goal of this meeting/Stem Cell (SC) Symposium – is to present fundamental knowledge with regard to hemobiological characteristics, as well as therapeutic application of native or ex vivo manipulated SCs in the fields of SC-transplants (self-renewal, differentiation and proliferation) and/or regenerative medicine (SC plasticity). In addition to investigations and clinical studies of normal SC, present research in cancer SCs (CSCs) will be discussed. Therefore, we will try to demonstrate the current state of the scientific research within conceptual and methodological SC areas, starting with exploration of different SC approaches in a "biological duel/battle" physician vs. disease.

Briefly, the self-renewal ability of primitive hematopoietic SCs provides maintaining of the continuity of their population in bone marrow – under conditions of physiological hematopoietic balance or "steady state hematopoiesis", but also in situation when it is partially disturbed. Less primitive populations of progenitors will give however, mature blood cells. Generally, SCs can be divided into embryonic and adult SCs. Embryonic SCs have the capacity to differentiate into all cell types. It has recently been demonstrated that some primitive populations of bone marrow derived adult SCs have similar potential, having ability to differentiate not only into all blood cells, but also into some somatic cells (trans-differentiation). In specific conditions, they can deliver osteocytes, chondrocytes, hepatocytes and other cells. Thanks to this capacity, similar to mesenchymal SCs, hematopoietic SCs can be used in regenerative medicine.

SCs are capable of providing repopulation of bone marrow in persons with partially or completely injured hematopoiesis – which is the basis of their "conventional" transplants. Those transplants secure complete and long-term hematopoietic reconstitution, associated with patients' overall recovery following high dose radio-chemotherapy. Thanks to their plasticity, therapeutic application of SCs is justified in the treatment of patients with cardiac, liver, pancreatic, brain and other organs/tissue damages. Clinical studies show that application/injection of SCs into a damaged or ischemic regions results in "SC-homing" and potential trans-differentiation into cell line of a damaged tissue (heart, arterial endothelium, etc). Some "angiogenetic-factors" stimulate formation of collaterals (capillaries and arterioles) in the process known as "neo-angiogenesis". The use of nanotechnology-based biomaterials and SCs are the next generation of "tools" for treatment and replacement of damaged organs. The idea and concept of SC and progenitor ex vivo expansion completely derives from the knowledge and facts provided by experimental hematology. Expanded hematopoietic SCs in clinical trials showed the ability to decrease post-transplant agranulocytosis. The discovery of "adult-neurogenesis" has opened a new era in modern neurobiology – the brain has the potential to regenerate. This approach could be applied to trace activated and/or CSs transplanted into the human brain (stroke, multiple sclerosis, etc). SC-based treatment is also attractive for inner ear related diseases, since the hair cells are very sensitive and do not regenerate. Recently several researchers have applied SCs into the inner ear with promising results (but these studies require further examinations). Finally, this Symposium will be also a great opportunity for a brief, conceptual presentation of some characteristics of

cancer SCs (CSCs), especially their possible role in diagnosis and search for advances in overall treatment of patients. Techniques and methodologies for the identification of cancer SCs will be discussed, as well as the specificity of their metabolism, respiration, genetic and epigenetic mechanisms, including DNA-methylation and "cancer issue/problem/outcome" modeling. Some differences and similarities between cancer and normal SCs will be presented, along with the concept of targets of anticancer therapy.

According to previously stated facts, it can be concluded that conventional SC transplant is an imperative in the treatment of hemato-oncological patients and some benign blood diseases, as well as certain other disorders (several autoimmune diseases – e.g. sclerosis multiplex). The concept of SCs plasticity enables their ever increasing therapeutic application in regenerative medicine (defects within certain organs/tissues – ischemic heart disease, liver damage, as well as deafness, osteogenesis imperfecta, wet and dry retinopathy, etc). Mechanisms that enable SCs trans-differentiation and/or cell-reprogramming – through "extrinsic" or "intrinsic" factors – are only partially clarified. However, achieved favorable clinical results prove the use of therapy with SCs in transplantation and regenerative medicine – with constant procedural/technical improvements (such as for example, the use of hypoxia as a natural cause for stem cell expansion).

## **NANOTECHNOLOGY AND STEM CELLS FOR TREATMENT AND REPLACEMENT OF DAMAGED ORGANS**

Alexander Marcus Seifalian  
Nanotechnology Regenerative Medicine Ltd  
London Bioscience Innovation Centre  
London, United Kingdom

Nanoparticles, nanotechnology-based biomaterials and stem cells are the next generations of biotechnology have been used for treatment and replacement of damaged organs.

Their research and development is based on a multidisciplinary team approach from basic science to the clinical. We have developed and patented a family of nanoparticles, nanocomposites materials and use stem cells in the development of human organs.



Using these novel materials 3D scaffold is fabricated using 3D bioprinter, and then the scaffold is functionalised by peptides, antibodies and or stem cells.

There are number of sources of autologous stem cells, these include adipose drive stem cells, endothelial progenitor stem cells, bone marrow stem cells, IPS, and others. Currently we have been concentrating on adipose drive stem cells.

In my lecture, data on manufacturing and evaluation as well as *in vitro* and preclinical testing will be presented. The route to translational from laboratories to clinical setting will be highlighted and commercialisation of these technologies will be discussed.

In conclusion application of nanotechnology and stem cells are next generation tool under development for the treatment of diseases tissue and potential for treatment of damaged tissue is excellent and is a \$multi billion industry.

## KONCEPT KANCERSKE MATIČNE ĆELIJE (KMĆ)

Prof. dr Mirjana Pavlović

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Analizirajući istraživanja u poslednjih nekoliko godina, procenjeno je sadašnje razumevanje koncepta kancerske matične ćelije da bi se istakla zrelost situacije za novu i kreativnu ciljnu terapiju tumora. Dok mnogi istraživači u polju tumorske terapije nastavljaju da nadgrađuju postojeće modele hemoterapije i zračenja, u naporu da poprave svoju efikasnost povećanjem njihove specifičnosti, poseban istraživački kadar koristi noviji put – usmeren prema kancerskoj matičnoj ćeliji. Novi koncept ukazuje na dva dobro definisana modela od kojih ni jedan ne može da kompletno opiše sve osobine:

- a) **Stohastički** (model klonalne evolucije): sve kancerozne ćelije imaju tumorigeni potencijal i proizvod su klonalne evolucije alteracijom izazvanom genskim mutacijama ili epigenetskim promenama.
- b) **Hijerarhijski**: tumori pokazuju hijerarhiju, sa subpopulacijom KMĆ s tumorigenim potencijalom mnogo većim od onog u drugim kancerskim ćelijama. Tumor je hijerarhijski organizovan sa matičnom kancerskom ćelijom na vrhu, praćen progenitorima, i diferenciranim ćelijama koje više nisu sposobne da proizvedu tumor.

Početni doprinos Dick-a (1994) postavio je evidentne kriterijume koncepta KMĆ primenjujući NOD/SCID model miša. Uspešno je transplantirao matične ćelije kancera akutne mijelogene leukemije (AML) humanih pacijenata u NOD/SCID mišji model, u kome su AML ćelije čoveka regenerisane. Klasični eksperimentni Al Hajj-a (kancer dojke) i Li-ja (kancer pankreasa) još čvršće su poduprli koncept. Fluorescentno obeležavanje detektovalo je klonalno propagirane, stabilne markere i visoku tumorigenost s rezistentnošću na terapiju – tipične znake funkcionalnosti ovih, inače retkih ćelija (0,1% totalne populacije). Retkost KMĆ-a zahteva razvoj terapijskih strategija različitih od konvencionalnih.

Kritičan značaj teorije KMĆ je u novom konceptu ciljne terapije tih ćelija koji uključuje originalne pristupe za precizno njihovo ciljanje, što rezultira smežuravanjem KMĆ i smrću tumora. Ovi tretmani su brojni i uključuju preciznu isporuku leka (nanopartikule/nanotehnologija, biomagnetizam, itd.). Specijalno dostignuće je daljinska kontrola dopremanja i raspodele leka primenom bežične manipulacije bazirane na mikročipu ili magnetu, što obezbeđuje raspodelu leka u pravom vremenu i njegovo praćenje. Bioprintovani (3D) tumori kao modeli KMĆ služe u svrhe istraživanja unutar različitih scenarija.



## CANCER STEM CELL CONCEPT

Prof Mirjana Pavlović

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Through analysis of over a range of several years, current understanding of the Cancer Stem Cell (CSC) concept is assessed to emphasize areas of opportunity for novel and creative targeted cancer therapy. While many cancer researchers continue to build upon existing models of chemotherapy and radiation in efforts to improve their effectiveness by increasing their specificity, a separate cadre of researchers is exploring a more novel route: CSCs. Novel concept indicates two well defined models, none of which completely can describe its features:

- a) **Stochastic** (clonal evolution): states that all cancer cells hold tumorigenic potential and they are the product of clonal evolution by the acquisition of genetic mutations and epigenetic changes.
- b) **Hierarchical**: tumors show hierarchy, with a subpopulation of CSCs having a tumorigenic potential much greater than that of other cancer cells. Tumor contains hierarchical/heterogeneous organization with stem cells at top, progenitors, and more differentiated cells, no longer able to produce tumors.

The initial efforts of Dick (1994) set the stage for an evidence-based concept of CSCs using the NOD/SCID mice model. He successfully transplanted acute myelogenous leukemia (AML) stem cells from human patients into the murine model, wherein the stem cells regenerated AML in the mice. Classical experiments of Al-Hajj (breast cancer) and Li (pancreatic cancer) were even more supportive. Fluorescent labeling has revealed clonally produced, stable markers, and high tumorigenicity and cancer resistance – the functionality of these, otherwise rare cells (0.1% total population). The rarity of CSC will require therapeutic strategies different from conventional ones.

Critical significance of CSC theory is in novel concept of targeted CSC therapy involving different, original approaches for precise target-CSCs which will shrink, ending up the life of tumor. This treatments are numerous, including drug delivery (nanoparticles/nanotechnology, bio magnetism, etc.). A special achievement is remote control of drug delivery by using a wirelessly controlled microchip, or magnet, producing real-time scheduling/tracking. The bioprinted (3D) tumors turned into CSC disease models serve better research purposes within various scenarios.

## **BIOLOGIJA I KLINIKA MATIČNIH I PROGENITORSKIH ĆELIJA HEMATOPOEZE UMNOŽENIH U KULTURI ZA TRANSPLANTACIJU**

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Koncept umnožavanja matičnih i progenitorskih ćelija hematopoeze u kulturi direktno se naslanja na spoznaje do kojih je došla eksperimentalna hematologija u toku poslednje tri decenije dvadesetog veka.

Te spoznaje su dovele do razumevanja funkcionalne heterogenosti odeljaka matičnih ćelija i progenitora hematopoeze kao i učešća svake od subpopulacija opredeljenih progenitora i matičnih ćelija u hematopoetskoj rekonstituciji posle transplantacije. Uprošćeno, opredeljeni hematopoetski progenitori su „odgovorni“ za prvi talas rekonstitucije posle transplantacije dok od najmanje dve populacije matičnih ćelija prisutnih u transplantatu zavise kratkotrajna i dugotrajna, to jest definitivna, hematopoetska rekonstitucija. Ovi principi, primenjeni na ćelije iz humane kostne srži, matične ćelije i progenitore mobilisane u perifernu krv ili one iz placentarne krvi, su omogućili realizaciju prvih protokola za umnožavanje progenitora i matičnih ćelija hematopoeze u kulturi u cilju povećanje broja opredeljenih progenitora i posledičnog ubrzanja hematopoetske rekonstitucije bez istovremenog uzrokovanja iscrpljenja odeljka matičnih ćelija i posledične insuficijencije transplantata i „gašenja“ hematopoetske rekonstitucije. Ipak, da bi se postigao ovaj cilj bilo je potrebno shvatiti neke osnovne principe funkcionisanja matične ćelije, pre svega njenu anaerobnu prirodu i u vezi s tim, uvideti da je atmosferska koncentracija kiseonika negativno deluje na očuvanje odeljka matičnih ćelija; bilo je potrebno realizovati kulture sa adekvatnim medijumima i koktelima citokina koji dovode do tzv „hipoksičnog odgovora“ ćelija u dovoljnoj meri da se dobije izraziti porast broja opredeljenih progenitora i potpuno očuvanje potencijala matičnih ćelija.

Protokoli za umnožavanje matičnih ćelija i progenitora u kulturi zasnovani na ovim principima su korišćeni za dobijanje ćelija upotrebljenih u kliničkim studijama. Te studije su pokazale da je moguće značajno skratiti ili potpuno „premostiti“ posttransplantacijsku agranulocitozu bez ugrožavanja dugotrajnog rekonstitutivnog potencijala transplantata ako su hematopoetske ćelije adekvatno umnožene u kulturi.

**BIOLOGY AND CLINICS OF EX VIVO EXPANSION OF HEMATOPOIETIC STEM AND PROGENITOR CELLS**

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The concept of ex vivo expansion of hematopoietic stem and progenitor cells is directly issued from the knowledge provided by experimental hematology during the last three decades of 20th century.

This knowledge enabled to realize the functional heterogeneity of the compartment of hematopoietic stem and progenitors cells and participation of each of several committed progenitors and stem cell classes in kinetics of ex vivo reconstitution after transplantation. Roughly, committed hematopoietic progenitors are responsible for the first wave of hematopoietic reconstitution while short-term and long-term repopulating hematopoietic stem cells are needed to maintain post-transplantation hematopoiesis during months and years i.e. for a sustained graft-generated hematopoiesis. These principles, transposed to human cells originating from bone marrow peripheral blood and cord blood, enabled to conceptualize the first protocols of ex vivo expansion aiming to accelerate hematopoietic reconstitution after transplantation without inducing the exhaustion of stem cells and consequent graft failure. However, it was necessary to get insight of anaerobic nature of hematopoietic stem cells and understand the negative influence of atmospheric oxygen concentration on stem cell maintenance to realize the appropriate culture media and cytokine cocktails mimicking “hypoxic effects” i.e. providing the conditions for amplification of committed progenitors in parallel with the maintenance of stem cells.

This way, the hematopoietic progenitor and stem cells expanded ex vivo were used for clinical trials in which they showed a capacity to significantly decrease or totally abrogate post-transplant agranulocytosis without impairing the sustained hematopoietic reconstitution originating from the graft.

## **MATIČNE ĆELIJE MOZGA, NJIHOVA ULOGA I DETEKCIJA U MOZGU ODRASLIH LJUDI**

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Otkrice neurogeneze, procesa stvaranja neurona, u mozgu odraslih sisara je otvorilo nove horizonte modernoj neurobiologiji: nasuprot stogodisnjoj dogmi da se novi neuroni ne formiraju posle rođenja, mozdan tkivo ipak ima mogućnost da se regenerise. Novi neuroni se svakodnevno radjaju u dvema regijama mozga: hipokampusu, centru za učenje i pamćenje, i u subventrikularnoj zoni, odakle migriraju prema olfaktornom bubusu. Hipokampalna neurogeneza predstavlja posebnu vrstu multicelularne plasticnosti: novorođeni neuroni se stvaraju od lokalnih stem celija kao rezultat adaptacije na potrebe tkiva. U animalnim modelima, novorođeni neuroni su važni za pamćenje i regulaciju stresa i raspoloženja. Kod ljudi, analiza datuma rođenja celija pomoću  $^{14}\text{C}$  metode je ustanovila da se oko 700 novih neurona dnevno integriše u hipokampus, ali njihova funkcija je za sada nepoznata jer ne postoji način da se ovi neuroni detektuju u mozgu ljudi.

U našim istraživanjima, našli smo da su izolovane stem celije mozga obogatene lipidima koji se mogu videti na spektru magnetne rezonance jer osciluju na frekvenciji od 1.28ppm. Da bi omogućili detekciju ovog signala u mozgu ljudi, mi smo razvili analitički metod za automatsko i objektivno merenje 1.28ppm signala u spektrima dobijenim magnetnom rezonancom koristeći 3T MRI skenere. Naša metodologija omogućava preciznu detekciju delova mozga gde neurogeneza postoji. Takođe, naša istraživanja su uspostavila prvu vezu između neurogeneze, starosti, i depresije kod ljudi. Jedan od značajnih rezultata ove studije je da elektrokonvulzivna terapija koja se rutinski primenjuje kod depresivnih pacijenata koji ne reaguju na lekove, dovodi do dvostrukog povećanja neurogenog signala posle prve terapije. Ovaj porast direktno korelira sa povećanjem volumena hipokampusa i rezolucijom depresivnih simptoma na kraju terapije.

Dakle, naše studije omogućavaju istraživanja stem celija i neurogeneze kod ljudi i ispitivanja značaja ovog procesa za razvoj depresije, demencije, i za procenju efikasnosti lekova koji utiču na ovaj proces. Takođe, ova metoda može da se koristi za detekciju aktiviranih matičnih celija kao i onih koje su transplantirane u mozak ljudi – prve takve intervencije se trenutno testiraju kao terapijski modaliteti za mozdani udar i multiplu sklerozu.

## **NEURAL STEM CELLS, THEIR ROLE AND DETECTION IN THE ADULT HUMAN BRAIN**

Prof Mirjana Maletic-Savatic  
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Texas Children's Hospital, Baylor College of Medicine, Houston, USA

The discovery of adult neurogenesis has opened a new era in modern neurobiology: the brain, after all, has the capacity to regenerate. In the mammalian brain, new neurons are continuously formed in two brain regions: hippocampus, the center for learning and memory, and the subventricular zone, from which new neurons migrate to the olfactory bulb. Adult hippocampal neurogenesis is one of the brain's most elusive multicellular forms of plasticity: the *de novo* formation of new neurons from neural stem cells is not merely static or restorative; rather, it is an adaptive response of the brain to our needs. In animal models, newborn neurons are important for cognition, mood and stress regulation. In humans, <sup>14</sup>C-retrospective cell birth dating estimates that about 700 new neurons are integrated daily into the human hippocampus, but their functional importance is not known because of the lack of a live and non-invasive measure.

Based on a series of experiments using magnetic resonance spectroscopy (MRS), we previously identified a fatty acid-related metabolite that is highly enriched in neural stem cells and visible at 1.28ppm on the resonance spectrum. To enable detection of the neural stem cells in the human brain, we developed an analytical algorithm that allows automated and objective quantitation of the 1.28ppm spectroscopic signal obtained by 3T MRS. Using this method, we can distinguish neurogenic and non-neurogenic areas in the human brain. Further, we discovered that the neurogenic signal is associated with age and depression. Strikingly, in medication-resistant depressed individuals, electroconvulsive treatment provokes a two-fold signal increase – a leading indicator that predicts subsequent hippocampal plasticity and clinical outcome.

Overall, we now have the means to study neurogenesis in the live human brain and provide new insights on the role of this process in human brain function, dysfunction and treatment response. Moreover, this method may be used to trace activated and/or stem cells transplanted into the human brain, already in clinical trials for stroke and multiple sclerosis.



**SPONZORSKA PREDAVANJA ACIBADEM**  
***ACIBADEM'S SPONSORED LECTURES***

## **INDICATIONS FOR HAPLOIDENTICAL TRANSPLANTATION.**

Prof. Ratip Siret

Department of Hematology, Acibadem Kozyatagi Hospital, Istanbul, Turkey.

Nowadays choosing between Haploidentical, HLA matched unrelated and HLA mismatched umbilical cord blood transplantations can be difficult. A significant number of patients are lost as a result of relapsed disease whilst awaiting for an HLA matched unrelated transplant. On the other hand, many patients planned for cord blood transplants are unable to proceed as a result of insufficient CD34+ cell number.

Developments in Haploidentical transplantation including alpha beta T-cell and CD19+ cell depletion, mesenchymal stem cell support and post transplant high dose cyclophosphamide lead to improved survival reaching a similar level as HLA matched unrelated transplants.

## **OUR LIVER TRANSPLANTATION EXPERIENCE**

Prof. Remzi Emiroğlu

First cadaveric liver transplantation was performed in 8 December 1988 in our country. Between 1988 and 2001 liver transplantation was practiced just in private hospitals. Since 2001 the government has been supporting the liver transplantation program. The formation of national transplantation organization has led to significant developments in liver transplantation.

Additionally, the evolution in medical technology has expedited the all steps of transplantation and also has enabled new surgical techniques. Afterall, the amount of liver transplantation has increased rapidly and also the variation of transplantation techniques has risen.

**SESIJA 2 – TRANSPLANTACIJA ORGANA I  
TKIVA U SRBIJI**

***SESSION 2 – ORGAN AND TISSUE  
TRANSPLANTATION IN SERBIA***

## **RAZVOJ TRANSPLANTACIJE ORGANA U SRBIJI**

Prof. dr Nebojša Stanković  
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Prava era transplantacije organa (TO) u svetu započinje 50-ih godina XX veka sa prvom uspešnom transplantacijom bubrega (J. Murray i D. Hume, 1954.) i koštane srži (D.Thomas, 1956.), a kasnije transplantacijom i drugih organa ( jetre, 1963. T. Starzl; pluća, 1963. J.Hardy; pankreasa, 1966. R. Lillehei i W. Kelly; srca, 1967. Ch. Barnard itd.).

Istorija transplantacije u Srbiji počinje početkom XX veka sa transplantacijom testisa, što je kasnije napušteno (dr Pjotr Vasiljevič Kolesnikov, 1926. u Zaječaru). Prva transplantacija bubrega u Srbiji urađena je 1973, godine u Gradskoj bolnici na Zvezdari (prof dr Vasilije Jovanović i Prim dr Milan Jovanović), a prva uspešna od živog srodnog davaoca urađena je u Urološkoj klinici KCS u Beogradu, 1975. (Akademik Sava Petković). Prva transplantacija jetre 1995. – u IKVB „Dedinje“ u Beogradu (prof dr Božina Radević), pankreasa 1996. (prof dr Božina Radević), srca 1996. – u IKVB „Dedinje“ (prof dr M. Huskić) i koštane stži od alogenog davaoca 1997. - u Institutu za majku i dete u Beogradu.

Danas se TO u transplantacionim centrima u Srbiji obavlja sporadično ( KCS: bubreg, jetra, srce, rožnjača; VMA: bubreg, jetra, koštana srž; KCV u N.Sadu: bubreg, jetra; KC u Nišu: bubreg; UDK „Tiršova“ u Beogradu: bubreg, jetra; Institut za majku i dete u Beogradu: koštana srž).

U poslednjih 20 godina stvorena je osnova za dalji razvoj TO u Srbiji. Međutim, broj i vrsta do sada objavljenih TO ne zadovoljava, u odnosu na lokalne potrebe kao i prema broju transplantacija u državama EU. I pored određenih pomaka, Srbija je i dalje na začelju u EU (iza su samo Albanija, Crna Gora, Makedonija i BiH).

Kadaverična TO je merilo kulturne i civilizacijske razvijenosti jedne evropske zemlje (Helsinčka Dekleracija, 1986.). Izazovi TO u Srbiji nisu samo medicinski problem, već pre svega etičko, organizacijsko, medijsko i finansijsko pitanje i drugo.

## **THE DEVELOPMENT OF ORGAN TRANSPLANTATION IN SERBIA**

Prof Nebojša Stanković  
Medical Military Academy, Belgrade, Serbia

First era of organ transplantation (OT) in the world has begun in 50's of XX th century with first successful kidney transplantation (J. Murray and D. Hume, 1954.) and bone marrow (D. Tomas, 1956.), and later transplantations of other organs (liver, 1963. T. Starzl; lungs 1963. J. Hardy; pancreas, 1966. R. Lillehei and W. Kelly; heart, 1967. Ch. Barnard and so on).

History of transplantation in Serbia has begun at the beginning of XXth century with testis transplantation, which was abandoned later (Dr Pjotr Vasiljevič Kolesnikov, 1926. in Zaječar). First kidney transplantation in Serbia was done in 1973. in Belgrade's city hospital on Zvezdara (prof. dr Vasilije Jovanović and primarius dr Milan Jovanović), and a first from alive related donor was done at Urological Clinic of KCS in Belgrade, 1975 (academic Sava Petković). First liver transplantation 1995. in IKVB „Dedinje“ in Belgrade (prof Božina Radević), pancreas 1996. (prof Božina Radević), heart 1996. – in IKVB „Dedinje“ (prof R. Huskić) and bone marrow from inventories donor 1997. – in Institute for mother and child in Belgrade.

Today, OT in transplantation centers in Serbia is practiced sporadically (KCS: kidney, liver, heart, cornea; VMA: kidney, liver, bone marrow; KCV in Novi Sad: kidney, liver; KC in Niš: kidney; UDK Tiršova in Belgrade: kidney, liver; Institute for mother and child in Belgrade: bone marrow.

The basis for future development of OT in Serbia was created in the last 20 years. But the number and category of so far published OT is unsatisfying with respect to local requirements and the number of transplantations in EU. Despite some progress, Serbia is still at the bottom in EU ( behind are only Albany, Monte Negro, Macedonia and BiH).

Cadaveric transplantation is a measure of cultural and civilization development of one European country (Helsinki Declaration, 1986). OT challenges in Serbia are not only medical problem, but first of all ethics, media and financial issue and other.



## **ULOGA UREĐAJA ZA MEHANIČKU POTPORU CIRKULACIJI LEVOM SRCU KOD PACIJENATA SA TERMINALNIM STADIJUMOM SRČANE INSUFICIJENCIJE – ISKUSTVO KLINIČKOG CENTRA SRBIJE**

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**Uvod:** Transplantacija srca (HTx) je realna opcija lečenja samo za mali broj pacijenata sa terminalnim stadijumom srčane insuficijencije (SI). Usled malog broja dostupnih donatorskih organa i sve većeg broja pacijenata nepodobnih za transplantaciju srca, uređaji za mehaničku potporu cirkulaciji levom srcu (LVAD), postaju sve više opcija lečenja ovih pacijenata. Cilj ovog rada je prikazivanje iskustva našeg centra u pogledu lečenja pacijenata sa uznapredovalim stadijumom SI primenom LVAD terapije.

**Metod:** LVAD je implantiran kod 38 pacijenata, kao vid dugoročne terapije SI u Kliničkom centru Srbije u periodu od 2013 do 2015; 9% je podvrgnuto HTx, nakon medijane od 13 meseci provedenih na LVAD-u. Većina pacijenata je bila muškog pola (94,7%). Najčešći uzrok SI je bila ishemijska kardiomiopatija (52,6%). U odnosu na INTERMACS klasifikaciju, 52,6% pacijenata je pripadalo grupi 4, 26,3% grupi 2. Medijana praćenja posledičnih ishoda (ukupno preživljavanje i neželjeni efekti) je bila 7 (23) meseci.

**Rezultati:** Prosečna starost pacijenata je bila  $50,24 \pm 14,6$ . Medijana vremena provedenog na potpori LVAD-om je bila (23) meseca. Ukupno, 30 dnevno, 6-mesečno i 1-godišnje preživljavanje je bilo 91,2%, 88,5% and 76,2%. 20 (52,6%) pacijenata je imalo neki vid neželjenih efekata. Serumski kreatinin, urea, ukupni bilirubin, infekcija i renalna insuficijencija su dijagnostikovani kao faktori rizika značajno povezani sa smanjenjem ukupnog preživljavanja u univarijantnoj Cox-regresionoj analizi ( $p < 0,05$ ), a renalna insuficijencija je kao nezavisni faktor rizika sveukupnog preživljavanja u multivarijantnoj Cox-regresionoj analizi ( $p = 0,035$ ).

**Zaključak:** Implantacija LVAD-a je povezana sa prihvatljivom stopom mortaliteta, sličnoj kao nakon transplantacije srca i predstavlja efektivnu opciju lečenja za pacijente sa terminalnom fazom srčanog popuštanja. Renalna insuficijencija je nezavisni faktor rizika ukupnog preživljavanja i česta je pojava nakon ugradnje LVAD-a. Utvrđivanje optimalnog vremena za ugradnju LVAD-a doprineće u budućnosti smanjenju stope pojave neželjenih efekata nakon implantacije ovih uređaja.

**Ključne reči:** Srčana insuficijencija, Transplantacija srca, Uređaji za mehaničku potporu levom srcu

## **ROLE OF LEFT VENTRICULAR ASSIST DEVICE THERAPY FOR PATIENTS WITH END-STAGE HEART FAILURE –EXPERIENCE OF CLINICAL CENTER OF SERBIA**

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**Background:** Heart transplantation (HTx) is a realistic option for only a small number of end-stage heart failure (HF) patients. Due to organ donor shortage and growing number of HTx ineligible patients, left ventricular assist device (LVAD) has become more beneficial option. The goal of this study was to report our single-center experience concerning treatment patients with advanced HF with LVAD support.

**Methods:** Overall, 38 patients received long-term LVAD at Clinical Center of Serbia from 2013 to 2015; 9% underwent HTx after a median duration of LVAD support of 13 months. The majority of subjects were male gender (94,7%). The most frequent etiology of the HF was ischemic cardiomyopathy (52,6%). Regarding the INTERMACS profile, the 52,6% of patients were profile 4, and 26,3% profile 2. The median follow up for consequently outcomes (overall survival and adverse events) was 7 (23) months.

**Results:** The mean age of patients was  $50,24 \pm 14,6$ . Median duration of LVAD support was 7 (23) months. The overall 30 day, 6-months and 1-year survival were 91,2%, 88,5% and 76,2%. Among patients adverse events were present in 20 (52,6%). Serum creatinine, blood urea nitrogen, total bilirubin, infection and renal failure were associated with a significantly decrease of overall survival rate in the Univariate Cox regression analysis ( $p < 0,05$ ), and renal failure was found to be an independent risk factor for overall survival in multivariate Cox regression analysis ( $p = 0,035$ ).

**Conclusion:** LVAD is associated with acceptable mortality rate, similar to heart transplant and it represents an effective treatment option for patients with end-stage HF. Renal failure is common following LVAD implantation and is an independent risk factor for overall survival. The resolution of optimal timing of LVAD implantation will contribute to reduce the rate of adverse events in the future.

**Key words:** Heart failure, heart transplantation, left ventricular assist device

## **TRANSPLANTACIJA SRCA – DVOGODIŠNJE ISKUSTVO KLINIČKOG CENTRA SRBIJE**

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**Uvod:** Pacijenti u terminalnom stadijumu srčane insuficijencije (SI) refrakterne na konvencionalnu medikamentoznu terapiju, imaju lošu prognozu preživljavanja. Transplantacija srca (HTx) predstavlja opciju lečenja za ovu grupu pacijenata, uprkos činjenici da usled nedovoljnog broja dostupnih donorskih organa i sve većeg broja pacijenata preko 70 godina starosti je dostupna samo malom broju pacijenata. Cilj ove studije je da prikaže iskustvo našeg centra u pogledu lečenja pacijenata sa krajnjim stadijumom SI koji su podvrgnuti HTx.

**Metod:** Transplantacija srca je urađena kod 14 pacijenata u našem centru u periodu od septembra 2013.g. do novembra 2015.g; 3 (21,4%) su transplantirana nakon medijane od 13 meseci provedenih na uređaju za mehaničku potporu cirkulaciji levom srcu (LVAD). 63 % pacijenata je pripadalo grupi 4 a 19 % grupi 2 u odnosu na INTERMACS klasifikaciju,. Jedan pacijent je pripadao INTERMACS profilu 1 (kardiogeni šok). Najčešći uzrok SI je bila idiopatska kardiomiopatija (CMP) i većina pacijenata su pripadala muškom polu (82%). Medijana praćenja posledičnih ishoda (ukupno preživljavanje i neželjeni efekti) je bila 12,5 (26) meseci.

**Resultati:** Prosečno godište pacijenata je bilo 49,55 ±7,2 godine. 6-mesečno i jednogodišnje preživljavanje pacijenata sa transplantacijom srca bilo je 63,6%, i predstavljaju odraz višeg ranog 30-odnevno mortaliteta (4/14). Dva pacijenta su umrla zbog multiorganskog popuštanja, jedan kao posledica krvarenja nakon korišćenja trojne antikoagulantne terapije i jedan usled postransplantacionog razvoja Guillain Barr sindroma.

**Zaključak:** U svetlu nedovoljnog broja donorskih organa, i sve veće upotrebe organa od marginalnih donora, ključ uspešnog transplantacionog programa svake zemlje leži u dobroj preoperativnoj selekciji pacijenata. Utvrđivanje optimalnog vremena za transplantaciju srca, doprineće smanjenju stope mortaliteta ovih pacijenata kao i stope razvoja neželjenih efekata.

**Ključne reči:** Srčana insuficijencija, Transplantacija srca, Uređaji za mehaničku potporu levom srcu

## **TWO – YEARS EXPERIENCE IN HEART TRANSPLANTATION IN CLINICAL CENTER OF SERBIA**

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**Background:** Patients with end-stage heart failure (HF), refractory to conventional medical therapy, show a poor short-term survival prognosis. Despite the fact that heart transplantation (HTx) can be performed in only a minority of patients due to organ donor shortage and increasing number of patients over 70, it's remains the therapy of choice for this group of patients. The aim of this study was to report our single-center experience concerning treatment patients with advanced HF who underwent (HTx).

**Methods:** 14 patients underwent heart transplant at our center from September 2013 to November 2015; 3 (21,4%) underwent HTx after a median duration of Left Ventricular Assist Device (LVAD) support of 13 months. Regarding the INTERMACS profile, the 63 % of patients were profile 4, and 19 % profile 2. One patient was in cardiogenic shock, INTERMACS profile 1. The most frequent etiology of the HF was idiopathic cardiomyopathy (CMP) and majority of patients are male gender (82%). The median follow up for consequently outcomes (overall survival and adverse events) was 12,5 (26) months.

**Results:** The mean age of patients was 49,55 ±7,2 years. Due to 30 day mortality rate of 36% (4/14), both overall 6 months and 1year survival, were lower 63,6% for all period of follow-up. Two of them died because of multisystem organ failure, one because of bleeding complication after using triple anticoagulation therapy and one due to post transplant Guillain Barr syndrome.

**Conclusion:** Due to growing number of using marginal donor hearts in the light of insufficient availability of donors, the key of the success of transplant program in every country is a good preoperative selection of patients. Determining of optimal timing of heart transplantation will contribute to reduce the mortality rate and rate of adverse events.

**Key words:** Heart Failure, Heart Transplantation, Left Ventricular Assist Device

**EXPANDED CRITERIA DONORS IN FUNCTION OF THE INCREASED NUMBER OF CADAVERIC KIDNEY TRANSPLANTATION AT THE MILITARY MEDICAL ACADEMY IN BELGRADE**

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Significant disproportion between the number of patients registered in the waiting lists for kidney transplantation and the number of available organs impose the need for assessment of the kidney transplantation suitability both from living and cadaveric Expanded Criteria Donors (ECD). Results of the Eurotransplant Senior Programme „Old to Old“ as well as better survival of the aged patients after kidney transplantation from the ECD in comparison with their survival on the chronic dialysis, have imposed the need for detailed evaluation of each ECD as potential kidney donor. ECD are defined according to the current definition -older than 60 years or donors aged 50 - 59 years with presence of one or two mentioned parameters: brain stroke as the cause of brain death and also presence of the arterial hypertension within the longer period, that is, when the serum creatinine is higher than 130 mmol/L in the time of donor realisation.

Within the period 2010.-2014., 23 cadaveric donors from MMA and other donor hospitals were realised: 7 of them were younger than 50 years, 10 donors were 50-60 years old and 6 of them were over 60. 17 donors were males and 6 females. 7 donors had characteristics of the donor under standard risk and 16 of them were ECD. Average age of all of them was  $51.6 \pm 13.7$  years, the youngest one was 2 and the oldest one 76 years old. Average age of the kidney recipient was  $46.2 \pm 10.1$  years and the average dialysis period before kidney transplantation was  $50.2 \pm 40.0$  months. 33 kidney recipients were males and 12 females. One-year and three-year recipient survival period was 88.9%, and of the graft 88.9%, namely, 82.23%. The serum creatinine levels in the kidney recipient after one and three years of the posttransplantation period were  $141 \pm 42$ , that is,  $141 \pm 99.1$  micromol/L. In the kidney recipient from the standard ECD the serum creatinine levels were not statistically different after the first and the third year of the kidney transplantation (Mann-Whitney test  $p > 0.05$ ). Zero kidney biopsy with pathohistologic scoring was used for making decision concerning the kidney allocation.

Clinical evaluation, experience of an explantational urologist and pretransplantation kidney biopsy together with histologic score assessment have great importance in the kidney allocation and choice of modality (transplantation of only one or both kidneys).

## **TRANSPLANTACIJA JETRE U SRBIJI**

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Transplantacija jetre predstavlja najsloženiju proceduru u oblasti transplantacije solidnih organa. Prva uspesna transplantacija jetre u svetu uradjena je 1965 god u USA. Pocetkom 80-tih u Zagrebu je uradjena prva transplantacija jeyre u SFRJ. 1995 god je u Beogradu uradjena prva trasplantacoja jetre u SCG a 2008 godine u Novom Sadu je uradjena prva transplantaciha jetre u Vojvodini.

Uprkos visedecenijskom iskustvu, program tranaplantacije jetre u Srbiji nije do danas zaziveo u punom obimu i prema potrebama pacijenata/oko 150 transplantacija godisnje/.Brojni su razlozi za to a mogli bi se podeliti u tri grupe:

1. Nedovoljan razvitak Donorskog programa uz izostanak kontinuirane podrške Ministarstva Zdravlja i RFZO
2. Nedostatak dovoljnog broja adekvatno edukovanog strucnog kadra-hirurzi,anesteziolozi...
3. Politizacija celokupnog programa uz nepostovanje strucnih iracionalnih faktora u odredjivanju transplantacionog centra/centara.

U ovom trenutku zvanicno postoje tri centra u Srbiji gde se obavlja transplantacija jetre.Gledajuci veliko iskustvo u oblasti resekcione a i transplantacione hirurgije jetre, kontinuitet u radu/1998 resekcije,2008 transplantacije/, te broj uradjenih transplantacija kao i rezultate, Klinicki Centar Vojvodine predstavlja vodecu ustanovu u Srbiji za ovu oblast. U daljem toku izlaganja bice prezentovani nasi rezultati.

## **LIVER TRANSPLANTATION IN SERBIA**

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Liver transplantation is the most complex procedure in solid organ transplantation field. First successful liver transplantation in the World was performed in the USA 1965. In former Yugoslavia, first liver transplantation was made in Zagreb at the beginning of 1980. First liver transplantation in Serbia and Montenegro was performed in Belgrade 1995, and in 2008, first liver transplantation was done in Novi Sad in Vojvodina. Despite of decades of experience, liver transplantation program in Serbia did not begin to fully live, according to patients needs (approximately 150 transplantations per year). There is a numerous reasons for that, and all could be divided into three groups:

1. insufficient development of the Donor program with absence of continued support of the Ministry of Health and Health Insurance
2. lack of adequate number of properly educated specialist (surgeons, anesthesiologist, nurses etc)
3. politization of the whole program with disrespect of the experts factors in determining of Transplantation Center.

As for now, officially there is three Centers in Serbia where liver transplantation is performing. Looking at huge experience in the field of liver resections, liver transplantations surgery, continuity in work as well as achieved results, Clinical Center Vojvodina presents leading institution in Serbia in this field. In the further course of this presentation, the our results will be presented.



## **TRANSPLANTACIJA BUBREGA U SRBIJI**

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Transplantacija bubrega je metod izbora u lečenju terminalne bubrežne insuficijencije. Do sada u svetu ima oko 400000 transplantiranih. U Evropi oko 30000 ljudi čeka na transplantaciju bubrega. U Srbiji se broj bubrežnih bolesnika uvećava za oko 15% i sada se na hemodijalizi nalazi oko 5000 ljudi. Prvu transplantaciju bubrega u SFRJ je izveo dr V. Frančišković u Rijeci 1971, a u Beogradu dr S. Petković 1975. Prvu transplantaciju bubrega sa živog davaoca na VMA su izveli Elaković i Kronja 30.01. 1996. godine, a prvu kadaveričnu transplantaciju Kronja, Elaković, Mišović i Milović 24.10.1998. godine. Do sada je u Srbiji učinjeno oko 1500 transplantacija bubrega, od toga u KC Srbije oko 900, VMA oko 410, KC Novi Sad oko 150, KC u Nišu 50, i KC Banja Luci 25. U Srbiji ima oko 50 000 vlasnika donorskih kartica. Na listi čekanja za kadaveričnu transplantaciju bubrega nalazi se oko 1000 osoba. Osnovni problemi u ranoj fazi transplantacije bubrega su hirurške komplikacije, ishemija bubrega, metabolički problemi i rane manifestacije ishemijsko-reperfuzione povrede sa oksidativnim i nitrozativnim stresom.

Hiperakutno i akutno odbacivanje je svedeno na minimum a hronično se nalazi u svetskim okvirima. Izračunate vrednosti glomerulske filtracije MDRD formulama smeštaju donore u grupu pacijenata sa trećim stepenom hronične bubrežne insuficijencije. Neophodno je redovno postoperativno praćenje donora kao potencijalnog pacijenta, kao i pažljiv odabir donora bez komorbiditeta. Najnoviji napredak u transplantaciji bubrega u VMA se beleži u transplantaciji preko pozitivnog crossmatch-a i preko krvno-grupne barijere. Jednogodišnjim preživljavanjem grafta u 90 % slučajeva i prosečnim trajanjem grafta od 10 g ova procedura bolesnicima znatno popravlja komfor i kvalitet života. Transplantacija bubrega društvu èini ustupak, jer je u dužem periodu znatno jeftinija od dijalize.



## **KIDNEY TRANSPLANTATION IN SERBIA**

Ass. prof Aleksandar Tomić  
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Kidney transplantation is the method of choice in the treatment of renal insufficiency. So far the world has about 400,000 transplanted. In Europe, about 30,000 people waiting for a kidney transplant. In Serbia, the number of kidney patients increased by about 15% per year and now undergoing dialysis are about 5000 people. The first kidney transplant in Yugoslavia has brought Dr. V. Frančičković in Rijeka in 1971, and in Belgrade Dr. S. Petkovic in 1975. The first kidney transplant from a living donor at the Military Medical Academy performed Prof. dr D. Elaković and Prof. dr G. Kronja 30.01. In 1996, a first cadaveric transplant Kronja, Elaković, Mišović and Milović 24.10.1998. So far in Serbia done about 1,500 kidney transplants, of which the Clinical Center of Serbia around 900, VMA around 410, KC Novi Sad about 150, KC Nis 50, and KC Banja Luka 25. In Serbia there are around 50,000 owners of donor cards. On the waiting list for a kidney transplant is around 1,000 people. The main problems in the early stages of kidney transplantation were surgical complications, kidney ischemia, metabolic problems and early manifestations of ischemia-reperfusion injury with oxidative and nitro stress.

Hyperacute and acute rejection are minimized and chronic rejection is as in average the world results. The calculated value of glomerular filtration MDRD formulas accommodations donors in the group of patients with third degree of chronic renal failure. It is necessary for regular postoperative follow-up of donors as a potential patient, and careful selection of donors without comorbidity. The latest advances in kidney transplantation in MMA is recorded in transplantation through positive crossmatch and across the blood-group barriers. With a one-year graft survival in 90% of cases and with 10 y average duration of graft, this procedure significantly improves comfort and quality of life of transplanted patients. Kidney transplantation makes a concession for society because in the long run considerably cheaper than dialysis.

## **SISTEM HLA I TRANSPLANTACIJA ORGANA**

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Odeljenje za tipizaciju tkiva, Institut za transfuziju krvi Srbije

Otkrića centralne uloge HLA u celularnom i humoralnom imunskom odgovoru kao i izraženog polimorfizma HLA doprinela su da tipizacija tkiva bude neizostavni deo procedure izbora parova za transplantaciju organa. Uvažavajući najnovija saznanja o kliničkom značaju sistema HLA, ovo pravilo se primenjuje u Srbiji od prvih transplantacija bubrega urađenih sedamdesetih godina prošlog veka. Stepenn podudarnosti davaoca i primaoca za povoljan ishod transplantacije se razlikuje u zavisnosti od organa koji se transplantira. U retrospektivnim studijama nije dokazan uticaj podudarnosti HLA na ishod transplantacije jetre. Povoljan efekat HLA-A, -B i -DR podudarnosti dokazan je za transplantacije ostalih organa, posebno bubrega i pankreasa gde se, uz podudarnost u ABO sistemu, smatra kriterijumom za izbor parova za transplantaciju.

Glavna laboratorijska ispitivanja za potrebe transplantacije bubrega su tipizacija HLA pacijenata i davalaca organa, kao i ispitivanje prisustva i specifičnosti anti-HLA antitela u serumu primaoca organa. Skrining anti-HLA antitela i unakrsna reakcija seruma pacijenta sa sopstvenim limfocitima i limfocitima davaoca primenjuju se za transplantacije svih solidnih organa. Pored testova komplement zavisne citotoksičnosti, u rutinski rad uvedeni su testovi molekularne tipizacije HLA kao i Luminex metode za detekciju i ispitivanje specifičnosti anti-HLA antitela. Definisane donor-specifičnih anti-HLA antitela novim osetljivijim metodama omogućilo je pouzdaniju procenu imunološkog rizika pri izboru parova za transplantaciju. Navedena ispitivanja u Srbiji obavljaju se u laboratorijama akreditovanim od strane Evropske federacije za imunogenetiku (EFI).

Odeljenje za tipizaciju tkiva Instituta za transfuziju krvi Srbije (ITKS), prva laboratorija za ispitivanje sistema HLA u Srbiji, učestvovala je u skoro svim transplantacijama organa sa živog ili kadaveričnog donora koje su urađene u glavnim transplantacionim centrima na ovom prostoru. Rad Odeljenja je organizovan po principu pripravnosti ekipa 24 h dnevno, sedam dana u nedelji, za potrebe realizacije programa kadaverične transplantaciju organa. Odlukom Ministarstva zdravlja Republike Srbije, Lista čekanja za kadaveričnu transplantaciju bubrega formirana je 1976. godine u ITKS i do danas se svakodnevno ažurira kao elektronska baza podataka o oko 600 pacijenata sa cele teritorije Republike Srbije. Automatskom obradom podataka za svakog kadaveričnog donora pravi lista potencijalnih primalaca odgovarajuće krvne grupe ABO, rangiranih prema stepenu podudarnosti HLA. Prateći savremene trendove u imunogenetici i tehnološke novine više od četiri decenije naša ustanova doprinosi unapređenju programa transplantacije organa u Srbiji.

## **SYSTEM HLA AND ORGAN TRANSPLANTATION**

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Recognizing the clinical importance of HLA, from the very beginning of organ transplantation program in Serbia, HLA testing has become the cornerstone of determining transplant suitability in both living and cadaver donor renal transplantation. There are two fundamental reasons for HLA testing is an essential component of successful organ transplant program. First, the HLA plays a central role in the cellular and humoral immune response that determine the outcome of a transplant and the second, the extensive HLA polymorphism poses a major barrier to successful transplantation. The effect of HLA matching on clinical outcome varies greatly with the organ being transplanted. In the case of liver transplantation, donor matching may actually be detrimental. In transplantation of other organs, the benefits of HLA-A, -B, and -DR matching are still evident, especially in renal and pancreas transplantations where is the ground rule in the allocation of cadaveric donor organs.

The HLA typing of both organ recipients and organ donors, determination of HLA antibodies in patient serum and cross-matching are the main immunogenetic tests prior to the transplantation. In Serbia, immunogenetic assessment of donors and recipients of living donor and cadaver organs is performed at tissue typing laboratories, actually accredited by the European Federation for Immunogenetics.

Till nowadays the Tissue typing department of Blood transfusion Institute, the first tissue typing laboratory in Serbia which manages immunogenetic part of organ transplantation program, was involved in almost all transplantations performed in main transplant centers in Serbia operating "on call" 24 hours a day, 7 days a week. Under the auspices of the Ministry of Health the staff of our Tissue Typing Department founded the National kidney recipient waiting list in 1976. and up to date is responsible for list keeping and informatics of central donor/recipient selection. Actually, there are about 600 kidney recipients registered on the waiting list.

As a result of major advances in technology, HLA-typing has evolved from serological-based typing to molecular HLA-typing and solid-phase anti-HLA-antibody detection assays, which have had a major influence in both allocation and outcome of transplanted kidneys. The identification of donorspecific anti-HLA-antibody (DSA) has become standard practice.

The availability of these sensitive assays has enable clinicians to perform identified donorspecific anti-HLA antibody, which has led to a more accurate assessment of immunological risk of potential transplant candidates and improvement in the program of organ transplantation in Serbia.

**SESIJA 3 – ORGANIZACIJA HITNE  
MEDICINSKE POMOĆI U URGENTNIM  
KARDIO I CEREBROVASKULARNIM  
STANJIMA**

***SESSION 3 – ORGANISATION OF  
EMERGENCY MEDICAL CARE IN CARDIO  
AND CEREBROVASCULAR EVENTS***

## **ORGANISATION OF EMERGENCY SERVICES AND COOPERATION WITH STROKE UNITS IN SWITZERLAND**

Thomas Kamber  
Medical Director of EMS Kantonsspital Aarau

Switzerland is a Federation of Cantons. These are responsible for the organization and the structure of the emergency medical services. Considering 26 health laws, differences in demography, topography, interests and financial situation, there is no typical Swiss emergency service. Nonetheless there is a national association with a mandate of the cantons to coordinate activities, setting quality standards and controlling them.

Key points of the quality are human resources (emergency physicians, paramedics, disponents of medical alarm center), infrastructure (rescue vehicles and equipment, intervention times), formation and continuous training.

The groundbased EMS is by far the most important part of Swiss rescue, but there is a long tradition of excellent cooperation with air borne rescue, alpine and water rescue, fire departments and the police. These “blue light” organisations are coordinated nationwide by the Federal Bureau of Civil Defence.

Since the development of new treatment protocols caring for stroke patients becomes a numerically fast growing task. In cooperation with the department of neurology, our EMS developed algorithms for preclinical identification and care, treatment in the emergency room and patient support during neuroradiological diagnosis and interventions. As the EMS is part of the department of Anesthesia, transfer between partners is fast and smooth.

A difficult part in the stroke treatment sequence is raising the awareness of the public for the problem of stroke. This campaign is a cooperative approach between neurologists, the Swiss Heart Association and the rescue system.

## **EMERGENCY STROKE CARE- UK EXPERIENCE, WHAT REALLY MATTERS**

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London, UK

Stroke is preventable and treatable disease. The traditional concept of perception, that stroke is simply a consequence of ageing that results in death or disability, has changed significantly.

Growing body of evidence suggests that our understanding and knowledge contribute to a better outcome of this disabling condition. More evidence-based practice and regular auditing as well as implementation of guidelines in practice, provide clinicians and patients with more supporting data and recommendations for better patient-centred care.

Stroke being health and resource burden, until recently, was not perceived as a high priority in UK National Health System. UK National Stroke Strategy outlines needs for immediate diagnosis, treatment and management including all aspect of care from initial response to life after stroke. Emergency Stroke Care protocols and guidelines take into account patients' needs and preferences.

Good communication between healthcare professionals, patients and their families and carers is essential.

The above presentation is aiming to provide some answers for challenging dilemmas present in current Emergency Stroke Care in UK. The emphasis of the talk will be also based on recognition that "one model does not fit all". Discussion will hopefully lead to potential solutions and adjustments into how patients can benefit more from improved emergency stroke care in Serbia.

## **LEČENJE AKUTNOG KORONARNOG SINDROMA (AKS) U SRBIJI: KOLIKO SMO BLIZU EVROPSKIM PREPORUKAMA?**

Ostojić, M., Orlić, B., Djedović, S., Tomašević, M., Beleslin, B., Stojković, S., Ašanin, M, Vukčević, V., Stanković, G., Arandjelović, A., Polovina, M., Lović, M, Dobrić, M.

u ime Stent for Life (S4L) inicijative u Srbiji

Kardiovaskularna oboljenja su vodeći uzrok mortaliteta (Mt) u većini zemalja; u Srbiji je to oko 50%, a u razvijenim zemljama oko 30%. AKS, naročito infarct sa ST-elevacijom (STEMI) ili bez-ST elevacije (NSTEMI) uprkos savremenim metodama lečenja koje smanjenjuju intrahospitalni Mt i dalje ima značajan dugoročni Mt. Sa otkrićem Čazova 1976. g da se sa intrakoronarnom streptokinazom može otvoriti okludrirana arterija je započeta era trombolize (T) u STEMI.

Uvedena je i prehospitalna T. Danas se smatra da je koronarna angioplastika (balonom i/ili stentom)(pPCI) bolja od T ako se uradi unutar 12 h od STEMI. pPCI je potrebno uraditi unutar 90/120 min od postavljanja dijagnoze u zavisnosti da li se bolesnik transportuje direktno/indirektno u PCI centar. Ako nije moguće ispuniti ova preprukama zadata vremena, preporučuje se tzv. farmako-invazivni pristup – administira se i.v T i bolesnik transportuje u PCI centar. I ako se T u bivšoj Jugoslaviji primenjuje od samog početka (osamdesetih godina XX veka) u toku 24 h godišnje, pPCI je primenjivana samo u radno vereme od 1984-2005 godine. Od 2005. kada je sklopljen ugovor sa Republičkim fondom zdravstvenog osiguranja pPCI je postala dostupna 24 h/365 dana. Godine 2009 Srbija potpisuje deklaraciju Evropskog udruženja kardiologa “S4L” čiji je jedan od ciljeva da se leči barem 600 STEMI sa pPCI na million stanovnika.

Iako je Srbija 2008 imala samo 180/1 milion stanovnika pPCI, 2014. se lečilo pPCI 650/1 milion stanovnika. Opravdanje za ne postizanje zadatih vremena u Srbiji je činjenica i da mnogo razvijenije zemlje još nisu dostigle takvu logistiku da ih postižu kod svih bolesnika.

**TREATMENT OF ACUTE CORONARY SYNDROME (ACS) IN SERBIA: IS IT CONCORDANT WITH EUROPEAN GUIDELINES?**

Ostojić, M., Orlić, B., Djedović, S., Tomašević, M., Beleslin, B., Stojković, S., Nedeljković, M, Ašanin, M, Vukčević, V., Stanković, G., Arandjelović, A., Polovina, M., Lović, M, Dobrić, M.

on behalf of Stent for Life (S4L) initiative in Serbia

Cardiovascular diseases are the leading cause of mortality (Mt) in the most countries; in Serbia it is around 50%, and in developed countries around 30%. ACS, in particular myocardial infarction with-ST-elevation (STEMI) and without-ST-Elevation (NSTEMI) despite decreased intra-hospital Mt, still has significant mid-long term Mt. With the discovery of intracoronary application of streptokinase by Chazov in 1976 the era of thrombolysis (T) has begun in the treatment of STEMI. Pre-hospital T has been introduced also.

Now-days the intracoronary angioplasty (ballooning and/or stenting)(pPCI) is the preferred over T in STEMI if done in the timely fashion within 90/120 min from the established diagnosis in patients transferred directly/indirectly to PCI center within the 12-24 h of the beginning of the chest pain. If pPCI could not be performed in the timely fashion than pharmaco-invasive approach is recommended – administration of T and immediate transportation to the PCI center. Despite the fact that T was available in former Yugoslavia since mid-eighties 24 h/365 days, pPCI was available during working hours only since 1984 up to 2005. Since 2005 when government insurance fund provided resources pPCI has become available 24 h/365 days. In 2009 Serbia joined S4L initiative with the aim to treat at least 600 STEMI per 1 million inhabitants by pPCI.

Despite the fact that Serbia in 2008 had only 180 pPCI/1-million in 2014 it reached 650/1-million. Justification that not all patients were treated within recommended timelines may be the fact that even most developed countries could not achieve it.



## **HITNA MEDICINSKA POMOĆ BEOGRAD: JUČE, DANAS, SUTRA U ZBRINJAVANJU AKS I AMU**

N sar. dr sc. med. Slađana Anđelić, dr Goran Čolaković, Dr Nada Emiš-Vandlik  
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Slađana Anđelić, GZZHMP Beograd

**Uvod:** Akutni koronarni sindrom (AKS) i akutni moždani udar (AMU) su hitna medicinska stanja i zahtevaju urgentan prehospitalni skrining i zbrinjavanje. Njihovo prehospitalno dijagnostikovanje nije jednostavno zbog širokog spektra simptoma i moguće diferencijalne dijagnoze.

**Cilj rada** je da predstavimo način organizacije GZZHMP: juče, danas, sutra u zbrinjavanju AKS i AMU.

**Metod rada:** Za kreiranje ovog rada korišćeni su monografija GZZHMP Beograd, aktuelni vodiči dobre kliničke prakse, interna stručno-metodološka uputstva za operatere 194 i ekipe na terenu vezane za prijem poziva, davanje insrukcija pozivaocu do dolaska ekipe HMP i prehospitalno dijagnostikovanje i lečenje AKS i AMU.

**Rezultati rada:** Od svog osnivanja 1. decembra 1904. godine do danas, menjali su se ne samo naziv ustanove i kadrovska struktura, već i načini zbrinjavanja bolesnika sa AKS i AMU. Od nekadašnje varoške ambulatorije bez kardioloških ekipa, nastao je Gradski zavod za hitnu medicinsku pomoć u Beogradu, koji trenutno u svakoj operativnoj smeni ima 22 ekipe koje funkcionišu po univerzalnom obrascu zbrinjavanja AKS i AMU. Unapređenje kvaliteta rada GZZHMP Beograd doprinelo je da se u optimalnom vremenskom roku postavi adekvatna prehospitalna dijagnoza i bolesnik transportuje u odgovarajuću zdravstvenu ustanovu. Neka buduća istraživanja eksperata iz ovih oblasti trebala bi da otkriju slabe karike u lancu zbrinjavanja u postojećem zdravstvenom sistemu.

**Zaključak:** Postupak zbrinjavanja AKS i AMU na prehospitalnom nivou u Beogradu je u skladu sa najnovijim vodiča dobre kliničke prakse. Primenom aktuelnih algoritama dobro uvežbana ekipa HMP doprinosi da se pravi pacijent u pravo vreme zbrine i transportuje na pravom mestu.

**Ključne reči:** akutni koronarni sindrom, akutni moždani udar, prehospitalno zbrinjavanje, juče, danas, sutra

## **EMERGENCY MEDICAL SERVICES OF BELGRADE: YESTERDAY, TODAY, TOMORROW**

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**Introduction:** Acute coronary syndrome (ACS) and acute ischemic stroke (AIS) are medical emergency conditions that require urgent pre-hospital screening and care. Their pre-hospital diagnostics is not simple because of a wide specter of symptoms and possible differential diagnosis.

**Objective:** The aim of the manuscript was to present the manner of organization of the Municipal Emergency Medical Services: yesterday, today and tomorrow.

**Methods:** In the creation of this manuscript we used the monograph of the EMS Belgrade, up-to-date guidelines of good hospital practice, internal-methodological guidelines for dispatchers 194 and teams answering the call in the field, instructions given to the caller pre-arrival of the EMS team and pre-hospital diagnostics and treatment of ACS and AIS.

**Results:** From its foundation on December 1, 1904 until today, not only the name of the institution and personnel structure has been changed, but also the manner of the care of patients with ACS and AIS. The Municipal Emergency Medical Services of Belgrade was developed from a past small-town healthcare facility without cardiology teams, which at this point of time has 22 teams in each work shift that functions according to the universal pattern of ACS and AIS patients care. Improvement of the work quality of Belgrade EMS has contributed to the adequate pre-hospital diagnosis that is now passed within the optimal time-limit and to the patients transport to the corresponding healthcare facility. Some future researches conducted by experts in these fields should reveal weak links in the chain of care in the present healthcare system.

**Conclusion:** In Belgrade, the procedure ACS and AIS care at the pre-hospital level is in accordance with the latest guidelines of good hospital practice. By the application of up-to-date algorithms, a well-trained EMS team contributes to the policy: the right patient in the right place, at the right time.

**Keywords:** acute coronary syndrome, acute ischemic stroke, pre-hospital healthcare, yesterday, today, tomorrow

**OKRUGLI STO – SARADNJA SA  
DIJASPOROM: ISKUSTVA I PREDLOZI**

***ROUND TABLE – COOPERATION WITH  
DIASPORA: EXPERIENCES AND  
SUGGESTIONS***

## **UVOD U DISKUSIJU OKRUGLOG STOLA O SARADNJI SA DIJASPOROM – PETNAESTOGODIŠNJE ISKUSTVO**

Mihael Podvinec  
Predsednik OBI

Iznose se iskustva iz saradnje dveju švajcarskih organizacije za razmenu znanja izmedju lekara, sa raznim ustanovama u Srbiji. Iz tih iskustava proizilaze predlozi, na koji način bi bilo moguće, uz pomoć lekarskih udruženja u Srbiji (SLD i Lekarskekomore) uspostaviti trajnu tribinu za razmenu znanja i za uzajamnu pomoć u edukaciji. Cilj bi bio, da se elektronskim putem održava stalni kontakt izmedjulekara u dijaspori i lekara u Srbiji, kako bi se u kratkom vremenskom roku saznalo šta lekari u Srbiji interesuje, a šta lekari iz dijaspore imaju da ponude.

Predloženi oblici rada bili bi:

- organizovana razmena predavanja o najnovijim dostignućima struke i nauke, u oba pravca
- održavanje kurseva znanja i umešnosti, sa praktičnim radom
- pomoć u objavljivanju naučnih radova u inostranstvu
- organizacija kratkih poseta lekara iz Srbije u renomiranim ustanovama u inostranstvu, sa unapred dogovorenim projektima.

## **INTRODUCTION TO THE ROUND TABLE DISCUSSION ON THE COOPERATION OF THE DIASPORA WITH PHYSICIANS IN SERBIA – 15 YEARS'S EXPERIENCE**

Mihael Podvinec  
President of OBI

Experiences from a 15-year long cooperation of two medical knowledge exchange organisations from Switzerland with Serbian institutions will be related. Founded on these experiences, propositions are made on the ways in which physicians from the diaspora could cooperate with the colleagues in Serbia. To this effect, the support from medical organisations in Serbia (Serbian Medical Society and the Medical Chamber) must be solicited. Ideally, a permanent contact in an online forum for mutual knowledge exchange and mutual support in matters of continuing education could be established. This would make an immediate exchange of information on desired subjects of educational events between the two sides possible.

Forms of knowledge exchange could be:

- lectures and seminars on the newest developments in science and clinical medicine, in both directions
- courses with hands-on training
- support in publishing scientific and clinical papers abroad
- organisation of short visits by Serbian trainees in renown medical institutions abroad, with an agreed programme.

**IT DOES NOT MATTER HOW SLOW YOU GO AS LONG AS YOU DO NOT STOP -  
BRITISH- SERBIAN MEDICAL ASSOCIATION (BSMA)-THE JOURNEY WE  
TRAVEL, WHAT REALLY MATTERS?**

Dr Olivera Potparic  
London, UK

Presenter, Dr Olivera Potparic, former President of British - Serbian Medical Association will provide information regarding the activities and future projects of this Charity Organisation. The emphasis of the discussion will be reflection on past, challenges of the present times and hopes for the future collaboration with Serbian Colleagues.

The following aspects and dilemmas will be covered:

- Aim of our Association
- Membership
- Why are we here where we are now?
- What has been done so far?
- Recognition or failure to deliver?
- Achievements and failures
- Are we taken seriously?
- Our Serbian Colleagues, how do we contribute?
- Can we do better?
- How to avoid obstacles?
- How to accept constructive criticism?
- How to develop two - way communication?
- How to develop " same- similar " frame of thinking?
- How to stand on the same platform ?
- How to be united in what we do together to achieve improved care for our patients?
- How to do more for our professional and personal development?
- Realistic expectations
- Feedback
- Recognition of our strength and weaknesses
- What is "doable", what is unachievable mission?

We need your help in shaping the future of our Medical Association.

## **EDUKACIJA MLADIH ISTRAŽIVAČA: POMOĆ NAUČNIKA IZ DIJASPORE**

Prof. dr Rajko Igić \*

Stroger Hospital of Cook County, Chicago, IL, USA i Zavod za kliničku farmakologiju, Medicinski fakultet, Banjaluka, Republika srpska, Bosna i Hercegovina (volonter)

Mnogi naši lekari svoja interesantna opažanja, inovacije i rezultate istraživanja ne publikuju u domaćim ili stranim recenziranim časopisima jer ne znaju prezentirati svoj rad. Pored toga, medicinsko pisanje zahteva veliki trud lekara-praktičara. Zato oni većinom izlažu saopštenja na lokalnim sastancima. Ta je situacija izraženija u medicinskim centrima udaljenijim od univerziteta. Na primer, spisak nekoliko stotina mahom nerecenziranih publikacija koje su objavili lekari iz Sombora popunio je čitavu knjigu, a među njima je mali broj radova u časopisima koje registruje *Medline/PubMed* (Tab. 1).

Tabela 1. Biomedicinske publikacije iz Sombora u časopisima koje registruje MEDLINE

Godina	2008.	2009.	2010.	2011.	2012.	2013.	2014.	2015.
Broj publikacija	2	4	0	4	3	4	2	1

**Kako podstaći publikovanje u prestižnijim časopisima?** 1) Studentima medicine treba posvetiti veću pažnju pri upoznavanju metodologije istraživačkog rada; 2) specijalizantima uvesti obuku o istraživanjima i pisanju naučnih saopštenja; 3) na doktorskim studijama obučiti studente pisanju međunarodnih istraživačkih projekata, dizajnu istraživanja, deskriptivnoj i inferencijalnoj statistici, izboru i određivanju veličine uzorka, pisanju naučnih saopštenja i uređivanju časopisa, a student mora isplanirati, izvesti i u prestižnom časopisu objaviti nezavisno istraživanje; 3) obezbediti domaćim časopisima kvalitetne rukopise da uđu u glavne baze podataka; 4) treba poboljšati kvalitet domaćih recenzenata (videti članak Recenzija rukopisa naučnih saopštenja, *Scripta Medica*, Banjaluka, 2013;44:54-8); 5) u Srbiji oformiti novu profesiju 'privatni urednik' da pruža pomoć lekaru pri sastavljanju rukopisa; 6) stvoriti klimu u ustanovama da se ceni publikovanje u prestižnim časopisima; 7) mladi lekari treba što pre da publikuju (prikaz slučaja, komentar, istorijski članak, vesti, tehničko saopštenje, pismo uredniku, i sl.); 8) država mora izdvajati više sredstava za nauku.

**Pomoć dijaspore.** Pozive za predavanja, konsultacije, demonstriranje metoda ili učešće u uređivanju i proceni rukopisa neće odbiti stručnjaci dijaspore. U dijasporu spadaju i strani studenti koji su studirali kod nas. Najpre ministarstvo za kulturu i informisanje, uz pomoć univerziteta, treba da sačini spisak svih lekara i istraživača u dijaspori. Te stručnjake mogu organizatori raznih biomedicinskih skupova (uključujući i aktivnosti koju priređuje *alma mater*) pozivati, a penzionisane pojedince vredi uključiti u razne stručne aktivnosti u zemlji.

---

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## **EDUCATION OF YOUNG INVESTIGATORS: HELP OF SCIENTISTS FROM DIASPORA**

Prof. dr Rajko Igić \*

Stroger Hospital of Cook County, Chicago, IL, USA and Department of Clinical Pharmacology, Medical Faculty, Banjaluka, Republic of Srpska, Bosnia and Herzegovina (as a volunteer)

Many medical doctors from Serbia do not publish their interesting observations, innovations, or other results because they do not know the basics of scientific writing and publishing. Such writing, also makes demands on the practitioners, like any other task done really well. Therefore, the majority of practitioners present reports mainly at local meetings. Such situation is more pronounced at the medical centers that are located at a greater distance from the universities. For example, a list of publications that medical doctors from Sombor filled up a whole book, but just a few were published in the journals that are recorded in the *Medline/PubMed* (Tab. 1).

Table 1. Publications from Sombor in the journals recorded in the *Medline* from 2008 to 2015.

Year	2008	2009	2010	2011	2012	2013	2014	2015
Number of publications	2	4	0	4	3	4	2	1

**How to stimulate publishing in reputed journals?** 1) Medical students should be acquainted with methodology of medical research and publishing; 2) residents need training in clinical research and medical writing; 3) at the doctoral studies, the students should learn how to write (international) research projects, use descriptive and inferential statistics, understand principle of probability, selecting and calculate sample size, and they should plan, perform, write and publish independent research study; 4) quality of our reviewers should be improved (see an article on this subject “Manuscript assessment of scientific papers“/*Recenzija rukopisa naučnih saopštenja*/, *Scripta Medica*, Banjaluka, 2013;44:54-8); 5) in Serbia a new profession, private editor, should be established in order to help physicians in medical writing; 6) the authors who publish from medical centers should be appreciated by their colleagues and peers; 7) young physicians should publish as soon as they finish medical school (case report, book presentation or book review, technical improvements, comments, news, technical note, letter to the editor, etc.); 8) government should better support scientific research.

**Help from the diaspora.** Many experienced physicians and biomedical researchers from diaspora will accept an invitation to present seminars, consultations, demonstration of methods, participate in journal editing or manuscript assessing, and to attend professional meetings. All foreigners who studied in Serbia or other parts of Yugoslavia belong to our diaspora. Ministry of Culture and Information, in cooperation with universities, should prepare a list of all physicians from diaspora, and organizers of various meetings (including the *alma mater* events) should invite biomedical professionals to participate. Retired persons from diaspora could be included in various professional activities in the country.

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**POMOC U PUBLIKOVANJU KNJIGA S AKTUELNIM TEMAMA U BIOMEDICINSKIM ISTRAZIVANJIMA : STA URADITI?**

Mirjana Pavlovic  
SAD

**1. Uspostavljanje relacije sa kolegama iz Srbije koji zele da napisu knjigu.**

Slobodno se obratite na moju e-mail adresu koja je prilozena

**2. Sta je Springer?**

Jedna od najvećih izdavačkih kuća u svetu, dakle internacionalnog karaktera. Sasvim nedavno se udružila sa Cold Spring Harbor, Nature Publishing, Mc Millan, etc., što je još više učvrstilo renome.

**3. Kakve knjige stampa Springer?**

- Kratke (briefs) do 125 strana, plasticne korice)
- Monografije ( veci broj od kratkih, krute korice)
- Editovane volumene(veći broj strana, krute korice)
- U posebnim slučajevima dobijate obojene primerke (visok nivo vase tehnicke obrade)

**4. Sta je vazno u izboru?**

Vrlo je vazna tematika, koja neosporno treba da je veoma aktuelna ili ako je monografskog tipa predstavlja specificno iskustvo lekara-istrazivaca.

**5. Gde mogu pomoci?**

Uspostavljanje kontakta, preporuka, revizija knjige, pomoc u finalizaciji-revizija jezika i strukture knjige, povremeno ukljucenje u knjigu ako je problematika vezana za moje istrazivacke domene.

U prikazu cu dati primere svoje saradnje u proslosti i trenutne, detalje rada na stampanju knjige izmedju autora (editor) i prestavnika Springera, njihove e-mail adrese i svoju rec da sto sam obecala nameravam i da uradim.



**HELP WITH BOOK PUBLISHING WITH EMPHASIS ON ACTUAL TOPICS IN BIOMEDICAL RESEARCH: WHAT WE COULD DO?**

Mirjana Pavlovic  
USA

**1. Establishment of the relationships with colleagues from Serbia who would like to publish the book**

Feel free to contact me through e-mail address enclosed: mpavlovi@fau.edu

**2. What is Springer?**

All of us know: one of the biggest publishing houses in the world, which means of International character. Quite recently it merged with Cold Spring Harbor, Nature Publishing, Mc Millan, etc., which has contributed to its renome.

**3. What kind of book does Springer publish?**

Briefs, up to 125 pages, plastic cover)

Monographies (bigger number of pages, hard cover)

Edited volumes(bigger number of pages, hard cover)

In special cases you can get colored samples (high level of technical performance)

**4. What is so important within the choice?**

The topic is of a great importance, how actual it is, or if it is monograph it has to present specific experience of the physician-researcher-scientist.

**5. How I can help?**

Establishment of the contact, recommendations, revisions of the books help in finalization-linguistic revision and structure of the book, sometimes involvement into the book if it is connected to my research domains

During presentation I will give examples of my collaboration in the past and current, details of the work on publishing between author(editor) and Springer Officials, their e-mail addresses and my word that what I have promised I intend to do.

**ISTRAŽIVAČKI PROJEKTI MLADIH LEKARA I BIOMEDICINSKIH STRUČNJAKA, MASTER I DOKTORSKI RADOVI U FRANCUSKOJ: STUDIJSKI BORAVCI I ZAJEDNIČKI MENTORSKI RAD FRANCUSKIH I SRPSKIH UNIVERZITETA; POST-DOKTORSKE STUDIJE**

Prof. dr Zoran Ivanović  
Francuska

Moja intervencija će se sastojati u iznošenju ličnog iskustva sa školovanjem kadrova iz Srbije kroz doktorske studije i post-doktorske staževe u istraživačkim jedinicama INSERM-a, CNRS-a i Univerziteta u Bordou sa posebnim osvrtom na Francusku ustanovu za krv.

U svetlu najnovijeg iskustva, mentorstva jedne doktorske teze koja se radu u „co-tutelle“ Univerziteta u Bordou i Beogradu, pokušaću da ukažem na slabe tačke i anahronosti u administrativnom pristupu kao i na strukturalne inkompatibilnosti dva različita pristupa koje otežavaju i možda onemogućavaju realizaciju takvih programa.

Biće izneti predlozi za poboljšanje i pojednostavljenje postupka a pre svega potreba za fleksibilnijim pristupom administracije i shvatanjem da postoje rešenja koja su različita od onih prisutnih u administrativnoj tradiciji Srbije.

**RESEARCH PROJECTS OF YOUNG MEDICAL DOCTORS AND BIOMEDICAL SCIENTISTS, MASTER AND PHD THESIS IN FRANCE: FELLOWSHIPS AND „CO-TUTELLE“ BETWEEN FRENCH AND SERBIAN UNIVERSITIES; POST-DOCTORAL FELLOWSHIPS**

Prof Zoran Ivanović  
France

My intervention will consist in presentation of personal experience related to the education of the students from Serbia through the PhD and post-doctoral programs in INSERM, CNRS and Bordeaux University Research Units with a special point on French Blood Institute.

In the light of the last experience, supervision of a PhD thesis performed in “co-tutelle” between the universities of Bordeaux and Belgrade I will try to stress the weak points as well as to reveal some anachronisms in administrative approach as well as some structural incompatibilities of two different systems, making difficult and maybe even impairing the realization of such a program.

Some propositions will be articulate to improve and simplify the procedures and above all, the need for more flexible approach of administration through the understanding that some solutions are possible even if they are different comparing to those in administrative tradition of Serbia.

## **LETNJA OBUKA U HJUSTONU**

Mirjana Maletic-Savatic  
SAD

U Hjustonu je 2011. godine osnovan Medical Student Advancement Program – MedSAP, preko koga svakog leta nekoliko studenata Medicinskog fakulteta iz Beograda dolaze na usavršavanje. Program sponzorise Srpsko-američka privredna komora Hjustona. Svaki student dobije svog mentora, u zavisnosti koja ga oblast medicine interesuje i učestvuje u svakodnevnom radu tog lekara – od klinike, do vizita i operacija. U toku diskusije za okruglim stolom, izneće se perspektive studenata koji su prošli kroz program i mogućnosti da se program proširi na specijalizante i druge lekare.

Kako je u Sjedinjenim Drzavama nemoguće biti lekar bez posebne sertifikacije i završene specijalizacije u akreditovanim ustanovama, druga mogućnost za unapredjenje znanja lekara uključuje formalna, didaktička predavanja; učestvovanje u naučnom radu preko zajedničkih projekata; pisanje radova za naučne časopise. Nadam se da će naša konferencija otvoriti mogućnost za ovakvu saradnju.

## **SUMMER INTERNSHIP IN HOUSTON**

Mirjana Maletic-Savatic  
USA

In 2011, Serbian-American Commerce association founded MedSAP, Medical Student Advancement Program, with the goal to enhance knowledge of medical students from the University of Belgrade, Serbia. Since then, every summer several students from Serbia come to Houston and spend 2-3 months embedded in daily medical practice. Each student has his/her own mentor, depending on the medical specialty they are interested in, and they participate in all daily activities of their mentors - from outpatient clinic, through daily rounds, to surgeries. During my round table discussion, I will talk about the perspectives of both mentors and students who participated in this program as well as about the possibilities to expand the program to physicians and specialty trainings.

As in the USA, it is impossible to be a physician without American Board-certified accreditation, another possibility to advance the knowledge is through formal didactic seminars; participation in joint scientific projects; and writing of manuscripts for medical journals. I hope that this mini-symposium will open the door for such collaborations.

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**Zahvaljujemo se svima koji su svojim savetima i predusretljivošću pomogli da se ovaj sastanak realizuje.**

**Posebnu zahvalnost dugujemo gospođi Gordani Antuljeskov, saradnicima iz Interlab Exim i Dijagfarm.**

# Perfekcija u zdravstvu

Svake godine više od 3.500.000 pacijenata iz celog sveta poseti Adžibadem Zdravstvenu Grupaciju radi lečenja. Još od 1991. godine Adžibadem je najcenjenija privatna zdravstvena grupacija u Turskoj koja pruža sveobuhvatnu dijagnostiku i usluge lečenja sa profesionalnim timom najvišeg kalibra uz pomoć najsavremenije medicinske tehnologije, snažne infrastrukture i po standardima odobrenim od strane JCI-a.



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