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## Errata

At the request of Prof. Dr. Sandra Stefan Mikić, Ph. D., author of the paper “ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF ACINETOBACTER SPP IN THE PERIOD 2012 - 2015”, published in the journal *Medical Review*, 3 - 4/2017, pages 99 – 106, we hereby provide the correct list of coauthors of this paper: **Sandra Stefan-Mikić, Siniša Sević, Ivana Hrnjaković Cvjetković, Vesna Milošević, Vedrana Petrić and Milica Rupar.**

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At the request of Dr. Uroš Milošević, author of the article “CENTRAL PANCREATECTOMY IN SURGICAL TREATMENT OF PANCREATIC INSULINOMA”, published in the journal *Medical Review*, 3 - 4/2017, pages 111 – 114, we hereby provide the correct email address of the author: [uros.milosevic@mf.uns.ac.rs](mailto:uros.milosevic@mf.uns.ac.rs).

*Na molbu dr Uroša Miloševića, autora rada „Centralna pankreatektomija u hirurškom tretmanu insulinoma pankreasa – prikaz slučaja“, objavljenog u dvobroju 3-4/2017, na stranama 111–114. objavljujemo ispravku koja se odnosi na imejl adresu autora, a koja bi trebalo da glasi **uros.milosevic@mf.uns.ac.rs**.*

**EDITORIAL****UVODNIK**

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## THERAPEUTIC EFFECTS OF PHYSICAL AGENTS IN THE TREATMENT OF CHRONIC PAIN

### MEHANIZAM DEJSTVA FIZIKALNIH AGENASA U TERAPIJI HRONIČNOG BOLA

**Ksenija BOŠKOVIĆ and Snežana TOMAŠEVIĆ TODOROVIĆ**

Chronic pain is a physiological response to tissue damage, often associated with emotional reaction, somatic and autonomic disorders, and changes in behavior [1]. Therefore, it requires a multidisciplinary approach among which physical agents have a very important place [2, 3]. In order to apply adequate physical agents in the treatment of chronic

pain, it is necessary to accurately determine pain characteristics, as well as to know the physiological mechanisms of action of the applied physical agent (**Table 1**) [4].

The explanation of therapeutic effects of physical agents is based on the theory of control and modulation of painful impulses at: 1) peripheral level (mechanosen-

**Table 1.** Potentials of physical therapy effects on chronic pain

**Tabela 1.** Mogućnosti delovanja fizikalne terapije na hronični bol

Process <i>Proces</i>	Therapeutic mechanism <i>Terapijski mehanizam</i>	Therapeutic interventions <i>Terapijske intervencije</i>
Transduction <i>Transdukcija</i>	Damage reduction <i>Redukcija oštećenja</i> Nocioreceptor excitability decrease <i>Smanjenje ekscitabilnosti nocioreceptora</i>	Protective positions/ <i>Zaštitni položaji</i> Exercises reducing joint stress and renewing the function/ <i>Vežbe koje redukuju zglobni stres i obnavljaju funkciju</i> Cryotherapy/ <i>Krioterapija</i> Small power laser/ <i>Laser male snage</i> Ultrasound/ <i>Ultrazvuk</i> Electrotherapy/ <i>Elektroterapija</i>
Transmission <i>Transmisija</i>	Competition (sensor receptors stimuli with faster conduction of „gate control“). Transmission decrease (decrease of hyperexcitability at the level of spinal ganglia and back horns of spinal cord)/ <i>Kompeticija (nadražaj senzornih receptora sa bržim provođenjem kroz „kontrolne kapije signala“). Smanjenje transmisije (smanjenje hiperekscitabilnosti na nivou spinalnih ganglija i zadnjih rogova kičmene moždine)</i>	TENS/ <i>TENS</i> Massage/ <i>Masaža</i> Heat/ <i>Toplota</i> Laser/ <i>Laser</i> Acupuncture/ <i>Akupunktura</i>
Perception <i>Percepcija</i>	Cognitive insight/ <i>Kognitivni uvid</i> Motivation-emotional processes <i>Motivaciono-emocionalni procesi</i>	Information/ <i>Informacija</i> Education/ <i>Edukacija</i> Support/ <i>Podrška</i>
Modulation <i>Modulacija</i>	Strengthening of pain control descendent mechanisms <i>Jačanje descendentnih mehanizama kontrole bola</i>	Information/ <i>Informacija</i> Education/ <i>Edukacija</i> Support/ <i>Podrška</i> Exercises/ <i>Vežbe</i> Electrotherapy/ <i>Elektroterapija</i> Acupunture/ <i>Akupunktura</i>

TENS - transcutaneous electrical nerve stimulation/*transkutana električna nervna stimulacija*

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### Abbreviations

TENS – transcutaneous electrical nerve stimulation

sitive, thermosensitive and chemosensitive pain receptors); 2) spinal level (segmental – presynaptic system); 3) supra-spinal (central blocking system) [5, 6]. The analgesic effects of physical therapy may be expressed on afferent or efferent segments of the consignment spinal system. In order to explain afferent analgesia, the theory most often used is “the gate control” i.e. the signal input gate control theory. The stimulation of peripheral thick fast-conducting nerve fibers activates dorsal horn neurons before signals arrive via A $\delta$  and C fibers that cannot additionally activate them (the gate has been closed). It is considered that most physical modalities achieve their effects in this way [7, 8].

The efferent analgesic system is complex. The voluntary stimuli from the cerebral cortex (suggestion, biofeedback and other cognitive demands) increase the process of release of the matter decreasing the pain. Those are endogenous opiates (enkephalins, endorphins) of the middle brain which decrease neurotransmitter release in afferent path of pain through the downstream paths, directly or indirectly, over serotonin to distal part of the first neurone of afferent path of pain, by presynaptic inhibition over  $\mu$  and partly kappa receptors. This inhibited state of the second neuron in the afferent path decreases the pain [9].

Physical therapy recognizes the term “fatigue process of the A $\delta$  afferent fibers” through axonal blockage (repetitive, high-frequency stimuli) as well as neuropeptide transmitters release (direct and modulated current) followed by pain transfer blockage on the peripheral and spinal level. Hyperstimulation analgesia and analgesia via application of transcutaneous electrical nerve stimulation (TENS), in addition to the already mentioned mechanisms of action, also act at supraspinal level, inhibiting the pain transfer up to conscious level at the somatosensory cerebral cortex [10, 11].

### Therapeutic effects of certain physical agents

*Kinesitherapy* is a therapy based on movement and exercise used in the management of chronic pain. Effects of this physical agent are explained by segmental blockage activation, suprasedgmental blockage activation, as well as by the psycho-tonus increase with the characteristics of joy, independence, communication and feeling of security [7, 11, 12].

*Galvanic current*, named after Luigi Galvani, is a direct current where ions move constantly, with the same intensity in one direction. The analgesic effects of direct current are explained by effects of ions on C afferent nerve fibers, as well as by application of different ionic content, while neuromodulatory effect is explained by release of neuropeptide transmitters [3, 9].

*Electrophoresis (iontophoresis)* in the chronic pain therapy is the use of galvanic current to introduce analgesic ions into the organism through non-

injured skin or mucosa. Aqueous solution medicine is inserted from electrode that has the same charge as the active component of the medicine. The analgesic effect is explained by the combination effects of the galvanic current and the given medicine.

*Diadynamic currents*, or Bernard’s currents, which belong to the group of low frequency direct currents, may be semi-wave and full-wave sinusoidal currents, 50 - 100 Hz frequency. These currents are the combination of 5 differently modulated impulses by their intensity, shape and amplitude (impulse one) and galvanic component: DF (diphase fixe), MF (monophase fixe), CP (courte “short” period), LP (long periods), RS (rhythmic syncope). By combining diadynamic currents of different modulation, we can enhance the desired effect even more, firstly in the form of analgesia, but also in vasodilatation, sympaticolytic effect or the possibility of muscle contraction [9, 10, 13].

*Transcutaneous electrical nerve stimulation (TENS)* is a basic physical therapeutic procedure for pain modulation and its effects are based on the pain entrance gate control theory and pain neurohumoral modulation, via endogenous opiate system. TENS is the use of low-frequency currents with rectangular impulses of certain duration; analgesia is achieved with electric stimulation of neuron inhibitory system of the spinal cord last horn, via descending paths mediated by opiates (endorphins and enkephalins) [3, 9].

*Interference currents* or *Nemec’s currents* are produced by 2 alternating currents of middle-frequencies, but more painlessly and deeply than each would individually; deep in the tissue, low-frequency alternating current is generated. In this way, the skin resistance is avoided, as well as discomfort. Interference currents act in an analgesic way and longer than other types of currents, on local increase of tissue blood supply and edema reduction, accelerate bone healing after fracture, stimulate recovery of the injured nerves, etc. [9, 13].

*High-frequency current* is applied as short-wave and micro-wave diathermy, with the purpose to heat deep muscular tissues. It belongs to alternating currents where dipoles change their orientation, tend to be positioned in direction of circuit flow and friction between dipole molecules and viscous environment heats the tissue. The analgesic effect of diathermy is explained by thermal conditioning of mesencephalic blockage and in humoral way - via thermal/stress reaction and excretion of cortisol [9, 10].

*Cryotherapy* is the use of low temperatures for therapeutic purposes. The analgesic effect is achieved through metabolic activities, slowing down nerves conduction in the treated region, decreasing the activity of the inflammatory mediator, as well as of enzymes responsible for destructive changes in some inflammatory rheumatic diseases [3, 9].

*Heat therapy* is mostly applied in the chronic pain therapy by application of surface and deep methods of heating. Heating causes vasodilation

and relaxation of muscles in the treated area. In this way oxygenation is increased, as well as acceleration of cellular metabolism. The initial feeling of a mild heat may have analgesic effects and results in decrease of local soreness and muscle spasm [9].

*Hydrotherapy* is one of the oldest methods of physical therapy; it is the use of water, especially thermal mineral water in order to treat different diseases. The therapeutic effect is reached by the combination of physical characteristics with heat, chemical and mechanical action, and also by the combination with exercises in the water. The analgesic effect of hydrotherapy is explained by the theory of the pain entrance gate control and segmental competitive blockage through the thermal-receptor stimulation, while humoral effect can be seen through heat and cold stress, i.e. through cortisol secretion [3].

*Laser therapy - low level laser* therapy is the use of red and infrared laser rays, i.e. stimulated light fotons on the region treated. The analgesic effect of laser therapy is explained by the mechanism of closing the entrance gate on ascendant path, with segmental competitive blockage through activation of peripheral axonal blockage i.e. blockage of A- $\delta$  afferent neural fibers; the neuromodulatory effect of laser therapy is explained by inhibition of inflammatory mediators formation [9, 14].

*Sonotherapy* is a method of using ultrasound at frequency higher than 20 kHz, directed by applicator to the certain region of the body where sound oscilations are transmitted into mechanical vibrations. The analgesic effect is explained by the influence on the painful pulses, via activation of mesencephalic system of blockade, while humoral effect

is explained by heat reaction and reduction of algogenic substances at the level of receptors [3, 9].

Ultrasonophoresis is a treatment where active ingredients are pushed through non-injured skin by ultrasound. The analgesic effect is explained by the combination of the galvanic current and given medication effect.

*Magnotherapy* is the application of constant or impulse magnetic field of low or high frequency. It affects chemical and physiological processes in the organism, acting at a molecular level; it changes the activity of neural and endocrine systems that represent the main regulatory systems in the organism, influencing metabolism, microcirculation and the blood content. This way, both the analgesic and anti-edematous effect are explained [9, 10].

*Acupuncture*, as part of the traditional Chinese medicine and a special philosophical approach to the human body and spirit, has been successfully applied as an additional method in the chronic pain therapy. The neural thalamic network is the gate towards the cortex and, in that way, cortical projections influence the analysis of all signals going through the thalamus. Also, the existance of interaction between somatosensory regions, close to the thalamus, has been found [15].

## Conclusion

Adequate pain assessment, associated with good knowledge of therapeutic effects of physical agents, and a multimodal approach to the treatment of pain, provide expected results in the management of chronic pain.

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## ORIGINAL STUDIES

## ORIGINALNI NAUČNI RADOVI

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Original study  
*Originalni naučni rad*  
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## ADAPTABILITY OF DIFFERENT CANAL SEALERS TO THE ROOT CANAL DENTIN – SCANNING ELECTRON MICROSCOPY ANALYSIS

ADAPTABILNOST RAZLIČITIH KANALNIH PUNJENJA ZA DENTIN KORENSKOG KANALA  
– ANALIZA ELEKTRONSKI SKENIRANIH MIKROFOTOGRAFIJA

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### Summary

**Introduction.** The aim of this *in vitro* study was to test and analyze the sealing ability of three endodontic materials used for permanent obturation, in between the dentin walls and the gutta-percha points, using a scanning electron microscope. **Material and Methods.** Forty-five recently extracted single-root teeth, treated by a step-back technique, were divided into three groups (15 teeth in each); the canals were filled with three different permanent obturation materials: N2 - zinc oxide root canal cement, Gutta Flow (Coltene), and Endomethasone N (Septodont). Their sealing ability and adhesive properties were analyzed using field emission gun scanning electron microscope, at the time when they were applied between the dentin walls of the canal and the gutta-percha. **Results.** The results of the scanning electron microscope analysis have shown that all the three sealers have good adhesion properties when used over the root canal walls in the apical third. Good adaptation of the filling used for the root canal walls in the middle and the cervical third was found only in teeth obturated using Gutta Flow, while samples obturated by N2 - zinc oxide root canal cement and Endomethasone showed the weakest adhesion, and greatest number of cracks between the sealer and the canal wall. **Conclusion.** When using a single-cone obturation technique, compared to other obturation materials, Gutta Flow shows considerably better adaptation to the root canal wall and the gutta-percha points in the apical, middle, and the cervical third of the root. **Key words:** Root Canal Filling Materials; Root Canal Preparation; Root Canal Obturation; Dentin; Microscopy, Electron, Scanning; Gutta-Percha

### Sažetak

**Uvod.** Cilj ove *in vitro* studije je testiranje i analiziranje sposobnosti zaptivanja tri različita endodontska materijala koji se upotrebljavaju za definitivno punjenje između dentinskih zidova i gutaperke poena, primenom elektronskog mikroskopa. **Materijal i metode.** Četrdeset pet ekstrahovanih jednokorenih zuba, tretiranih *step-back* tehnikom bili su podeljeni u tri grupe (po 15 zuba u svakoj od njih), kanali su bili ispunjeni trima različitim materijalima za definitivnu opturaciju kanala: cink-oksidi eugenolom, *Gutta Flow* (Coltene) i *Endomethasone N* (Septodont). Elektronskim mikroskopom sa emisijom polja analizirani su adhezivna sposobnost i zaptivanje materijala za punjenje između dentinskih zidova korenskog kanala i gutaperke. **Rezultati.** Analiza elektronski skeniranih mikrofotografija pokazala je da sva tri materijala imaju dobru adheziju karakterističnu za njihovu primenu na zidovima kanala korena u apikalnoj trećini. Dobra adaptacija punjenja za zidove kanala korena u srednje i cervikalne trećine pronađena je samo na uzorke opturiranih metodom *Gutta Flow*, a uzorci koji su bili opturirani sa cink-oksidi eugenolom, i *Endomethasone*-om N imali su najslabiju adheziju i najveće prisustvo pukotina između silera i zida kanala. Kada se primenjuje *single-cone* tehnika za opturaciju kanala, *Gutta Flow* pokazuje znatno bolju adaptaciju za zid korenskog kanala i gutaperke u apikalni deo kao i u srednjoj i cervikalnoj trećini korena u poređenju sa drugim materijalima za opturaciju kanala.

**Gljučne reči:** materijali za punjenje kanala korena zuba; preparacija kanala korena zuba; opturacija kanala korena zuba; dentin; skenirajuća elektronska mikroskopija; gutaperka

### Introduction

The endodontic treatment is a complex procedure which includes preparation, instrumentation, and root canal obturation.

A successful outcome of endodontic therapy depends on numerous factors, including appropriate canal instrumentation, successful irrigation and decontamination of the whole root canal system, as well

### Abbreviations

SEM	– scanning electron microscope
NiTi	– nickel titanium
EDTA	– ethylenediaminetetraacetic acid
FEG-SEM	– field emission gun - scanning electron microscope
N2	– zinc oxide root canal cement
NaOCl	– sodium hypochlorite
AHplus	– epoxy-amine resin

as complete obturation, using biocompatible materials [1, 2].

One of the main purposes of the root canal filling materials is to prevent penetration of microorganisms and their products, in order to prevent reinfection of the root canal system. That is why the biocompatibility of the obturation material, the antimicrobial effect, as well as the sealing and adaptation ability of the material used over dentin walls, are important preconditions for achieving that goal [3].

For years, gutta-percha has been the most commonly used material for permanent obturation of root canals. As it does not have the ability to bond to dentin, it is mostly used in combination with sealers or cements that fill the space gap between the gutta-percha and the root canal wall, and between the gutta-percha and the dentin walls [4].

In order to achieve quality permanent sealing, as well as complete obturation of the whole canal space, it is necessary to prevent micro crack formation, which in turn prevents micro leakage that occurs between the canal walls, the filling material, and the gutta-percha points after certain period of time [5].

One of the most important properties that permanent obturation cements must possess is viscosity (the fluidity) of the material, in order to fill in the space between the gutta-percha and the dentin walls better, and be able to reach and fill in all the irregularities of the canal space and to obturate the holes of the lateral and the accessory canals [6].

Gutta Flow (Coltene/Whaledent, Altstätten, Switzerland) is a cold liquid self-bonding cement composed of powdered gutta-percha, polydimethylsiloxane and nanosilver particles. The structure and the size of the particles enable good adaptability because of its leakage ability and expansion of 0.2% when bonding [7].

The solubility of Gutta Flow is virtually equal to zero, which should ensure good sealing for a longer period of time.

The sealing ability is the main characteristic that needs to be tested for every material or technique that is used for permanent obturation of the root canal system. Nowadays, many techniques are used for evaluation of the adhesion level of the root canal filling materials. These methods include penetration of ink, the fluid filtration method, the radioactive isotopes method, penetration of bacteria and scanning electron microscope (SEM) analysis [8, 9].

The SEM analysis enables evaluation of the sealing and the adhesion properties of the sealer to the

root canal wall, as well as to the gutta-percha point, at various levels of sectioning [10].

The purpose of this *in vitro* study was to test and analyze the sealing ability of three endodontic materials used for permanent obturation, applied between the dental walls and the gutta-percha points, using SEM.

### Material and Methods

This *in vitro* study examined forty-five single-root upper anterior intact teeth (incisors) recently extracted due to periodontal reasons. The teeth were cut transversely, down to the level of the enamel-cement junction, using a high speed diamond burr, under water coolant and the crowns were removed from the root part of the teeth. The working length of the canals was established 0.5 mm short of the apex, using K-file # 10. The instrumentation was performed using nickel titanium (NiTi) hand files size #40, by a step-back technique. During the canal preparation, 5 ml 3% sodium hypochlorite was used as an irrigant. Towards the end of canal preparation, root canals were irrigated with 1 ml 15% ethylenediaminetetraacetic acid (EDTA) followed by 2 ml 3% sodium hypochlorite to remove the smear layer. Finally, the root canals were rinsed with 2 ml deionized water and dried with paper points. The roots were divided into three groups (15 in each) and the canals were filled with three different permanent obturation materials: the first group was obturated with Endomethasone N (Septodont) and gutta-percha point, the second with Gutta Flow system (Coltene), and the third group with zinc oxide root canal cement (N2) (Hager&Werken) and gutta-percha point. The root canal sealer was applied using a #25 lentulo spiral. Then, a single Master gutta-percha point #35 was inserted in each of the canals down to the previously determined length. The excessive gutta-percha cones were removed and the cervical part of the root samples were obturated using glass-ionomer cement (Fuji IX GP, GC Japan).

The root samples were placed and kept in a physiological saline for 7 days, at a temperature of 37°C, in order to enable bonding of the material intended to be used for permanent obturation. After this period of time, the teeth were cut transversely on three levels: in the cervical third, in the middle third, and in the apical third, i.e. 10, 5, and 2 mm from the apex.

These surfaces that were previously cut were polished and appropriately prepared for field emission gun scanning electron microscope (FEG-SEM) analysis. The adhesion and the sealing properties of the sealer used between the dental walls of the canal and the gutta-percha were analyzed under different magnifications, ranging from x 100 to x 200. These representative micrographs were taken in order to classify the results, using modified Ray and Seltzer criteria [11] as follows:

- **Grade 1.** Exceptionally good adhesion – flat line of contact at the border between the sealer

and the dentin, without presence of flaws and space gaps, with considerable penetration of the material in the openings of the dental tubules;

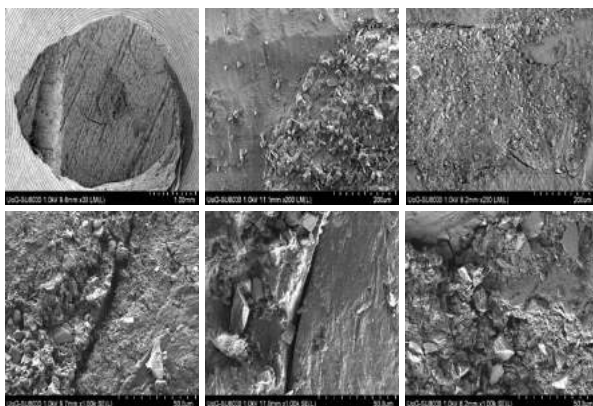
- **Grade 2.** Good adhesion – slightly uneven contact surface on the border between the sealer and the dentin wall, with a few noticeable cracks and space gaps;
- **Grade 3.** Relatively good adhesion – space gaps on the contact surface between the sealer and the dentin of the canal walls was noticed, with unclear and uneven contact surface on the area of bondage.

### Results

The micrographs of root samples obturated with N2, Gutta Flow, and Endomethasone cut transversely in the apical third are shown in **Figure 1**. Good adaptation and bondage of sealers with the dentin walls was noticed.

At the contact surface of the gutta-percha and the three types of sealers, presence of a few cracks was evidenced. The adhesion at the apical third of all of tested materials was ranked with grade 2.

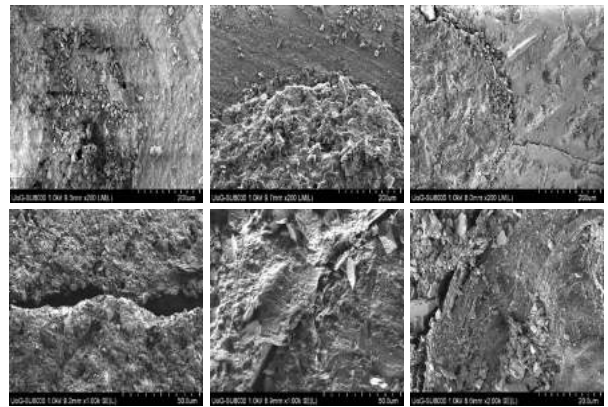
At cross sections of samples made in the middle third (**Figure 2**), a slightly uneven contact surface on the bondage area of the sealer and the dentin walls was found, as well as presence of a small number of cracks and space gaps in root canals filled with Endomethasone and N2 (relatively good adhesion – grade 3). A bit better edge closure and less number of cracks were evidenced in samples filled with Gutta Flow (good adhesion – grade 2). At the contact area between the Gutta Flow and the gutta-percha points, a continuous contact was evidenced, without presence of cracks or space gaps (grade 1).



Endomethasone Gutta Flow N2  
Endometazon Tečna gutaperka Cink-oksidi eugenol

**Figure 1.** SE micrographs of permanent obturation of the root canals by Endomethasone, Gutta Flow and N2 (Transverse cross-section in the apical third)

*Slika 1. Elektronski skenirane mikrofotografije permanentno opturiranih zubnih kanala korišćenjem: endometazona, tečne gutaperke i cink-oksidi eugenola (transverzalni poprečni presek apikalne trećine korena)*



Endomethasone Gutta Flow N2  
Endometazon Tečna gutaperka Cink-oksidi eugenol

**Figure 2.** SE micrographs of permanent obturation of the root canal using Endomethasone, Gutta Flow and N2 (Transverse cross-section in the middle third)

*Slika 2. Elektronski skenirane mikrofotografije permanentno opturiranih zubnih kanala korišćenjem: endometazona, tečne gutaperke i cink-oksidi eugenola (transverzalni poprečni presek srednjeg dela korena)*

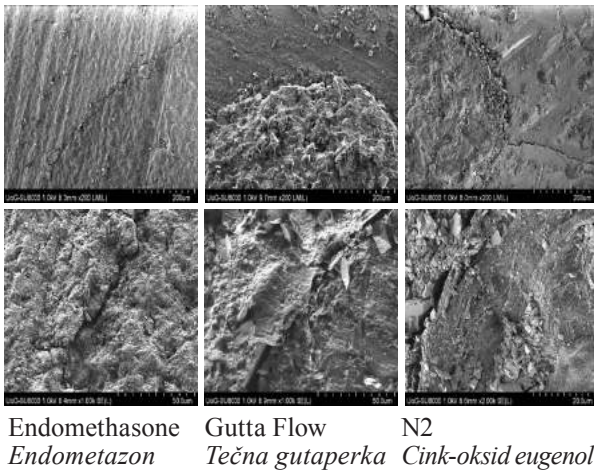
In the cervical third (**Figure 3**), the adhesion of sealers Endomethasone and Gutta Flow to the dentin was good, with slightly uneven contact surface and small number of cracks (grade 2), while the adhesion in the root canals filled with N2 could be ranked as relatively good, because of the presence of space gaps between the dentin and the sealer (grade 3).

### Discussion

Obturation of the root canal is the last phase of the endodontic therapy, which is particularly significant for the long-term success of the endodontic therapy. For many years, gutta-percha is the most commonly used material for permanent obturation of the root canals. Due to its inability to bond to the dentin, it has been used in combination with sealers or cements that fill in the space gap between the gutta-percha and the root canal wall [12].

Based on the previous tests, modern endodontics prefers lesser thickness of the sealer, due to its contraction and dissolution, and occurrence of micro leakage. Of all filling techniques, the largest volume of the sealer compared to the gutta-percha point appears in the single cone technique, which enables occurrence of space gaps in the filling, thus resulting in lower quality. By calibrating the gutta-percha points in the preparatory period, one enables to lower the volume of the sealer even in the single cone technique [13].

Today, there are more techniques that are used for evaluation of the root canal walls filling such as penetration of ink, fluid filtrating method, radioactive isotope method, penetration of bacteria. The SEM analysis allows evaluation of the sealing and adhesion ability of the sealer to the wall of the root



**Figure 3.** SE micrographs of permanent obturation of the root canals using Endomethasone, Gutta Flow and N2. (Transverse cross-section in the cervical third)

**Slika 3.** Elektronski skenirane mikrofotografije permanentno opturiranih zubnih kanala korišćenjem: endometazona, tečne gutaperke i cink-oksidi eugenola (transverzalni poprečni presek cervikalnog dela korena)

canal and the gutta-percha point on various levels of sectioning.

The adaptation of the sealer to the root canal walls depends of the presence or the absence of a smear layer. Previous tests have shown that the use of sodium hypochlorite (NaOCl) in combination with EDTA as a solution for irrigation of the root canals is exceptionally effective for removal of the smear layer [14]. In the present study, 3% NaOCl in combination with EDTA for root canal irrigation was used.

The results of SEM analysis have shown that all the three sealers have good adhesion to the root canal walls in the apical third. In the middle and the cervical third, there was good adaptation of the sealer only in the samples obturated with Gutta Flow, while the samples obturated with N2 and Endomethasone show weak adhesion of the sealer and noticeable presence of cracks in-between the sealer and the canal wall. Exceptionally good adhesion of the sealer was not found in any of the samples.

In their study, Vujasković et al. came to a conclusion that Gutta Flow shows great adhesion to the root canal wall and the gutta-percha point, without presence of gaps and cracks [15].

El Ayouti found that even with the presence of a small number of gaps in the same material, Gutta Flow shows good adaptability to the wall of the canal. As a sealer based on a resin, Gutta Flow has a homogenous structure with particles of gutta-percha that allow leakage of the sealer in the open dentin tubules and lateral canals, and complete obturation of the space between the canal wall and the gutta-percha point [16].

According to Varun Kapoor, Gutta Flow is a good alternative for thermoplastic gutta-percha, in all of the cases where application of lateral compac-

tion was contraindicated, providing good apical obturation [17].

Better sealing of apical depressions and lateral canals while applying Gutta Flow was evidenced by various authors [18–20].

According to Dhanya Kumar, Gutta Flow enables significantly better sealing in the apical 3 mm of the root canal as a result of a better leakage in the lateral canals and present depressions in the apical third of the tooth. Unlike in the apical third of the tooth, the technique of vertical condensation of gutta-percha has shown better adaptation to the walls of the root canal in the middle third of the tooth compared to Gutta Flow [21, 22]. The research of Upadhyay and associates pointed to significantly more superior sealing of the root canal over the whole length when using Gutta Flow, compared to zinc oxide eugenol sealer and lateral condensation of the gutta-percha [10].

Single-cone technique includes application of one gutta-percha point, at a room temperature, and a sealer (of various thickness), depending on the adaptation of the point to the walls of the root canal. Studies show lower effectiveness of the single-cone technique in the sealing of the canal system because of a greater thickness of the sealer, which may be expected in the absence of the gutta-percha's condensation and presence of variability in the shape of the root canals, that aren't always corresponding to the shape of the instruments that are used for this treatment and the master points. Porosities, contraction, cement dissolution and a lower adaptation of the master point in the middle and the cervical third, especially in root canals with irregular shape, are main flaws of this technique [13].

In the present study, Gutta Flow has shown better adaptation to the walls of the root canal in the middle and the cervical third of the tooth, compared to the other two sealers. Along with liquid consistency, the size of the particles ( $< 0.9 \mu\text{m}$ ), and the ability of Gutta Flow to expand while bonding by 0.2% additionally improving the adaptation, this may be the reason for better adhesion in the middle and the cervical third of the samples obturated with Gutta Flow. To the opposite, another in vitro research shows that Gutta Flow has maximum apical leakage compared to epoxy-amine resin (AH plus) as a sealer, which may be due to the weak chemical bondage between the gutta-percha particles and the master gutta-percha [23].

Savariz et al. have tested the sealing ability of Gutta Flow and AH plus, in combination with various sealing techniques, for a period of 3, 30, and 120 days. Their test results showed that after a certain period of time Gutta Flow shows greater capacity for sealing apically and coronary compared to AH plus, regardless if the single cone technique or lateral condensation was applied. The application of Gutta Flow as the only solution for filling the root canal without application of a master point has resulted in greater coronal and apical leakage [24].

## Conclusion

The results of scanning electron microscope analysis have shown that in single cone technique of obturation, Gutta Flow shows better adaptation

to the wall of the root canal and the gutta-percha points than Endomethasone and zinc oxide root canal cement, and that it is better in the apical compared to the middle and the cervical third of the root.

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## THE QUALITY OF VOICE AND SPEECH BEFORE AND AFTER SURGICAL TREATMENT OF BILATERAL RECURRENT LARYNGEAL NERVE PARALYSIS

*KVALITET GLASA I GOVORA PRE I NAKON HIRURŠKOG LEČENJA OBOSTRANE TRAJNE ODUZETOSTI POVRATNOG GRKLJANSKOG ŽIVCA*

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### Summary

**Introduction.** Bilateral recurrent laryngeal nerve paralysis usually occurs after thyroid surgery. In bilateral vocal cord paralysis, the voice is clear or slightly hoarse. The aim of this study was to determine whether the quality of voice and speech significantly deteriorates after the surgical treatment of bilateral recurrent laryngeal nerve paralysis. **Material and Methods.** The study included 16 patients with bilateral vocal cord paralysis and 16 age- and sex-matched healthy controls. The patients underwent partial arytenoidectomy with posterior cordectomy at the Clinical Center of Vojvodina in the period from January to April 2014. The quality of voice and speech was determined before and after surgical treatment by subjective, objective, aerodynamic voice analysis, and analysis of spontaneous speech, and then compared to the control group. **Results.** The results of this study showed that in patients with bilateral vocal cord paralysis the voice and speech quality was significantly worse compared to the healthy subjects. The results of subjective and aerodynamic analysis showed that there was a statistically significant deterioration in voice quality after the surgical treatment ( $p < 0.05$ ;  $p = 0.001$ ). The values of objective analysis and analysis of spontaneous speech parameters did not significantly change after the surgery ( $p > 0.05$ ;  $p = 0.401$ ). **Conclusion.** The patients with bilateral vocal cord paralysis have a poorer voice and speech quality compared to the healthy subjects. After the surgical treatment, patients presented with a lower voice quality, but there were no significant changes regarding the ability of spontaneous speech.

**Key words:** Vocal Cord Paralysis; Voice Quality; Surgical Procedures, Operative; Treatment Outcome; Postoperative Complications; Speech; Recurrent Laryngeal Nerve; Acoustics

### Introduction

The voice production refers to the optimal coordination among the respiratory, phonatory, resonance, and articulation subsystems, and changes at any level of this complex mechanism lead to certain voice and speech quality disorders [1–5]. Bilateral vocal cord paralysis usually occurs as an effect of operations and reoperations of malignant thyroid gland tumors, because of the close anatomical connection [5, 6]. The number of causes leading to recurrent laryngeal nerve paralysis

### Sažetak

**Uvod.** Obostrana trajna oduzetost povratnog grkljanskog živca najčešće nastaje kao posledica operacija tumora štitaste žlezde. Kod obostrane oduzetosti povratnog grkljanskog živca, glas je čist ili neznatno promukao. Cilj istraživanja bio je da se utvrdi da li se kvalitet glasa i govora značajno pogoršava posle hirurškog lečenja trajne obostrane oduzetosti povratnog grkljanskog živca. **Material and Methods.** Analiza je obuhvatala 16 pacijenata sa obostranom oduzetošću glasnica i 16 zdravih osoba slične uzrasne i polne distribucije. Pacijenti su operisani metodom parcijalne aritenoidektomije sa zadnjom hordektomijom u Kliničkom centru Vojvodine, u periodu od januara do aprila 2014. godine. Kvalitet glasa i govora kod pacijenata, pre i nakon hirurškog tretmana, utvrđen je subjektivnom, objektivnom, aerodinamičkom analizom glasa i analizom spontanog govora i upoređen sa kontrolnom grupom. **Rezultati.** Rezultati ove studije pokazali su da je kvalitet glasa i govora kod pacijenata sa obostranom oduzetošću glasnica značajno lošiji u poređenju sa zdravom grupom. Razultati subjektivne i aerodinamičke analize pokazali su da postoji statistički značajno pogoršanje kvaliteta glasa posle hirurškog tretmana ( $p = 0,001$ ;  $0,026$ ). Vrednosti parametara objektivne analize i analize spontanog govora nisu se značajno promenile posle operacije ( $p = 0,401$ ;  $0,876$ ). **Zaključak.** Pacijenti sa obostranom oduzetošću glasnica imaju lošiji kvalitet glasa i govora u poređenju sa zdravima. Posle hirurškog tretmana glas ima lošiji kvalitet, ali u pogledu sposobnosti spontanog govora nema značajnih promena.

**Ključne reči:** paraliza glasnih žica; kvalitet glasa; operativne hirurške procedure; ishod lečenja; postoperativne komplikacije; govor; povratni laringealni nerv; akustika

requires a systematic and multidisciplinary approach to diagnosis and therapy, whereas functional recovery of the nerve depends on the cause and severity of the injury [6]. Bilateral paralysis of the recurrent laryngeal nerve manifests as dysphagia, slight changes in voice quality, dyspnea, aspiration and stridor, which increase during physical activity and sleep [7]. According to the literature data, surgical techniques can eliminate the symptoms, but cannot restore the vocal fold physiological mobility [8]. Early surgical treatment is indicated in patients with aspiration pneumonia, dyspnea, non-

**Abbreviations**

MPT	– maximum phonation time
MPTa	– MPT of sound a
MPTs	– MPT of voiceless sound s
MPTz	– MPT of voiced sound z
GIRBAS scale	– G - grade, I - instability, R - roughness, B - breathiness, A -asthenia, S – strain
FO	– fundamental laryngeal tone
BRLNP	– bilateral recurrent laryngeal nerve paralysis

productive cough, and with poor response to vocal therapy [6]. Voice and speech disability after emergency tracheotomy has a strong impact on patients' psychosocial life, which is why the surgeons have now developed various alternative surgical techniques, such as total arytenoidectomy, partial arytenoidectomy with posterior cordectomy, laser-assisted arytenoidectomy, CO<sub>2</sub> laser cordectomy, laterofixation, etc. Laterofixation is the first alternative to tracheotomy in fresh bilateral lesions up to 8 weeks old. If the nerve does not recover after 10 to 12 months post laterofixation, or more than six-month after the injury, the submucosal arytenoidectomy is indicated. Arytenoidectomy is an irreversible method that permanently changes the relationships in the glottic part of larynx, making breathing easier, but the voice becomes worse because of the insufficient glottic occlusion. Therefore, some patients refuse or give up the intervention, despite severe breathing difficulties. The optimal treatment of bilateral vocal cord lesions has not yet been found.

The aim of this study was to determine whether the quality of voice and speech significantly deteriorates after the surgical treatment of bilateral recurrent laryngeal nerve paralysis (BRLNP). We also hypothesized that in patients with bilateral vocal cord paralysis the quality of voice and speech is significantly lower compared to the healthy subjects.

**Material and Methods**

The analysis included 16 patients, 5 male (31.25%) and 11 female patients (68.75%), aged 40 to 80 years, with bilateral vocal cord paralysis following thyroid gland tumor surgery using partial arytenoidectomy with posterior cordectomy in the period from January to April 2016. The other group included 16 age- and

sex-matched controls of healthy subjects. The study was conducted at the Ear, Nose and Throat Clinic of the Clinical Center of Vojvodina. Each patient's quality of voice and speech was examined pre- and postoperatively, and the results were compared to the healthy subjects. Subjective, objective, acoustic, and aerodynamic analysis were used to test the voice quality. The GIRBAS scale (G - grade, I - instability, R - roughness, B - breathiness, A -asthenia, S - strain) was used for subjective acoustic analysis. The evaluation of the voice using GIRBAS scale implies that three voice therapists independently examined the voice. The scale has four levels: 0 - normal voice, 1- somewhat worse, 2 - moderately worse, 3 - significantly worse. Using the Praat software package, parameters of objective acoustic analysis, the fundamental laryngeal tone (F0), jitter (the variable vocal fundamental laryngeal tone in short intervals) and shimmer (the intensity fluctuations of each vocal cord vibration) were examined. Reference values of these parameters were determined by the above mentioned software program. Within the aerodynamic analysis, the maximum phonation time (MPT) (the longest time of phoning the sound /a/) was measured as well as the friction of voiceless sound /s/ and voiced sound/z/ (MPTs, MPTz). Aerodynamic tests estimated the ratio of respiration and phonation. This method determines the vital capacity and MPT. The MPT is a parameter that indicates the possibility of a vocal apparatus to maintain phonation in a certain period. The patients were asked to take a deep breath and try to articulate one vowel sound with a comfortable height and intensity as long as possible. This was measured by a stopwatch. The test was performed in a standing position. Each patient tried this for three times and the longest value was used. The function of spontaneous speech was also examined in a way that each patient was asked to give some information about himself/herself in one breath. Statistical analysis was done using the software package Microsoft Excel 2010. Regarding statistical functions offered by this program, the arithmetic mean, standard deviation, and T-test were used.

**Results**

The results of subjective, aerodynamic analysis, and analysis of spontaneous speech showed that there

**Table 1.** The parameters of objective acoustic analysis (Jitter, Shimmer, F0) in patients before and after the surgery (\*\*p>0.05)

**Tabela 1.** Parametri objektivne akustičke analize (podrhtavanje, treperenje, fundamentalna frekvencija) kod pacijenata pre i posle operacije (\*\*p>0,05)

	Median <i>Medijana</i>	Standard deviation (SD) <i>Standardna devijacija (SD)</i>	T-test/ <i>T-test</i>	p/p
F0 - before surgery/ <i>pre operacije</i>	182.0000	77.79803	0.864	0.401**
F0 - after surgery/ <i>posle operacije</i>	195.2500	92.83713		
Jitter - before surgery/ <i>Podrhtavanje pre operacije</i>	189.5000	481.58876	-0.939	0.363**
Jitter - after surgery/ <i>Podrhtavanje posle operacije</i>	400.0569	673.64207		
Shimmer - before surgery/ <i>Treperenje pre operacije</i>	1587.0625	3950.93632	-0.595	0.561**
Shimmer - after surgery/ <i>Treperenje posle operacije</i>	2524.2500	4975.42820		

*FO - fundamentalna frekvencija*



**Table 2.** The parameters of aerodynamic analysis (MPTa, MPTs, MPTz) and analysis of the spontaneous speech in patients before and after the surgery (\* $p < 0.05$ ; \*\*  $p > 0.05$ )

**Tabela 2.** Parametri aerodinamičke analize (maksimalno vreme fonacije – MVF) i analize spontanog govora kod pacijenata pre i posle operacije (\* $p < 0,05$ ; \*\*  $p > 0,05$ )

	Median Medijana	Standard deviation (SD) Standardna devijacija (SD)	T-test T-test	p/p
MPTa – before surgery/MVFa pre operacije	9.3750	4.66011	4.071	0.001*
MPTa – after surgery/MVFa posle operacije	5.5625	1.99896		
MPTs – before surgery/MVFs pre operacije	11.1875	4.53459	2.505	0.026*
MPTs – after surgery/MVFs posle operacije	10.5000	2.87518		
MPTz – before surgery/MVFz pre operacije	9.5625	5.13769	3.716	0.002*
MPTz – after surgery/MVFz posle operacije	5.4375	2.39357		
Number of words – before surgery/Broj reči pre operacije	3.6875	0.70415	0.159	0.876**
Number of words – after surgery/Broj reči posle operacije	3.6250	1.08781		

MVFa - MVF samoglasnika a; MVFs - MVF suglasnika s; MVFz - MVF suglasnika z

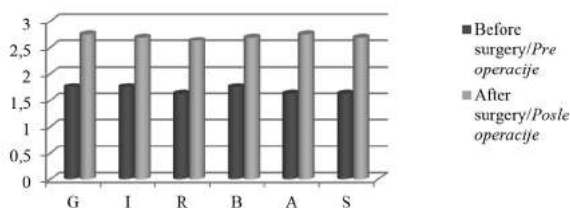
was a statistically significant difference in the voice and speech quality between the healthy control group and patients with bilateral vocal cord paralysis. The parameters of objective acoustic analysis, F0 and jitter, did not show lower voice quality in patients with bilateral laryngeal paralysis compared to healthy controls, unlike the parameter shimmer. The results of subjective acoustic analysis showed that there was a statistically significant deterioration in the voice quality after the surgical treatment (**Graph 1**). The parameters of the objective acoustic analysis did not statistically change after the surgery compared to the preoperative values ( $p=0.401$ ;  $0.363$ ;  $0.561$ ) (**Table 1**). After the surgical treatment of BRLNP, the parameters of aerodynamic analysis statistically changed compared to the preoperative ones ( $p=0.001$ ;  $0.026$ ;  $0.002$ ;  $0.026$ ) (**Table 2**). The analysis of the number of words spoken per breath showed that there was no statistically significant change in speech after the surgery ( $p=0.876$ ). **Graph 2** shows parameters of aerodynamic analysis and analysis of the spontaneous speech.

## Discussion

Based on previous studies, we investigated the quality of voice and speech in patients with bilateral vocal cord paralysis after partial arytenoidectomy with posterior cordectomy. In our study, there was a higher

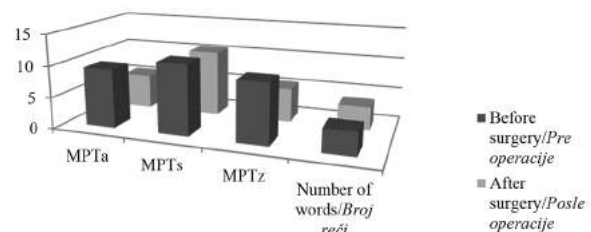
incidence of female patients (68.75%) compared to male patients (31.25%), which is in accordance with the literature data [9]. In BRLNP, vocal cords are placed in the medial or paramedial (phonation) position, which further reduces the airway, disables inspiration, with a high risk for aspiration and suffocation. The results of subjective, aerodynamic analysis, and analysis of spontaneous speech showed that the quality of voice and speech in patients with bilateral vocal cord paralysis is significantly poorer compared to the healthy subjects, regardless the paramedian position of the vocal cords, as we assumed. The parameters of objective acoustic analysis, F0 and jitter, did not show a decrease in the voice quality in patients with bilateral vocal cord paralysis compared to healthy controls, unlike the parameter shimmer. This means that the voice retains the frequency range after the lesion, but loses the strength and endurance, because of passive vocal cords vibrations.

The results of our subjective and aerodynamic voice analysis confirmed that the quality of voice significantly deteriorated after partial arytenoidectomy with posterior cordectomy. Arytenoidectomy provides a larger airway for respiration, which reduces the voice quality, because of the insufficient occlusion on the glottic level. The same results were obtained by many other authors [10–14]. Comparing the parameters of objective acoustic analysis, we found that the mean val-



**Graph 1.** The parameters of subjective acoustic analysis before and after the surgery (GIRBAS scale)

**Grafikon 1.** Parametri subjektivne akustičke analize pre i posle operacije (stepen disfunkcije - G; promenljivost kvaliteta fonacije - I; hrapavost glasa - R; pneumofoničnost - B; slabost glasa - A; napetost glasa - S)



**Graph 2.** A graphical representation of preoperative and postoperative mean values of the parameters of aerodynamic acoustic analysis and analysis of spontaneous speech  
**Grafikon 2.** Grafički prikaz preoperativnih i postoperativnih srednjih vrednosti parametara aerodinamičke analize i analize spontanog govora

ues of F0 ranged from 182.00 Hz preoperatively to 165.25 Hz postoperatively, while the mean values of jitter ranged from 189.500 preoperatively to 400.0569 postoperatively. Despite the obvious differences, the standard deviation was high; therefore, this difference was not significant. Other authors have reported similar results when examining the impact of total, partial, and laser-assisted arytenoidectomy and CO<sub>2</sub>-laser cordectomy on the voice quality [11, 12, 15–18]. On the other hand, Gorph et al. [19] showed that the parameters of objective acoustic analysis (shimmer, jitter) were worse after the endoscopic laser medial arytenoidectomy. Considering the results of objective acoustic analysis in our and other studies, it may be assumed that the parameters of objective acoustic analysis are closely related to the type of surgical technique. However, we did not examine the correlation between the applied surgical technique and subjective, objective and aerodynamic analysis of voice quality. Maybe in the future we will investigate which of these analyses has the highest correlation with the applied surgical technique.

The number of spontaneous words spoken per breath, which represents the integration of vital lung capacity, vocal cords and resonatory function, showed no statistical deterioration after partial arytenoidectomy

with posterior cordectomy, which was unexpected. No deterioration in spontaneous speech can be explained by the fact that patients with bilateral vocal cord paralysis have difficulties with respiration, but resonatory and phonatory functions are acceptable. On the other hand, after surgery, the patients' respiratory function is established, the resonatory function remains the same, but their phonatory function becomes abnormal. In both cases, one of the three components of this complex mechanism is damaged and two others work properly, which might be the reason why the ability of spontaneous speech did not significantly change in patients after the surgical treatment.

### Conclusion

We can conclude that patients with bilateral vocal cord paralysis have a poorer voice and speech quality compared to the healthy subjects. After partial arytenoidectomy with posterior cordectomy, the quality of voice is slightly worse, but there are no significant changes regarding the ability of spontaneous speech. Improvements in surgical techniques and introduction of new ones in the future will probably help preservation of the voice and speech quality.

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## EVALUATION OF BODY COMPOSITION AND MUSCULAR STRENGTH IN DIFFERENT SPORTS

### PROCENA TELESNOG SASTAVA I MIŠIĆNE SNAGE KOD RAZLIČITIH SPORTOVA

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#### Summary

**Introduction.** Body composition measurements and dynamometric parameters are very reliable indicators of performance and progress in the training process. The aim of this study was to assess the body composition and muscle strength and to establish the correlation between these parameters in various sports. **Material and Methods.** The study was conducted at the Department of Physiology, Laboratory of Functional Diagnostics, Faculty of Medicine in Novi Sad. It included 45 male examiners: 15 handball players, 15 football players, and 15 sprinters. The following parameters were measured: body weight, body height, body mass index, skinfold thickness, and dynamometric parameters of calf extensors and forearm flexors. **Results.** In comparison to football players and sprinters, handball players presented with statistically significantly higher body mass index ( $p < 0.05$ ). In terms of skinfold thickness, there were statistically significant differences ( $p < 0.05$ ) between the groups. The values of dynamometric parameters of calf extensors (average value of load of the calf extensors, maximum value of load of the calf extensors, strength of muscle contraction of calf extensors) showed no statistically significant differences between the groups of athletes ( $p > 0.05$ ). Compared to football and handball players, sprinters had significantly higher values of dynamometric parameters of forearm flexors (average value of load of forearm flexors, maximum value of load of forearm flexors, strength of muscle contraction of forearm flexors). **Conclusion.** In the group of handball players there was a positive correlation between the percentage of the body fat and muscle power in both examined muscle groups; however, among the football players and sprinters, a correlation was found between the body composition and strength of calf extensors.

**Key words:** Body Composition; Muscle Strength; Sports; Athletic Performance; Body Mass Index; Skinfold Thickness; Exercise Test

#### Sažetak

**Uvod.** Određivanje telesnog sastava i merenje dinamometrijskih parametara su veoma pouzdani pokazatelji uspešnosti i napredovanja trenaznog procesa. Cilj rada bio je procena telesnog sastava i mišićne snage kao i utvrđivanje postojanja njihove povezanosti kod različitih sportova. **Materijal i metode.** Ispitivanje je sprovedeno na Zavodu za fiziologiju u Laboratoriji za funkcionalnu dijagnostiku Medicinskog fakulteta u Novom Sadu. **Studija je obuhvatila** 45 osoba muškog pola: 15 rukometaša, 15 fudbalera i 15 sprintera. Izmereni su: telesna težina, telesna visina, indeks telesne mase, debljina kožnih nabora i dinamometrijski parametri ekstenzora potkolenice i fleksora podlaktice. **Rezultati.** Uočene su statistički značajno više vrednosti indeksa telesne mase kod rukometaša u odnosu na fudbalere i sprintere ( $p < 0,05$ ). Statistički značajna razlika ( $p < 0,05$ ) postoji u pogledu vrednosti debljine kožnih nabora između posmatranih grupa. U vrednostima dinamometrijskih parametara ekstenzora potkolenice: prosečna (Aen) i maksimalna (MAXen) vrednost savladanog opterećenja ekstenzora potkolenice, snaga mišićne kontrakcije ekstenzora potkolenice (Pen) između posmatranih grupa sportista nisu nađene statistički značajne razlike ( $p > 0,05$ ). U poređenju sa fudbalerima i sprinterima, rukometaši imaju značajno više vrednosti dinamometrijskih parametara fleksora podlaktice: prosečna (Afr) i maksimalna (MAXfr) vrednost savladanog opterećenja fleksora podlaktice, snaga mišićne kontrakcije fleksora podlaktice (Pfr). **Zaključak.** U grupi rukometaša postoji pozitivna korelacija između procenta telesne masti i snage obe ispitivane mišićne grupe, dok kod fudbalera i sprintera korelacija postoji između telesnog sastava i snage ekstenzora potkolenice. **Gljučne reči:** telesna kompozicija; mišićna snaga; sportovi; sportski učinak; indeks telesne mase; debljina kožnog nabora; vežbe, testovi

#### Introduction

Today, professional sports function as strictly controlled systems and nothing is random. The entire training process is conducted by a multidisci-

plinary team of experts that cover all aspects necessary for optimal development of each athlete. An integral part of this process is monitoring the progress of athletes and training results. Methods used to achieve the best results are various and nu-

**Abbreviations**

BH	– body height
BM	– body mass
BMI	– body mass index
BF %	– body fat percentage
Aen	– average value of load of the calf extensors
MAXen	– maximum value of load of the calf extensors
Pen	– strength of muscle contraction of calf extensors
Afr	– average value of load of forearm flexors
MAXfr	– maximum value of load of forearm flexors
Pfr	– strength of muscle contraction of forearm flexors
WHO	– World Health Organization
CT	– computerized tomography
MRI	– magnetic resonance imaging

merous. Among other methods, determination of body composition and measurements of dynamometric parameters, are highly reliable indicators of performance and progress in the training process.

Body height (BH) and body mass (BM) are the fundamental indicators of body growth and development. They are the result of the genetic potential and their interaction with environmental factors [1]. Determination of body composition provides information about the relationship between the fat and muscle mass, which is essential in monitoring the training process and sports achievements. The amount and distribution of fat and muscle mass are affected by many factors such as age, sex, race, diet, physical activity, etc. [2]. Due to a balanced diet and intense physical activity, athletes have different anthropometric parameters and energy capacity compared with non-athletes [3].

There are many methods which are used to analyze the body composition. The most reliable methods are computerized tomography (CT) and magnetic resonance imaging (MRI). These methods are too expensive and complicated for routine use. However, there are simpler, but less precise methods, which are easily accessible, cheaper and can be applied in large samples. In everyday practice, the most frequently used methods are anthropometric measurements and bioelectrical impedance method.

Measurements of muscle strength are among the most specific and the most accurate assessments of the functional state of the locomotor system. In addition, the muscular strength in athletes is also an indirect indicator of sports achievement [4]. Muscles have different strength, which depends on the needs, and muscle strength is directly proportional to the muscle profile. Methods for assessing muscle strength include subjective assessment of muscle strength, manual muscle test, dynamometry and dynamography.

The aim of this study was to evaluate body composition and muscle strength in different sports, as well as to establish the correlation between anthropometric and dynamometric parameters of athletes.

**Material and Methods**

The study included 45 male participants who were divided into three groups. The first group included 15 handball players, the second included 15 football players, and the third group included 15 sprinters. The study was conducted at the Laboratory of Functional Diagnostics of the Department of Physiology, Faculty of Medicine in Novi Sad. The subjects were healthy at the time of testing, and after a detailed explanation of the test protocol, they signed a voluntary informed consent to participate in the research.

The athletes underwent basic anthropometric measurements, analysis of body composition, and anthropometric determination of the percentage of body fat mass based on the skinfold thickness, as well as dynamometric measurement of muscle strength.

The following anthropometric parameters were measured - BM, BH, 8 body circumferences (forearm, flexed and relaxed upper arm, chest, waist, hip, mid-thigh and calf), 7 skinfold thickness sites (chest, subscapular, middle axillary, biceps, triceps, abdominal, suprailiac, supraspinal, front thigh and medial calf). Stadiometer with an accuracy of 0.1 cm was applied for the measuring the BH. The BM was measured by medical decimal scales with sliding weights with an accuracy of 0.1 kg. Tape measure with precision of 0.1 cm was used to measure body circumferences. Holtain Koln caliper with an accuracy of 0.1 mm was used to

**Table 1.** Average values of BM, BH, age (years) and sports experience (years) of examinees

**Tabela 1.** Prosečne vrednosti telesne mase, telesne visine, godina života i sportskog staža ispitanika

	Body weight (kg) <i>Telesna masa (kg)</i>	Height (cm) <i>Visina (cm)</i>	Age (years) <i>Starost (god)</i>	Sport experience (years) <i>Sportsko iskustvo (god)</i>
<b>Handball players/Rukometaši</b>				
X	92.8	189	21	8
SD	8.9	8.9	1	2
<b>Football players/Fudbaleri</b>				
X	80.8	186	20	9
SD	5.7	5	1	2
<b>Sprinters/Sprinteri</b>				
X	74	182.1	19	7
SD	7.6	3.6	2	2

**Table 2.** The values of BMI and BF %  
**Tabela 2.** Vrednosti BMI i BF %

	Handball players/Rukometaši	Football players/Fudbaleri	Sprinters/Sprinteri
BMI (kg/m <sup>2</sup> )	25.9	23.4	22.3
BF (%)	12	10	8

BMI - indeks telesne mase; BF % - % telesne masti

**Table 3.** Values of Aen, Maxen, Pen, Afr, MAXfr and Pfr  
**Tabela 3.** Vrednosti Aen, MAXen, Pen, Afr, MAXfr i Pfr

Parameters/Parametri	Handball players/Rukometaši	Football players/Fudbaleri	Sprinters/Sprinteri
Aen (kg) - X ± SD	182 ± 29.3	177 ± 32.7	174 ± 35.4
MAXen (kg) - X ± SD	193 ± 29.1	189 ± 30.1	185 ± 33.4
Pen (W) - X ± SD	987 ± 219	974 ± 217	893 ± 180.5

Legenda: Aen - prosečna vrednost savladanog opterećenja ekstenzora potkolenice, MAXen - maksimalna vrednost savladanog opterećenja ekstenzora potkolenice, Pen - snaga mišićne kontrakcije ekstenzora potkolenice, Afr - prosečna vrednost savladanog opterećenja fleksora podlaktice, MAXfr - maksimalna vrednost savladanog opterećenja fleksora podlaktice, Pfr - snaga mišićne kontrakcije fleksora podlaktice

measure skinfold thickness. The measurements were performed on the right side of the body at 7 sites, according to the standards of the International Society for the Advancement of Kinanthropometry [5]. These values were used to calculate the total body fat by using a regression equation.

According to the World Health Organization (WHO) recommendations, normal body mass index (BMI) is 18.5–24.9 kg/m<sup>2</sup>, overweight - 25–29.9 kg/m<sup>2</sup>, and all values over 30 kg/m<sup>2</sup> are considered as obesity. Reference values for body fat in athletes depend on the sports discipline. Fleck and Wilmore [6] recommended the following: for handball players – 10–12%, football players - 10% and for sprinters 8–16%.

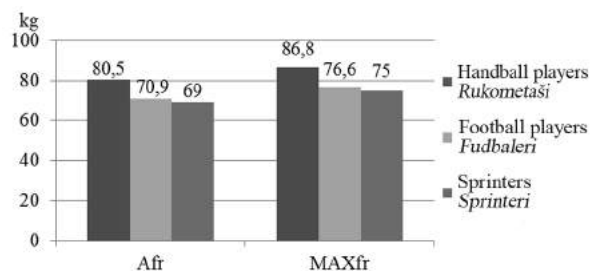
Dynamometric testing of the strength of the calf extensors and forearm flexors was performed using the machine Concept 2 DYNO. Maximum (MAXen and MAXfr) and average values (Aen and Afr) of load in kilograms (kg) and strength of muscle contractions of the calf extensors and forearm flexors (Pen and Pfr) expressed in watts (W) were analyzed.

The results were statistically analyzed, especially the mean value (X), standard deviation (SD), student's t-test, and Pearson's coefficient of correlation (r).

## Results

The average values of BM, BH, age (years), and sports experience (years) in all three groups of athletes, are presented in **Table 1**. Between the tested groups, in terms of BM, there was a statistically significant difference ( $p < 0.05$ ), while in terms of BH, there were no statistically significant differences ( $p > 0.05$ ) between handball and football players and sprinters, but between handball players and sprinters there was a statistically significant difference ( $p < 0.05$ ).

Values of BMI and body fat percentage (BF %) are presented in **Table 2**. Between handball and football players, as well as handball players and sprinters, there was a statistically significant difference in the BMI ( $p < 0.05$ ), but between football players and



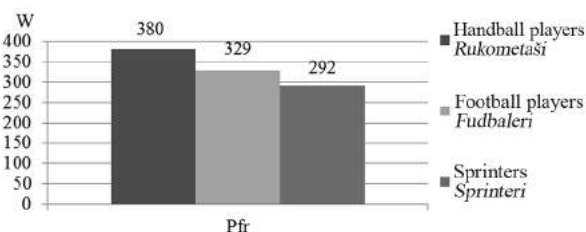
**Graph 1.** The average and maximum values of load of forearm flexors

**Grafikon 1.** Prosečna i maksimalna vrednost savladanog opterećenja fleksora podlaktice

sprinters, no significant difference ( $p > 0.05$ ) was found. However, there was a statistically significant difference in values of BF % ( $p < 0.05$ ) between the groups of athletes.

The Aen, Maxen and Pen of calf extensors are shown in **Table 3**. In all observed groups of athletes there was not a statistically significant difference ( $p > 0.05$ ) between measured values.

The Afr and MAXfr in the examined groups of athletes are presented in **Graph 1**. There were statistically significant differences in the values of Afr and MAXfr ( $p < 0.05$ ) between handball and foot-



**Graph 2.** The strength of muscle contraction of forearm flexors

**Grafikon 2.** Snaga mišićne kontrakcije fleksora podlaktice

ball players, and handball players and sprinters. However, between football players and sprinters there were no statistically significant differences in values of the observed parameters ( $p > 0.05$ ).

The values of Pfr are shown in **Graph 2**. There was a statistically significant difference ( $p < 0.05$ ), in the values of Pfr, among handball and football players, as well as handball players and sprinters, but between football players and sprinters, a difference was not found ( $p > 0.05$ ).

There was a positive correlation between the BF % and all observed dynamometric parameters of calf extensors: Aen, Maxen, Pen ( $r = 0,42$ ) in groups of handball and football players, while in the group of sprinters, the correlation was found between body composition and BF % and Pen ( $r = 0,41$ ).

## Discussion

The training process in elite athletes is highly specialized and requires constant upgrading. Its main task is to maximize the sport results fueled by high individual and team potential.

This study included three groups of professional athletes: handball players, football players and sprinters. By analyzing the basic anthropometric parameters, it was established that handball players were significantly heavier compared to football players and athletes. In terms of BH, handball players were the highest, but not statistically significantly higher from football players; however, the difference was statistically significant compared to the BH of sprinters. These basic anthropometric differences can be attributed to the specific requirements of individual sports, which influence the initial selection of athletes at an early age.

There was a statistically significant difference ( $p < 0.05$ ) in the BMI between handball and football players, and handball players and sprinters, while no significant difference ( $p > 0.05$ ) was found between football players and sprinters. In handball players the average BMI was  $25.9 \pm 2.6 \text{ kg/m}^2$ , football players  $23.4 \pm 1.2 \text{ kg/m}^2$  while in sprinters it was  $22.3 \pm 2.1 \text{ kg/m}^2$ . These results were expected, and explained by difference in BM of examined groups. Our results are in accordance with literature findings where handball players also presented with higher BMI [7]. According to the reference values of the WHO, the BMI in handball players may be regarded as increased. The BMI takes into account only the height and weight of the individual; the body composition is not taken into account [8], and therefore it is not considered a good indicator in terms of the amount of body fat mass in athletes, because high values indicate a developed muscle mass, rather than an increased amount of adipose tissue [9].

There was a statistically significant difference among the observed groups of athletes in assessment of BF % ( $p < 0.05$ ). The average BF % among handball

players was  $12 \pm 3\%$ , among football players it was  $10 \pm 2\%$ , and among sprinters  $8 \pm 3\%$ . These values are in the range of reference values for given sports disciplines. Skinfold thickness measurement provides a good estimate of body fat mass in people with normal weight and normal distribution of fat mass, because it reflects the subcutaneous adipose tissue.

The differences in motor skills, sources of energy for muscle contraction and psychological profile in certain sports, imposed a division of sports into groups. In one group of sports, training of endurance is dominant, while in the other, the emphasis is on developing power [10, 11]. However, all sports apply strength training. The volume and intensity of training in different sports is different [12].

In respect to Aen, MAXen, and Pen of calf extensors, measured in handball players, football players and sprinters, no statistically significant differences were found ( $p > 0.05$ ). The values were high in all three groups, because of the training process where, among other things, strength exercises of the lower extremities were dominant. In terms of Afr, MAXfr, and Pfr of forearm flexors, there were statistically significant difference in values ( $p < 0.05$ ) between handball and football players, and handball players and sprinters, while no statistically significant difference was found ( $p > 0.05$ ) between football players and sprinters. Significantly higher values of all parameters were found in handball players, due to a specific training, which includes a wide variety of exercises developing strength of the upper extremities and the development of explosive throwing strength, important in handball. Unlike handball players, football players and sprinters do not have strength training of the upper limbs, so it is not so emphasized.

In handball and football players, there was a correlation between the BF % and Aen, MAXen, and Pen of calf extensors. On the other hand, in the group of sprinters, a correlation exists only between the BF % and Pen of calf extensors. The registered correlation may be explained by specific requirements of individual sports and development of muscular strength of certain muscle groups, which is reflected on the body composition of sprinters.

## Conclusion

There are significant differences between the examined groups related to the values of body fat measured by anthropometric methods. In athletes, the body mass index is not a good indicator of the amount of body fat. The dynamometric parameters of the calf extensors were high in all three groups, whereas the dynamometric parameters of the forearm flexors were significantly higher in the group of handball players. The parameters of body composition were in positive correlation with the dynamometric parameters of lower extremities in all three groups of athletes.

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## PROFESSIONAL ARTICLES

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### SIGNIFICANCE AND ROLE OF HOMEOSTATIC MODEL ASSESSMENT IN THE EVALUATION OF GLUCOSE REGULATION MECHANISMS

#### ZNAČAJ I UPOTREBA PARAMETARA MODELA HOMEOSTAZE U PROCENI GLIKOREGULATORNIH MEHANIZAMA

Stanislava NIKOLIĆ<sup>1-4</sup>, Nikola ĆURIĆ<sup>1-4</sup>, Romana MIJOVIĆ<sup>1-4</sup>, Branislava ILINČIĆ<sup>1-4</sup> and Damir BENC<sup>1,3,5</sup>

#### Summary

**Introduction.** Mathematical formulas, such as homeostatic model assessment indexes, proved to be useful for the estimation of insulin resistance. Nevertheless, numerous published results point to a considerable variability of their reference values. The aim of this study was to use homeostatic model assessment indexes and evaluate levels of insulin resistance in nondiabetic patients. **Material and Methods.** The study included 486 individuals (mean age  $36.84 \pm 12.86$ ; 17% of males and 83% of females). Blood sampling was performed in order to determine glucose and insulin plasma levels, at the 0<sup>th</sup> and 120<sup>th</sup> minute of the oral glucose tolerance test. The indexes were calculated by the use of homeostatic model assessment 2 calculator, homeostatic model assessment of insulin resistance, homeostatic model assessment of insulin sensitivity, and homeostatic model assessment of  $\beta$ -cells function. The results were statistically analyzed using a *Data Analysis* programme. **Results.** In the examined population, the average glycemic values of the oral glucose tolerance test were within the euglycemic scope (Gluc 0 =  $4.76 \pm 0.45$  mmol/L; Gluc 120 =  $5.24 \pm 1.17$  mmol/L), while the average values of calculated homeostatic model assessment indexes were: insulin resistance -  $1.41 \pm 0.82$ ;  **$\beta$ -cells function - 131.54  $\pm$  49.41%, and insulin sensitivity - 91.94  $\pm$  47.32%.** According to study cut-off values, homeostatic model assessment of insulin resistance was less than 2. We found 84 (17.28%) individuals with increased insulin resistance. Also, we set the lowest reference value for homeostatic model assessment of insulin sensitivity at less than 50%. With the probability of 66.67% ( $\bar{x} \pm 1SD$ ), basal insulin level under 11.9 mIU/L can be considered to correspond to physiologic level of insulin resistance. **Conclusion.** The follow-up of increased insulin resistance and altered secretion of pancreatic  $\beta$ -cells, at early stages of glucose regulation disturbances, may be useful in assessing dynamics and level of glucose regulation disturbances and their appropriate treatment. **Key words:** Insulin Resistance; Prediabetic State; Insulin; Blood Glucose; Glucose Tolerance Test; Early Diagnosis; Models, Theoretical; Risk Factors; Diabetes Mellitus, Type 2; Insulin-Secreting Cells

#### Sažetak

**Uvod.** Za relativno brzu procenu insulinske rezistencije primenjuju se matematički izrazi, poput modela za procenu homeostaze. Međutim, podaci iz literature ukazuju na veliku varijabilnost njihovih graničnih vrednosti, namećući potrebu za njihovim određivanjem u našoj populaciji. Cilj rada bio je da se ispita nivo insulinske rezistencije pomoću indeksa homeostaze u grupi pacijenata bez dijabetesa. **Materijal i metode.** U studiju je uključeno 486 ispitanika, od kojih su 17% osobe muškog pola. Prosek godina života ispitanika je 36,84. Svim ispitanicima laboratorijski je određivana koncentracija glukoze i insulina, iz uzoraka plazme, u toku nultog i 120. minuta oralnog testa tolerancije glukoze, a zatim primenom kalkulatora 2 homeostaze, izračunati sledeći indeksi: indeks insulinske rezistencije, indeks insulinske senzitivnosti i sekretorni indeks oslobađanja insulina. Rezultati su statistički obrađivani programom *Data Analysis* i potom prikazani grafički i tabelarno. **Rezultati.** Na ispitivanoj populaciji, srednje vrednosti glikemije u nultom i 120. minutu oralnog testa tolerancije glukoze su unutar euglikemijskog opsega ( $4,76 \pm 0,45$  mmol/L i  $5,24 \pm 1,17$  mmol/L), dok su srednje vrednosti izračunatih indeksa homeostaze: indeks insulinske rezistencije ( $1,41 \pm 0,82$ ); sekretorni indeks oslobađanja insulina ( $131,54 \pm 49,41\%$ ) i indeks insulinske senzitivnosti ( $91,94 \pm 47,32\%$ ). Prema preporuci iz literature i rezultatima studije, definisana je gornja *cut-off* vrednost indeks insulinske rezistencije  $< 2$ . U ispitivanoj populaciji je bilo 84 ispitanika (17,28%) sa povišenom insulinskom rezistencijom. Takođe, postavili smo donju graničnu vrednost za indeks insulinske senzitivnosti na  $< 50\%$ . Sa verovatnoćom od 66,67% ( $\bar{x} \pm 1SD$ ), može se smatrati da vrednosti bazalnog insulina ispod 11,9 mIU/L odgovaraju fiziološkom nivou insulinske sekrecije. **Zaključak.** Praćenje promene insulinske rezistencije i sekrecije beta ćelija pankreasa, u početnim fazama poremećaja glikoregulatornog sistema, mogao bi biti od koristi u proceni dinamike i težine narušavanja glikoregulatornog sistema i eventualnom preduzimanju pravovremenih, odgovarajućih terapijskih mera.

**Ključne reči:** insulinska rezistencija; predijabetes; insulin; šećer u krvi; oralni glukoza tolerans test; rana dijagnoza; teoretski modeli; faktori rizika; dijabetes melitus, tip 2; insulin-sekretujuće ćelije



**Abbreviations**

T2DM	– type 2 diabetes mellitus
HOMA	– homeostatic model assessment
HOMA-IR	– homeostatic model assessment of insulin resistance
HOMA-S	– homeostatic model assessment of insulin sensitivity
HOMA-B	– homeostatic model assessment of secretory $\beta$ -cells capacity
QUICKI	– quantitative insulin sensitivity check index
OGTT	– oral glucose tolerance test
CLIA	– direct chemiluminescence immunoassay

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**Introduction**

The incidence of type 2 diabetes mellitus (T2DM), associated with obesity, physical inactivity and unhealthy diet, is increasing worldwide, especially in developing countries [1]. It is characterized by abnormalities in insulin secretion and elevated insulin resistance leading to increased glucose levels [2]. Years before the T2DM is diagnosed, patients usually have a few or even no signs or symptoms typical for the disease itself. Therefore, it is of great importance to have a suitable diagnostic tool which may point to the initial pathophysiological processes in apparently healthy population.

The gold standard for the assessment of insulin sensitivity and/or resistance is the glucose clamp technique. However, these tests are expensive and difficult to perform, and as such they are not suitable for routine use [3].

According to the results primarily obtained by clamp techniques (euglycemic, hyperinsulinemic, and hyperglycemic clamp), certain mathematical models were developed. These equations are based on simple, single determination of glucose, insulin

or C-peptide levels, and as such, relatively accurately estimate the level of insulin resistance, as well as the secretory capacity of pancreatic  $\beta$ -cells.

These mathematical equations, described in 1985, called homeostatic model assessment (HOMA) indexes, comprise two different formulas: homeostatic model assessment of insulin resistance (HOMA-IR), and homeostatic model assessment of  $\beta$ -cell capacity (HOMA-B) [4]. Since that time, other mathematical expressions have been developed, such as quantitative insulin sensitivity check index (QUICKI), and McAuley index which assesses the degree of insulin sensitivity [5]. At the same time, the existing formulas have been upgraded by glucose and insulin levels obtained from oral glucose tolerance test (OGTT), as well as the demographic and anthropometric data (body mass index, age, and gender). These equations are known as Stumvoll indexes [6].

The fact that these relatively simple mathematical models highly correlate with the clamp technique, has enabled their use in a large number of clinical and epidemiological studies. However, in clinical practice, the most widely used are HOMA indexes: HOMA-IR and HOMA-B, using both glucose and insulin under basal conditions.

Insulin resistance is associated with an increased cardio-metabolic risk in obese people as well as in individuals with altered glucose control. Considering that insulin resistance is the pathophysiological basis of T2DM, there is a need for its measurement, as well as for setting the reference (cut off) intervals, especially in people at increased risk of developing T2DM [7]. In most of the published papers, HOMA-IR value taken for the upper limit is less than 2.5 [8].

The aim of this study was to analyze the level of insulin resistance using HOMA indexes in subjects with clear euglycemic values in basal conditions, as well as at the 120<sup>th</sup> minute of the OGT-test.

**Table 1.** Mean values and standard deviations of all of examined parameters (n = 486)

**Tabela 1.** Srednje vrednosti i standardne devijacije analiziranih parametara u celom ispitivanom uzorku

n=486	$\bar{x}$	SD
Mean age (years)/ <i>Godine života (god)</i>	36.84	12.86
Gluc 0 (mmol/L)/ <i>Gluc 0 (mmol/l)</i>	4.76	0.45
Gluc 120 (mmol/L)/ <i>Gluc 120 (mmol/l)</i>	5.24	1.17
Ins 0 (mIU/L)/ <i>Ins 0 (mIU/l)</i>	11.14	6.59
Ins 120 (mIU/L)/ <i>Ins 120 (mIU/l)</i>	52.40	46.46
HOMA-IR/ <i>HOMA-IR</i>	1.41	0.82
HOMA-B (%)/ <i>HOMA-B (%)</i>	131.54	49.41
HOMA-S (%)/ <i>HOMA-S (%)</i>	91.94	47.32

**Legend:** Gluc 0 and Gluc 120 – plasma glucose level during the 0<sup>th</sup> and 120<sup>th</sup> OGT test; Ins 0 and Ins 120 – plasma insulin level during the 0<sup>th</sup> and 120<sup>th</sup> OGT test; HOMA-IR - calculated index of insulin resistance (homeostasis model assessment, calculator HOMA 2); HOMA-B - calculated index of insulin secretion (homeostasis model assessment, calculator HOMA 2); HOMA-S - calculated index of insulin sensitivity (homeostasis model assessment, calculator HOMA 2)

**Legenda:** *Gluc 0 i Gluc 120 – koncentracija glukoze u toku oralnog testa tolerancije glukoze; Ins 0 i Ins 120 – koncentracija insulina u toku oralnog testa tolerancije glukoze; HOMA-IR – izračunati indeks insulinske rezistencije; HOMA-B% - izračunati indeks insulinske sekrecije; HOMA-S% - izračunati indeks insulinske senzitivnosti*

**Table 2.** The significance of differences of examined parameters  
**Tabela 2.** Značajnost razlika ispitivanih parametara

	HOMA-IR>2 $\bar{x} \pm SD$ n=84	HOMA-IR<2 $\bar{x} \pm SD$ n=402	P
Gluc 0 (mmol/L)	4.91 ± 0.48	4.72 ± 0.42	p < 0,001
Gluc 120 (mmol/L)	5.88 ± 1.31	5.11 ± 1.10	p < 0.001
Ins 0 (mIU/L)	22.27 ± 7.45	8.81 ± 3.09	p < 0.001
Ins 120 (mIU/L)	106.28 ± 67.90	41.14 ± 30.36	p < 0.001
HOMA-IR	2.79 ± 0.89	1.12 ± 0.39	p < 0.001
HOMA-B (%)	200.90 ± 58.68	117.05 ± 31.97	p < 0.001
HOMA-S (%)	38.44 ± 8.89	103.12 ± 44.34	p < 0.001

**Legend:** Gluc 0 and Gluc 120 – plasma glucose level during the 0<sup>th</sup> and 120<sup>th</sup> OGT test; Ins 0 and Ins 120 – plasma insulin level during the 0<sup>th</sup> and 120<sup>th</sup> OGT test; HOMA-IR - calculated index of insulin resistance (homeostasis model assessment, calculator HOMA 2); HOMA-B - calculated index of insulin secretion (homeostasis model assessment, calculator HOMA 2); HOMA-S - calculated index of insulin sensitivity (homeostasis model assessment, calculator HOMA 2)

**Legenda:** Gluc 0 i Gluc 120 – koncentracija glukoze u toku oralnog testa tolerancije glukoze; Ins 0 i Ins 120 – koncentracija insulina u toku oralnog testa tolerancije glukoze; HOMA-IR – izračunati indeks insulinske rezistencije; HOMA-B% - izračunati indeks insulinske sekrecije; HOMA-S% - izračunati indeks insulinske senzitivnosti

## Material and Methods

The study included 486 subjects who were examined at the Center for Laboratory Medicine, Clinical Center of Vojvodina, from January 2014 to December 2015.

All the participants have undergone adequate preparation, including eight-hour, overnight fasting, as well as half an hour standstill before blood sampling. Blood was collected in EDTA (venous blood collection tubes) vacutainer tubes, centrifuged at a speed of 4000 rpm for 10 minutes. Glucose and insulin levels were determined from obtained plasma samples.

Glucose determination was done using a specific enzyme, GOD-pap method (reference range from 4.0 to 6.1 mmol/L), while insulin was measured using an automated immunometric system (ADVIA Centaur system XP), based on direct chemiluminescence immunoassay (CLIA). The sensitivity and the range of insulin was 0.5 to 300 mIU/L. The recommended reference value for the basal insulin values was 3.0 – 25.0 mIU/L.

Based on the measured values, exclusion criteria were as follows: fasting glucose during 0<sup>th</sup> of OGT testing > 6.1 mmol/L; glucose during 120<sup>th</sup> minute of OGT testing > 7.8 mmol/L. According to the above criteria, the study included only nondiabetic, euglycemic subjects [9].

HOMA indexes were calculated in all participants. According to HOMA2 calculator, the following indexes were determined: HOMA-IR (insulin resistance index), HOMA-S (index of insulin sensitivity %) and HOMA-B (index of  $\beta$ -cells secretory capacity %). HOMA2 calculator was downloaded from the official website of the University of Oxford, Oxford Centre for Diabetes, Endocrinology and Metabolism [10]. The content of the formulas used by the mentioned calculator is not known, but it most

certainly represents a perfected model in comparison to previously defined HOMA equations.

The results were statistically analyzed using a *Data Analysis* program, and then presented in graphical and tabular forms.

## Results

The study included 401 (83%) women, and 85 (17%) men. The average age of respondents was  $36.84 \pm 12.86$ , the youngest participant was 19 years old, and the oldest 70 years old (**Table 1**).

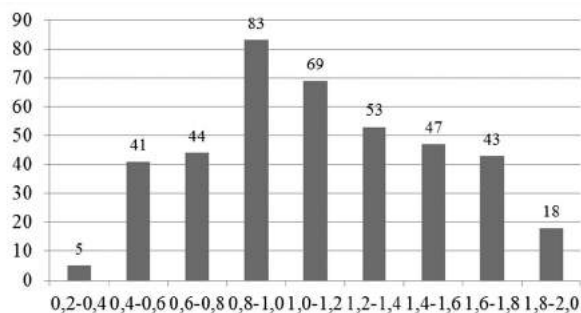
In the examined subjects, both average glycemic values (at 0<sup>th</sup> and 120<sup>th</sup> minute) of OGTT were within the euglycemic range (Gluc 0 =  $4.76 \pm 0.45$  mmol/L; Gluc 120 =  $5.24 \pm 1.17$  mmol/L). The mean values of calculated HOMA indexes are presented in **Table 1** (HOMA-IR =  $1.41 \pm 0.82$ ; HOMA-B =  $131.54 \pm 49.41\%$  and HOMA-S =  $91.94 \pm 47.32\%$ ) (**Table 1**).

The upper cut-off value for HOMA-IR has been defined to be less than 2 (**Table 2**).

Based on study results, 84 (17.28%) individuals manifested increased insulin resistance, while 402 participants had HOMA-IR values less than 2.0 and accounting for 82.7% (healthy subjects without insulin resistance) of the total of examined subjects (**Table 2**). According to the results presented in **Graph 1**, most subjects (83) had the interval of HOMA-IR values between 0,8 and 1,0 (**Graph 1**).

The T-test showed a statistically significant difference of all analyzed parameters between the group with initially elevated insulin resistance (HOMA-IR>2) and healthy subjects (HOMA-IR<2) (**Table 2**).

By definition, HOMA-S index represents the percentage of deviation from the expected, ideal 100% insulin sensitivity. Therefore, only the lowest reference value for HOMA-S less than 50% was set (**Table 2**).



**Graph 1.** Histogram of HOMA-IR distribution in the group of subjects without insulin resistance (HOMA-IR < 2)

**Grafikon 1.** Histogram distribucije učestalosti insulinske rezistencije u grupi zdravih ispitanika (HOMA-IR < 2)

**Legend:** x-axis: intervals of HOMA-IR; y-axis: frequency of HOMA-IR intervals

**Legenda:** na apcisi (x – osa) intervali vrednosti insulinske rezistencije; na ordinati (y – osa) učestalost vrednosti insulinske rezistencije u datom intervalu

No overlap in the mean basal insulin values ( $-1SD < \bar{x} < +1SD$ ) has been established between the two groups with ( $5.72 < 8.81 < 11.9$  mIU/L) and without ( $14.82 < 22.27 < 29.72$  mIU/L) elevated insulin resistance. With the probability of 66.67% ( $\bar{x} \pm 1SD$ ), basal insulin level under 11.91 mIU/L can be considered to correspond the physiologic level of insulin resistance (**Table 3**).

Linear correlation analysis revealed a statistically significant connection of a moderate degree between calculated HOMA-IR values and Ins 120 ( $r = 0.632$ ,  $p < 0.01$ ). A high degree of positive correlation was observed between HOMA-IR and HOMA-B ( $r = 0.831$ ,  $p < 0.01$ ), while there was a high degree of negative correlation between HOMA-IR and HOMA-S (**Table 4**).

## Discussion

This study included a total of 486 subjects with normal blood glucose levels during the 0<sup>th</sup> and 120<sup>th</sup> OGT-test (baseline glucose < 6.1 mmol/L and 120<sup>th</sup> glucose < 7.8 mmol/L, respectively). Since the glucose reference range during OGT testing is inde-

pendent of gender and age, the study included 83% of women and 17% of men, with an average age of 36.8 years (range - 19–70 years) [11].

Based on the values and results obtained in the study, the recommended cut-off value for HOMA-IR less than 2 was accepted [12]. The adequacy of the defined upper limit has been confirmed by analyzing the calculated value of HOMA-IR in the entire examined population. In the group of participants without insulin resistance, the level of HOMA-B and HOMA-S had the slightest deviation from the optimal values defined according to the euglycemic population (HOMA-S = 103.12%; HOMA-B = 117.05%) [4].

At the same time, the lower reference limit for HOMA-S to less than 50% has been established. HOMA-S represents a very important parameter because it defines condition of insulin resistance in peripheral tissues more closely. This index enables assessment of peripheral tissues insulin sensitivity. Due to lower insulin sensitivity, the insulin resistance is increased. Disturbances of insulin resistance represent the first link in the chain of numerous pathophysiological events leading to disruption of the complex metabolic processes in the body. Initially, higher insulin secretion is compensated with elevated insulin resistance, introducing the system in a vicious circle, until the collapse of glucose regulation and other metabolic homeostasis mechanisms resulting in a permanent expression of hyperglycemia and clinical manifestations of T2DM.

Based on the upper limit for HOMA-IR, 17.28% (84 of 486) of participants presented with elevated insulin resistance. This result is in accordance with numerous results obtained from different studies conducted in various populations. Japanese authors determined the upper limit value for HOMA-IR at 2.4 [13]. Another study established reference value for HOMA-IR at 2.05, and it included adult population in Spain [14]. Similar to our values, Swedish group of authors defined the limit for HOMA-IR at 2.0 [15], while HOMA-IR indexes were higher among Italians (HOMA-IR = 2.77) [16] and the French [17]. The study conducted among the adult population in the USA set a cut off value at 4.39 [18].

**Table 3.** Basal insulin levels and HOMA-S % in the groups of subjects with and without elevated insulin resistance  
**Tabela 3.** Vrednosti bazalnog insulina i HOMA-S% u grupi zdravih i grupi ispitanika sa povišenom insulinskom rezistencijom

	HOMA-IR < 2 N = 402			HOMA-IR > 2 N = 84		
	1 SD	$\bar{x}$	+ 1 SD	1 SD	$\bar{x}$	+ 1 SD
Ins 0 (mIU/L)	5.72	8.81	11.91	14.82	22.27	29.72
HOMA-S (%)	58.78	103.10	147.47	47.33	38.44	29.55

**Legend:** Ins 0 - plasma insulin level during the 0<sup>th</sup> of OGT test; HOMA-B% - calculated index of insulin secretion (homeostasis model assessment. calculator HOMA 2);  $\bar{x}$  – mean value; SD – standard deviation

**Legenda:** Ins 0 – koncentracija insulina u toku oralnog testa tolerancije glukoze; HOMA-S% – izračunati indeks insulinske senzitivnosti;  $\bar{x}$  – srednja vrednost; SD – standardna devijacija

The differences between the defined reference values of HOMA indexes can be explained by numerous facts. It is noteworthy that in many studies HOMA indexes have been calculated according to the original equation, using plasma values of glucose and insulin measured in basal conditions (original HOMA model equations). It is known that this original equation is defined based on the earlier generation of insulin tests, and as such underestimates insulin sensitivity and insulin resistance and overestimates the secretory capacity of pancreatic  $\beta$ -cells [4]. In contrast, in this study, HOMA2 computer model was used, which is more reliable and widespread providing the ability of calculating three different HOMA values at the same time (HOMA-IR, HOMA-B and HOMA-S). This model offers a non-linear solution. It is calibrated according to the latest generation of insulin or even c-peptide values as a direct indicator of insulin secretion. HOMA2 calculator is widely used in hyperglycemic states, taking into account the renal glucose loss [4].

Obesity and socioeconomic status are also important factors for the development of insulin resistance, which can explain the significantly higher value of the index among Americans compared to other populations, including our examinees [15]. A Mexican study dealt with the influence of heritage on the level of insulin resistance. The results of that study proved that Mexicans of Indian origin had higher HOMA indexes than those whose origins were European [19]. This is an interesting fact considering that the population of Vojvodina is multi-ethnic and future studies should take into account the ethnicity of the population being tested.

The participants were divided into two groups, based on the set cut-off HOMA-IR and were statistically different in all parameters (plasma glucose and insulin during the 0<sup>th</sup> and 120<sup>th</sup> minute of OGTT, HOMA-B and HOMA-S). Both groups had blood glucose levels in the reference range (from

4.0 to 6.1), with significantly higher values in the group with elevated insulin resistance (4.91 mmol/L vs. 4.72 mmol/L) (Table 2).

Also, the baseline plasma insulin was significantly lower in the group without elevated insulin resistance (8.81 mIU/L vs. 22.27 mIU/L). These insulin levels may be used in a rough estimation of insulin resistance and increased insulin secretion. Although the reference value of baseline insulin levels is between 3.0 and 25.0 mIU/L (manufacturer's recommendation), according to this study, with the probability of 66.67% ( $\bar{x} \pm 1SD$ ), basal insulin level under 11.91 mIU/L can be considered to correspond to physiologic level of insulin resistance.

Numerous publications were aimed to define the upper limit for insulin levels under basal conditions. McAuley and associates have set the limit at 12 mIU/L [20–22]. Other studies have defined the upper reference range at 16 mIU/L [23]. In this study, we noticed that the limit at 15.0 mIU/L resulted in the absence of false-negative patients (none of the 84 subjects with insulin resistance had the basal insulin level less than 15.0 mIU/L), and only 2 participants were false-positive (only 2 of 403 subjects without insulin resistance had fasting insulin levels above 15.0 mIU/L).

HOMA-B defines a compensatory mechanism which maintains the level of glucose in the optimal range. Since HOMA-B is about the degree of deviation of beta cells activity from the optimal glucose homeostasis, it provides very useful information on the current level of the compensatory mechanism in advanced stages of the disorder.

The study focuses on subjects whose glucose levels did not reflect a realistic insight into the physiological mechanism of glucose regulation, during the period when the pancreatic beta cells were sufficient to maintain glucose in the reference range. **Therefore, it is very important to detect elevation of insulin resistance using indirect methods**

**Table 4.** Linear correlation

**Tabela 4.** Linearna korelacija

	HOMA-IR n=486	
	r	p
Gluc 0 (mmol/L)	0.311	< 0.001
Gluc 120 (mmol/L)	0.300	< 0.001
Ins 0 (mIU/L)	0.998	< 0.001
Ins 120 (mIU/L)	0.632	< 0.001
HOMA-B (%)	0.831	< 0.001
HOMA-S (%)	-0.775	< 0.001

**Legend:** r-Pearson's coefficient of correlation; p - statistical significance; Gluc 0 and Gluc 120 – plasma glucose level during the 0<sup>th</sup> and 120<sup>th</sup> OGT test; Ins 0 and Ins 120 – plasma insulin level during the 0<sup>th</sup> and 120<sup>th</sup> OGT test; HOMA-IR - calculated index of insulin resistance (homeostasis model assessment, calculator HOMA 2); HOMA-B % - calculated index of insulin secretion (homeostasis model assessment, calculator HOMA 2); HOMA-S % - calculated index of insulin sensitivity (homeostasis model assessment, calculator HOMA 2)

**Legenda:** r-Pirsonov korelacioni koeficijent; p – statistička značajnost; Gluc 0 i Gluc 120 – koncentracija glukoze u toku oralnog testa tolerancije glukoze; Ins 0 i Ins 120 - koncentracija insulina u toku oralnog testa tolerancije glukoze; HOMA-IR – izračunati indeks insulinske rezistencije; HOMA-B%- izračunati indeks nsulinske sekrecije; HOMA-S%-izračunati indeks insulinske senzitivnosti

that can measure the degree of insulin resistance, particularly in people with an increased risk of disruption of glucose regulatory mechanisms, obesity and poor physical activity. For individuals with detected elevated HOMA-IR it is necessary to repeat the testing in order to exclude certain conditions that may compromise the credibility of the obtained results (tests performed in non-standard conditions). After confirming the elevation of HOMA-IR and/or reduction of HOMA-S, it is recommended to monitor these individuals in appropriate time intervals, since it is thought they are at increased risk for developing T2DM. In addition to regular laboratory monitoring of this population and calculation of HOMA indexes, it is very useful to implement education for these persons. However, today there is very little data available on monitoring and taking appropriate measures in nondiabetic population with early established increase in insulin resistance [24]. Therefore, it would be of particular importance to continuously monitor individuals with established insulin resistance, ac-

ording to set criteria (HOMA-IR >2). Eventually, slightly elevated insulin resistance will cause changes in blood glucose levels. The follow-up of changes in insulin resistance and secretion of pancreatic beta cells, may be useful in assessing the dynamics and severity of disruptions of glucose regulatory mechanisms, as well as in taking adequate therapeutic measures in due time.

## Conclusion

Continuous monitoring of individuals with elevated insulin resistance will give more precise answers about the efficacy of homeostatic model assessment indexes in early detection of the glucose regulation disturbances. The calculated homeostatic model assessments of insulin sensitivity (%) and of secretory  $\beta$ -cells capacity (%) are useful indicators that provide additional information necessary for proper interpretation of homeostatic model assessment of insulin resistance.

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## MONITORING THE QUALITY OF ORAL HEALTH AMONG THE POPULATION OF SCHOOLCHILDREN

*PRAĆENJE KVALITETA ORALNOG ZDRAVLJA KOD POPULACIJE ŠKOLSKE DECE*

**Slađana J. VASILJEVIĆ<sup>1</sup> and Aleksandra T. CVETKOVIĆ<sup>2</sup>**

### Summary

**Introduction.** Improvement of the quality of dental care is necessary for efficient prevention of oral diseases. The aim of this study was to analyze: the efficiency of the recommended work quality parameters in the Dental Health Care Service of the Health Center Zemun in 2014 and 2015; compare 7- and 12-year-olds in terms of having all healthy teeth and topical application of fluoride; presence of orthodontic anomalies in 12- and 14-year-olds, and assess the caries index (decayed-missing-filled teeth) in 12-year-old children. **Material and Methods.** The retrospective study included 7-, 12-, 14-, and 18-year-olds and assessed their oral health in 2014 (n = 4.317) and 2015 (n = 6.575). **Results.** A higher percentage of examinees kept their dental appointments in 2015 than in 2014 (82% and 60%, respectively). Out of 3.723 seven-year-olds, 36.6% had all healthy teeth, as well as 43.69% out of 3.170 of 12-year-olds. Out of 3.723 seven-year-olds, 65.26% had topical application of fluoride, as well as 78.73% out of 3.170 of twelve-year-olds. High percentages of orthodontic anomalies were found in both fourteen and eighteen-year-olds in 2015 (p<0.05). The average decayed-missing-filled teeth index in twelve-year-olds was 1.30 in 2014 and 1.68 in 2015. **Conclusion.** A higher percentage of all healthy teeth, and of topical application of fluoride in twelve-year-olds compared to the seven-year-olds, indicates that seven-year-olds keep their dental appointments more regularly, and consequently the prevention of oral diseases is more successful. Since the presence of orthodontic anomalies is high in both fourteen and eighteen-year-olds, and fewer children of both age groups respond to regular dental checkups, an intensified prevention of oral diseases is necessary in children.

**Key words:** Oral Health; Quality Control; Child; Adolescent; Preventive Dentistry; Dental Caries; Fluorides, Topical; Malocclusion

### Introduction

The generally accepted definition of healthcare quality, which proved to be useful in the development and formulation of strategies, regardless of the available resources, points out that the quality healthcare provides the most effective and safe prevention and treatment for healthcare users, efficiently organizing its resources, without unnecessary losses, and meeting high level demands [1]. Constant quality improvement is a continuous process aimed at achieving greater ef-

### Sažetak

**Uvod.** Unapređenje kvaliteta stomatološke zdravstvene zaštite predstavlja proces čiji je cilj efikasna preventiva bolesti usta. Cilj rada je analiza efikasnosti primene preporučenih parametara kvaliteta rada u Službi za stomatološku zdravstvenu zaštitu u 2014. i 2015. godini u Domu zdravlja Zemun; uporediti decu u sedmoj i dvanaestoj godini u pogledu postojanja svih zdravih zuba i lokalne aplikacije fluorida; odrediti prisustvo ortodontskih anomalija kod četrnaestogodišnjaka i osamnaestogodišnjaka, i ustanoviti indeks karijesa kod dvanaestogodišnjaka. **Materijal i metode.** Procena kvaliteta oralnog zdravlja dece u 7, 12, 14. i 18. godini života obavljena je retrospektivnom analizom podataka iz 2014. (n = 4 317). i 2015. (n = 6 575) godine. **Rezultati.** Znatno veći procenat dece je pregledan 2015. godine (82%) nego 2014. godine (60%). Od 3 723 sedmogodišnjaka, 36,6% imalo je sve zdrave zube, a takođe i 43,69% od 3 170 dvanaestogodišnjaka. Od 3 723 sedmogodišnjaka, 65,26% imalo je lokalnu aplikaciju fluorida, kao i 78,73% od 3 170 dvanaestogodišnjaka. Ortodontske anomalije su zabeležene u većem procentu kod četrnaestogodišnjaka i osamnaestogodišnjaka tokom 2015. god. (p < 0,05). Prosečan indeks karijesa kod dvanaestogodišnjaka godine 2014. je iznosio 1,30, a godine 2015 1,68. **Zaključak.** Povećan procenat svih zdravih zuba, kao i povećan procenat lokalne aplikacije fluorida kod dvanaestogodišnjaka u odnosu na sedmogodišnjake ukazuje na to da je posećenost stomatologu redovnija kod sedmogodišnjaka, pa je i prevencija uspešnija. Visok procenat ortodontskih anomalija kod četrnaestogodišnjaka i osamnaestogodišnjaka, a znatno manji broj dece obe uzrasne grupe koja koji dolaze na sistematski stomatološki pregled razlozi su za intenzivniji rad na preventivi bolesti usta kod dece.

**Ključne reči:** oralno zdravlje; kontrola kvaliteta; dete; adolescent; preventivna stomatologija; zubni karijes; topikalni fluoridi; malokluzija

iciency and success at work, as well as at increasing the satisfaction of customers and health care providers.

Organized efforts to assess and improve the quality of healthcare are of more recent date. In Europe, the activities to ensure quality have escalated after the adoption of the World Health Organization program, "Health for All" [2] and formulation of specific objectives pertaining to the improvement of the quality [3]. Since then, the activities and mechanisms for quality improvement have become more numerous and more diverse.

**Abbreviations**

DMFT – decayed-missing-filled teeth

In accordance with the Strategy for healthcare reform [1], the Institute of Public Health of Serbia “Dr. Milan Jovanović Batut”, prepared detailed guidelines for health care institutions in terms of reporting data on work quality indicators [4, 5]. The recommended quality of work indicators for the Dental Health Care Service included the number of children aged 7 and 12 years covered by dental examination and topical application of fluoride, and the number of children with orthodontic anomalies aged 14 and 18 years.

The aim of this study was to analyze the recommended quality of work parameters for the Dental Health Care Service of the Health Center Zemun in the period 2014 and 2015; determine whether there were differences between children aged seven and twelve years with all healthy teeth and topical application of fluoride; differences between fourteen- and eighteen-year-olds in terms of untreated orthodontic anomalies, as well as to determine the caries index, and distribution of decayed-missing-filled teeth (DMFT) in twelve-year-olds in this period.

**Material and Methods**

This retrospective study included 7-, 12-, 14-, and 18-year-old schoolchildren having preventive check-ups at the Health Center Zemun during 2014 and 2015. The total number of examined children during 2014 and 2015 was 7.202 and 7.961, respectively. The total number of children who responded to preventive dental check-ups in 2014 and 2015, was 4.317 and 6.575, respectively.

We determined the percentage of children who responded to systematic dental examinations, the number of children with all healthy teeth, and percentage of topical application of fluoride in seven- and twelve-year-olds, as well as the caries index in 12-year-olds. The presence of orthodontic anomalies was determined in 14- and 18-year-olds. The number of participants under orthodontic treatment in 2014 and 2015 was 631 and 1.311, respectively.

Statistical data processing: frequencies and percentages were used as descriptive statistics. Differences between groups were determined by  $X^2$  test. Statistical significance was defined at the level of probability of the null hypothesis of  $p \leq 0.05$  to  $p < 0.01$ . Statistical processing and analysis was done using SPSS ver. 20 (Statistical Package for Social Sciences).

**Results**

In comparison with 2014, a significantly higher percentage of children were covered by systematic dental examination (60% and 82%, respectively) during 2015 (**Table 1**). However, out of the total number of children who were scheduled for systematic dental check-ups during both years, 72% of children were actually examined (**Table 1**).

Out of 3.723 examined seven-year-olds, 1.364 (36.6%) had all healthy teeth, and out of 3.170 examined 12-year-olds, 1.385 children (43.69%) had all healthy teeth. Out of 3.723 seven-year-olds, 2.430 (65.26%) had topical application of fluoride, as well as 2.496 (78.73%) of 3.170 twelve-year-olds. There were no statistically significant differences between the data obtained in 2014 and 2015 ( $p > 0.05$ ) (**Graph 1**).

The response of children to preventive dental examination was not satisfactory neither in 2014 nor in 2015. More orthodontic anomalies were found in fourteen- and eighteen-year-olds in 2015 than in 2014 ( $p < 0.05$ ). In relation to the examined population of eighteen-year-olds, the presence of orthodontic anomalies was significantly higher ( $p < 0.05$ ) in 2015 than in 2014 (**Graph 2**).

In 2014, there were 1.134 cases of caries, 68 extractions and 1.056 fillings in twelve-year-olds, while the total DMFT-12 was 2.258 (average DMFT-12 = 1.30). In 2015, among children of the same age, there were 1.877 cases of caries, 285 extractions, 1.430 fillings, the total DMFT-12 = 3.592, and the average DMFT-12 = 1.68. The total DMFT index was significantly higher ( $p < 0.05$ ) in 2015 (**Graph 3**).

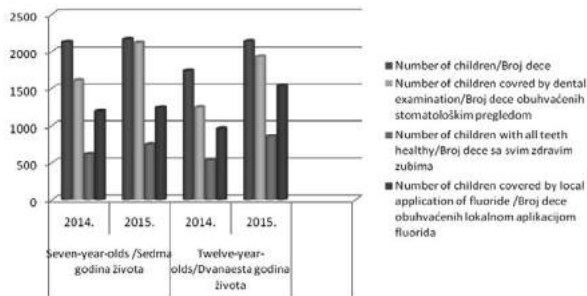
**Discussion**

Our study points to the increasing trend of dental preventive examinations in the total population of schoolchildren, indicating the introduction of a quality culture and continuous monitoring of the quality of work. However, it is evident that the number of children who respond to systematic preventive dental examinations declines with age. Dental checkups are more regular in younger children (seven-year-olds), which means that the timely prevention of caries is successful, so that the percentage of twelve-year-olds with all healthy teeth is larger. Prevention programs in most developed countries have resulted in permanent decline of tooth decay in children [6, 7], so it is necessary to revitalize the preventive health care in our country, according to recommendations, strategy and protocol already adopted [1, 8].

**Table 1.** The ratio of planned and completed dental examinations of schoolchildren in 2014 and 2015  
*Tabela 1. Odnos planiranih i izvršenih stomatoloških pregleda školske dece u 2014. i 2015. godini*

Period/Period	Planned number of children <i>Planirani broj dece</i>	Number of children covered by dental examination <i>Broj dece kod kojih je izvršen stomatološki pregled</i>	% %
1. 2014	7.202	4.317	60%
2. 2015	7.961	6.575	82%
3. Total/ <i>Ukupno</i>	15.163	10.892	72%



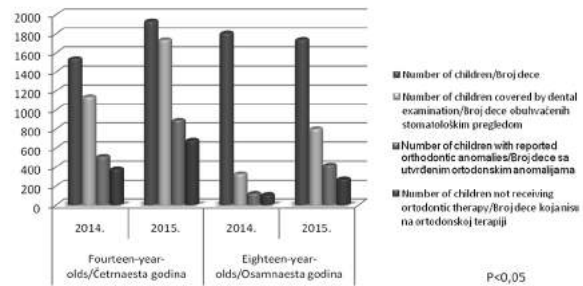


**Graph 1.** The number of children with all healthy teeth and topical application of fluoride in relation to the dental examination ( $p > 0.05$ )

**Grafikon 1.** Broj dece sa svim zdravim zubima i lokalnom aplikacijom fluorida u odnosu na stomatološki pregled ( $p > 0,05$ )

The importance of topical application of concentrated fluoride is confirmed in our tests, too. The percentage of children examined follows the number of services performing topical application of fluoride. The coverage of children receiving topical concentrated fluoride is defined by the Protocol on the application of fluoride and prevention of caries in children and young people in Serbia [8]. However, the fluoride-prophylaxis is not well known about in Serbia, especially in rural areas [9], which points to the necessity of promoting oral health in all, and especially in less developed countries [10–12]. Preventive fluoride agents are recommended for children who are at high risk for dental caries, although they are not profitable economically for large-scale massive application [13, 14].

The presence of untreated orthodontic anomalies is extremely high in both examined age groups. A reduced number of examined eighteen-year-olds is due to failure to respond to timely dental examination at the health center and/or visit to private dental office. It is possible that the incidence of orthodontic anomalies and caries is much higher among unscreened children of this age [15]. Such high percentage of children with untreated orthodontic problems can be reduced only by improving preventive work at an earlier age [16]; otherwise, the treatment of orthodontic anomalies is going to be more complicated and more expensive.



**Graph 2.** The number of children with established orthodontic anomalies (1,400 in 14-year-olds, 542 in 18-year-olds), ( $p < 0.05$ )

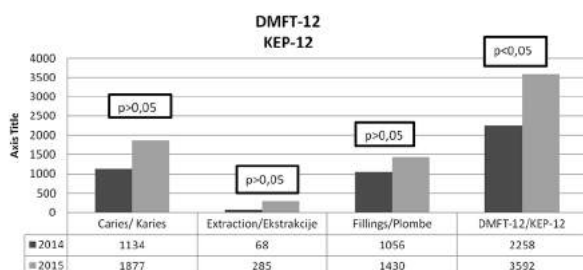
**Grafikon 2.** Broj dece kod kojih je utvrđeno prisustvo ortodontskih anomalija (u 14.godini 1400, u 18. godini 542), ( $p < 0,05$ )

The ratio of caries, extracted and filled teeth in twelve-year-olds was significantly higher in 2015, but still lower than the average in Serbia, which is 2.6. The DMFT-12 index (the sum of the numbers of caries, extracted, and filled teeth in twelve-year-olds) is considered a very good indicator of oral health. Average caries index in twelve-year-olds in the European countries ranges from 0.7 to 4.2, and in most countries of the European Union, the index is between 0.5 and 1.5 [3]. In developed European countries, this index has been constantly improving since the beginning of the nineties, but in the countries of Eastern and Central Europe, it is still a public health problem. Slow improvement in these countries is attributed to the change in the health system due to political and economic changes. The economic crisis, restructuring the system of dental health care, lack of continuous implementation of health care program measures for children and youth [8], and perhaps privatization in the health care system, has led to decreased use of free health care for children [17], therefore our analysis is limited only to children who responded to medical check-ups at the public health centers.

It is of utmost importance to start the prevention of oral health as early as possible [17], in order to ensure the prevention of oral health by reliable effects [18, 19], which is defined by the dental health care quality parameters [20]. Great importance in prevention is to organize dental services and social engagement [21].

## Conclusion

All quality indicators point to the unsatisfactory quality of oral health in children and youth examined at the Health Center Zemun. In order to improve the oral health of children, it is essential to support the adoption of healthy behaviors with regard to oral hygiene, fluoride prophylaxis, nutrition and regular visits to the dentist to control the oral health, through health and educational interventions. Improvements can be expected if the prevention programs are planned at the national level and with revitalization of preventive health care.



**Graph 3.** The number of dental caries, extraction, filled teeth and DMFT index in twelve-year-olds in 2014 and 2015

**Grafikon 3.** Broj karijesa, ekstrakcija i plombiranih zuba i indeks karijesa kod dvanaestogodišnjaka 2014. i 2015. godine

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## CASE REPORTS

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Case report

*Prikaz slučaja*

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<https://doi.org/10.2298/MPNS1706167D>

## SYNCOPE DUE TO SINUS NODE DYSFUNCTION AFTER SURGICAL PATCH CLOSURE OF ATRIAL SEPTAL DEFECT – A CASE REPORT

*SINKOPA ZBOG DISFUNKCIJE SINUSNOG ČVORA NAKON HIRURŠKOG ZATVARANJA ATRIJALNOG SEPTALNOG DEFEKTA – PRIKAZ SLUČAJA*

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### Summary

**Introduction.** Sick sinus syndrome, a frequent cause of syncope, refers to a combination of symptoms caused by sinus node dysfunction. **Case report.** We report the case of a 38-year-old female patient presenting with recurrent syncope, who underwent surgical patch closure of atrial septal defect three years before admission. Ambulatory twenty-four-hour Holter monitoring was done capturing only sinus tachycardia. A series of examinations were warranted after admission, and recurrent syncope was found to be the result of sinus node dysfunction. This syndrome rarely occurs after surgical closure of atrial septal defect. The patient underwent permanent pacemaker implantation. **Conclusion.** A rigorous search for every possible cause of syncope is mandatory. A structural, multidisciplinary approach is required in order to achieve an optimal outcome.

**Key words:** Sick Sinus Syndrome; Syncope; Tachycardia; Postoperative Complications; Pacemaker, Artificial; Heart Septal Defects, Atrial

### Introduction

Syncope is a sudden and brief loss of consciousness followed by spontaneous recovery. Syncope develops because of temporary reduction in blood flow to the brain with consecutive cerebral oxygen deprivation. Therefore, syncope is defined as a transient, self-limited loss of consciousness with an inability to maintain postural tone that is followed by spontaneous recovery. Various causes are well described in the literature and include cardiac, vascular, neurological, metabolic and miscellaneous origins [1]. Sometimes it is difficult to determine the real cause of syncope, so numerous analyses need to be performed. Sick sinus syndrome (SSS) refers to a combination of symptoms such as dizziness, confu-

### Sažetak

**Uvod.** Sinkopa je iznenadni i kratki gubitak svesti sa gubitkom posturalnog tonusa i najčešće spontanom oporavkom. Postoje brojni uzroci sinkope. Sindrom bolesnog sinusnog čvora, tzv. sik sinus sindrom, odnosi se na kombinaciju simptoma kao što su konfuzija ili sinkopa uzrokovane bolešću sinusnog čvora. **Prikaz slučaja.** Prikazan je slučaj 38-godišnje bolesnice sa istorijom sinkope. Pre tri godine podvrgnuta je hirurškom zahvatu zatvaranja pretkomorskog septalnog defekta. Ambulantni 24-satni monitoring holterom kod naše pacijentkinje pokazao je samo sinusnu tahikardiju. Ostale ambulante analize takođe su bile u granicama normale. Nakon niza pretraga, uz multidisciplinarni pristup i ponavljanje monitoringa holterom utvrđeno je da je sinkopa rezultat disfunkcije sinusnog čvora kao retke komplikacije hirurškog zatvaranja pretkomorskog septalnog defekta. Potom je podvrgnuta implantaciji veštačkog vodiča srčanog ritma – pejsmejker. **Zaključak.** Treba pomno istražiti sve moguće usroke sinkope uz poseban akcenat na multidisciplinarni pristup pacijentu.

**Cljučne reči:** disfunkcija sinusnog čvora; sinkopa; postoperativne komplikacije; pejsmejker; pretkomorski septalni defekt

sion etc. (symptoms and signs of end-organ hypoperfusion) caused by sinus node dysfunction (SND). SND is a frequent cause of syncope, and in this case it was a result of cerebral hypoperfusion.

We report here the case of a patient with history of syncope and dizziness. Three years before admission the patient underwent surgical repair of atrial septal defect (ASD) by pericardial patch closure of ASD. Recurrent syncope was a result of SSS and this syndrome rarely occurs after surgical patch closure of ASD.

### Case report

A 38-year-old woman was referred to our department due to repeated episodes of syncope during the past month. Three years before, she underwent

### Abbreviations

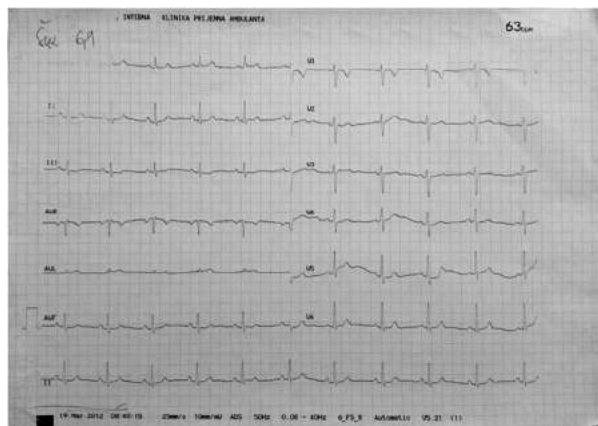
SSS	– sick sinus syndrome
SND	– sinus node dysfunction
ASD	– atrial septal defect
ECG	– electrocardiogram
DDDR	– dual chamber rate adaptive pacemaker
CHD	– congenital heart disease
SVASD	– sinus venosus atrial septal defect

a surgical patch closure of secundum ASD. She denied having other medical issues in the past and she was a non-smoker. She did not use any medications during the previous year.

Several months prior to admission, she started having symptoms of dizziness and weakness, and three months ago, she had the first episode of syncope. She did not have a chest pain, typical for angina. The patient was evaluated by a neurologist in ambulatory settings. A transcranial Doppler examination showed bilateral patency of carotid arteries, without significant stenosis. Computed tomography of the brain and electroencephalogram were requested. Ambulatory 24-hour Holter monitoring was done and it showed only sinus tachycardia with maximum heart rate 135/min during physical effort.

On admission, the patient was fully alert and oriented. Her vital signs (blood pressure, pulse and respiration) unremarkable. Physical examination of the heart, chest, abdomen and extremities were normal. No neurological deficit was present. Laboratory test results were within the normal range.

The chest X-ray showed no abnormalities. Both awake and asleep electroencephalography showed normal results. Computed tomography (CT) of the brain did not show any signs of intracranial hemorrhage or ischemia. Echocardiography showed slightly dilated right ventricle (3,5 cm) and patch closure of ASD, essentially preserved left-ventricular systolic function and no other abnormalities. Several electrocardiograms (ECG) were within normal limits (**Figure 1**).



**Figure 1.** Electrocardiogram of our patient on admission (no significant abnormalities)

**Slika 1.** Elektrokardiogram pacijentkinje na prijemu (bez značajnih abnormalnosti)

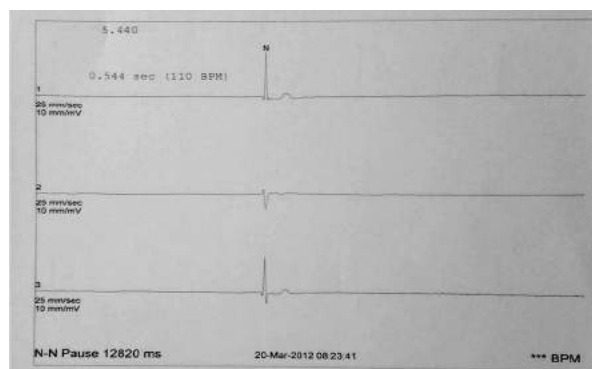
During the 24-hour Holter recording, the patient was in normal sinus rhythm with an average heart rate of 68/min, and maximum heart rate 137/min. PQ (time it takes for the sinus impulse to travel from the atria to the ventricles) and QT (measure between Q wave and T wave in the heart's electrical cycle) interval were within normal ranges, without signs of pre-excitation. Only rare atrial premature contractions were recorded. In the morning hours (08h 03 min to 08h 25min) a few significant sinus pauses were registered that correlated with the occurrence of syncope. The longest episode was 12820 ms (**Figure 2**).

The patient was diagnosed with symptomatic SND and underwent permanent pacemaker implantation (dual chamber rate adaptive pacemaker - DDDR). She did not suffer from syncope, weakness or dizziness after the treatment.

### Discussion

Sinus node dysfunction is a term used for numerous rhythm abnormalities such as: persistent sinus bradycardia, persistent sinus arrest with escape rhythms, and chronotropic incompetence [2, 3]. This disorder is often associated with conduction system diseases and supraventricular tachyarrhythmias (in this case, SND is termed tachy-brady syndrome) [3]. Most people with SSS are asymptomatic or oligosymptomatic. Well-described symptoms of SND are bradycardia, fainting (syncope), fatigue, weakness, dyspnea, angina, disturbed sleep, confusion, and palpitations.

The most common cause of SND is idiopathic sinoatrial node fibrosis, sometimes accompanied by degeneration of lower elements of the conducting system. Risk factors for development of SND in-



**Figure 2.** Holter monitoring - a few significant sinus pauses were registered in the morning hours (08 h 03 min to 08 h 25 min); the longest episode was 12820 ms, as shown above. This figure shows only the beginning of this longest episode, the whole pause is not shown due to technical circumstances

**Slika 2.** Monitoring holterom – nekoliko značajnih sinusnih pauza u jutarnjim satima (8 h i 3 min. do 8 h i 25 min.); najduža epizoda trajala je 12 820 ms (prikazano gore). Na slici je prikazan samo početak najduže epizode; cela pauza nije prikazana iz tehničkih razloga

clude: age, medications, hyperkalemia, myocardial infarction, heart surgery, sleep apnea, diphtheria, hemochromatosis, muscular dystrophy, amyloidosis (many ischemic, inflammatory and infiltrative disorders). In younger patients, SND is often secondary to other cardiac processes/disease [4] and it may be present in patients who have undergone surgery for congenital heart disease, including ASD. In addition, the later in life ASD is repaired, the more likely arrhythmia will develop. The cause of SND in these patients is probably related to the underlying structural heart disease and surgical trauma (of the sinus node and/or sinus node artery). When repairing ASDs, sinus venosus atrial septal defect (SVASD), SND often occurs because ASD is closely related to the sinus node tissue [4, 5]. Postoperative SND is more common in patients after SVASD repair than after secundum ASD repair [6].

The only effective treatment for patients with chronic symptomatic SND is pacemaker implantation. It is important to mention that asymptomatic patients do not require device therapy. Pacemakers are indicated in patients with certain symptomatic bradyarrhythmias caused by SND and in patients with frequent, prolonged sinus pauses [3]. Symptomatic bradyarrhythmias are the most common indications for pacemaker placement. Approximately one-half of devices are implanted for SND. Our patient was symptomatic, with very significant periods of asystoles (12 820 ms), so she underwent pacemaker implantation (DDDR) as mentioned above.

We believe that a certain number of syncope patients remain misdiagnosed. For example, in our case, a psychiatrist made a diagnosis of anxiety-depressive

disorder with panic attacks and dissociative reactions. On the other hand, it was difficult to establish the real diagnosis because the ambulatory Holter monitoring and serial ECG-s showed no abnormalities, as well as laboratory reports and neurological examinations. It is often difficult to capture the moment when syncope occurs on Holter or ECG. Differentiating true syncope from other similar non-syncopal conditions (e.g. epilepsy, severe metabolic disorders, intoxications, psychogenic pseudo-syncope etc.) is the first diagnostic step with huge influence on the subsequent diagnostic strategy. Among the neutrally mediated investigations, the tilt-test and carotid sinus massage are the most useful. The most useful cardiac examinations here are echocardiography, prolonged ECG monitoring, stress test, electrophysiological study and implantable loop recorder [7]. Patients with unexplained syncope are more likely to have an underlying arrhythmia mechanism than unselected patients with syncope. However, arrhythmias causing syncope may occur at varying and long intervals, giving standard ECG-a and short-lasting ECG monitoring little chance of providing symptoms vs. ECG correlation when compared with continuous long term ECG-monitoring (sometime a few days of ECG monitoring may be valuable). A structured, multidisciplinary approach to evaluation of syncope is the best model to achieve an optimal outcome [8].

### Conclusion

In conclusion, a structured multidisciplinary approach to syncope of unexplained origin is the best model to achieve an optimal outcome.

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## FOREIGN BODY INGESTION – GLASS IN COLON AND RECTUM – A CASE REPORT AND LITERATURE REVIEW

*PROGUTANA STRANA TELA – STAKLO U KOLONU I REKTUMU – PRIKAZ SLUČAJA I PREGLED LITERATURE*

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### Summary

**Introduction.** Ingestion of foreign body is one of the most complex and serious emergency conditions to diagnose. Accidental ingestion is more frequent in children than in adults, whereas intentional ingestion is usually found in cases of mental disorders, prisoners, attempted suicides, and in persons with intellectual disabilities. **Case report.** Glass ingestion is very rare and it is very difficult to predict the consequences of its passing through the gastrointestinal tract. We report a case of accidental swallowing of a large quantity of glass pieces in the ascending colon and rectum diagnosed by abdominal X-ray. The patient did not have any signs of perforation. An expectant attitude was taken, and the elimination occurred naturally.

**Key words:** Foreign Bodies; Deglutition; Accidents; Glass; Diagnosis; Treatment Outcome; Gastrointestinal Tract

### Introduction

Ingestion of a foreign body is not a common emergency condition in small hospitals. Accidental ingestion is more frequent in children. Intentional ingestion is usually found in cases of mental disorders, prisoners, attempted suicides, and in persons with intellectual disabilities. The most frequently ingested foreign bodies are pieces of food, most often bones, toothpicks, but real foreign bodies are orthodontic implants, needles, nails etc. [1].

Glass foreign bodies are among the most unusual ingested foreign bodies, and it is difficult to predict the consequences of their passing through the gastrointestinal tract (GIT). We report a case of accidental swallowing of a large quantity of glass pieces, diagnosed by X-ray in the ascending colon and the rectum. The patient did not have signs of perforation, so an expectant attitude was taken, and elimination occurred naturally.

### Case report

A 36-year-old woman with intellectual disabilities was admitted to the Clinic due to abdominal pain. Her anamnesis showed that she had allegedly had stom-

### Sažetak

**Uvod.** Progutano strano telo predstavlja veoma kompleksno i hitno stanje, teško za postavljanje dijagnoze. Slučajno gutanje je češće kod dece nego kod odraslih, a namerno gutanje nalazi se obično kod osoba sa psihološkim poremećajima, kod zatvorenika, osoba koje pokušaju suicid, te kod osoba sa poremećajima u mentalnom razvoju. Staklo je vrlo retko strano telo koje se guta i kod kojeg je teško predvideti posledice prolaska kroz gastrointestinalni trakt. **Prikaz slučaja.** Mi izveštavamo o nenamernom gutanju veće količine komada stakla koji su radiološki dijagnostikovani u ushodnom kolonu i rektumu. Pacijent nije imao znakove perforacije. Zauzet je ekspektativan stav, te je prirodnim putem došlo do eliminacije.

**Ključne reči:** strana tela; gutanje; nesreće; staklo; dijagnoza; ishod lečenja; gastrointestinalni trakt

ach pains for a month. Physical findings showed painful sensitivity in the upper right quadrant, with no signs of peritonitis. The abdominal X-ray showed a great number of intensive shadows in the area of the ascending colon and the rectum (**Figure 1**). Digital rectal examination produced a lump of stool with pieces of glass.

Upon admission, a computed tomography (CT) of the abdomen was performed (**Figure 2**). In the area of the ascending colon and the rectum there were numerous hyperdense areas of various shapes and sizes, mostly with sharp contours, and the character of a foreign body, with a density of 500 to 1500 HJ, 5 to 20 mm in diameter. The colonic loop was distended, especially in the area of the transverse colon, with a lumen up to 5 cm in width.

Due to the persistent pain, surgical exploration was considered, but in the absence of signs of perforation, an expectant attitude was taken, and laxatives were prescribed. The patient presented with a gradual regression of pain, and a control X-ray confirmed that the foreign bodies shifted through the intestines (**Figure 3 and 4**) but they were filled with air, at multiple air fluid levels.

A rectoscopy was performed to establish the condition of the mucous membranes of the rectum, showing

**Abbreviations**

CT – computed tomography  
GIT – gastrointestinal tract



**Figure 1.** Abdominal X-ray showing a great number of intensive shadows in the area of the ascending colon and the rectum

*Slika 1. Rendgenogram abdomena pokazuje veći broj intenzivnih senki u području ascendentnog kolona i rektuma*



**Figure 2.** Abdominal CT in the area of the ascending colon and the rectum showing numerous hyperdense areas

*Slika 2. Kompjuterizovana tomografija abdomena, u području ascendentnog kolona i rektuma veći broj hiperdenznih area*

intact mucous membranes, with several balls of stool. In each ball there was a piece of glass (**Figure 5 a and b**).

On the fifth day of hospitalization, X-ray of the native abdomen indicated the absence of glass (**Figure 6**), but showed several air fluid levels.

On the twelfth day of stay, the patient was discharged in a satisfactory general condition.

**Discussion**

Most intentionally or accidentally ingested foreign bodies pass through the GIT without complications, and only a minority require surgical intervention [2–4]. The occurrence of abdominal pain alerts the physician of possible complications, primarily perforation with the resulting peritonitis. Fatal cases after ingestion have also been described, due to intestinal obstruction [5].

The intestines have a significant ability to protect themselves from perforation in cases of ingestion of sharp objects, such as glass. When a sharp object is stuck in the intestinal mucous, an area of ischemia with a large central concavity develops. The walls of the intestines increase the lumen at the place of contact, enabling easier passage of the sharp object [6]. Moreover, when a sharp object is swallowed, the flow of the intestinal content and the relaxation of the intestinal walls tend to direct the head of the object to the front, and the sharp end to the back [7]. When it arrives in the colon, the foreign body is covered with faecal material, protecting the intestinal wall.



**Figures 3 and 4.** The X-ray confirmed that the foreign bodies shifted through the intestines, but they were filled with air at several air fluid levels

*Slike 3 i 4. Rendgenogram abdomena pokazuje pomeranje stranih tela kroz creva, ali crevima ispunjenim vazduhom i sa nekoliko aerolikvidnih nivoa*





**Figure 5 a and b.** One of the balls of stool containing a piece of glass

**Slika 5 a i b.** Jedna od "kuglica" stolice u kojoj se nalazi komadić stakla

Isolated groups of glass in the rectum (**Figures 1 and 2**) cause concern, because it is forgotten that this collection has already passed through the digestive tract, wrapped in stool, which protects the intestinal wall. In this case, the inability of the patient with intellectual disabilities to describe in detail how the ingestion occurred, that is, how the glass entered the GIT, led to difficulties in diagnosis and therapy.

The aim of clinical evaluation was to identify the type, quantity, size and location of the foreign bodies in the rectum. As a rule, removal of a foreign body from the rectum requires experience, with particular care when using various means of extraction, to minimize damage to the mucous membrane. Most foreign bodies can be successfully removed trans-anally, under appropriate anesthesia and using appropriate instruments. Alternative methods are the use of a Foley catheter [8], trans-anal vacuum extraction of glass foreign bodies [9], and trans-anal minimally invasive surgery [10].

Only a small number of foreign body cases, if they go deeper into the sigmoid colon, require extraction by



**Figure 6.** X-ray of the native abdomen indicated the absence of glass

**Slika 6.** Rendgenogram nativnog abdomena ukazuje na odsustvo stakla, ali sa nekoliko aerolikvidnih nivoa

colonoscopy [11]. Rare cases with signs of perforation, peritonitis, or pelvic sepsis, Fournier gangrene [12], or unsuccessful manual extraction, require open surgery or laparoscopy, by massaging (milking) towards the anus or a colostomy. After removal of the rectal foreign body, a proctosigmoidoscopy is mandatory, to exclude injury to the mucous membrane [13].

## Conclusion

In the case presented, it was clearly a matter of glass that had passed through the gastrointestinal tract. The attitude of waiting and monitoring the clinical condition of the patient seemed most appropriate; otherwise unnecessary resection of the large intestine would have been performed. This approach requires a great deal of patience, constant monitoring, and a prompt reaction in the case of intestinal perforation.

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## RHABDOMYOLYSIS AND INFLUENZA A (H3N2) INFECTION – A CASE REPORT

### *RABDOMIOLIZA I INFLUENZA A (H3N2) INFEKCIJA – PRIKAZ SLUČAJA*

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Siniša SEVIĆ and Maja RUŽIĆ

#### Summary

**Introduction.** Extrapulmonary complications of influenza infections are often unrecognized. The aim of this paper is to point to rhabdomyolysis as a potentially life threatening complication of influenza. **Case Report.** A month after the onset of influenza complicated by bronchopneumonia, the general condition of a nineteen year old female deteriorated with development of progressive muscle weakness and dark-colored urine. Despite intensive hydration and antibiotic therapy, her condition got worse, laboratory findings showed pancytopenia, hypoalbuminemia and creatine phosphokinase about 1000 times higher than normal. Influenza A H3N2 was confirmed by polymerase chain reaction analysis of the throat swab sample. Electromyoneurography showed severe acute polyneuropathy of muscles innervated by perineal nerve and signs of polymyositis; pathohistological examination of gastrocnemius muscle biopsy sample confirmed chronic myositis with necrotic neurogenic atrophy. In spite of intense hydration, the patient's status continued deteriorating, so methylprednisolone was administered. Six weeks later, the patient was discharged in a good general condition, with blood test results within reference ranges, with weakness of foot dorsiflexors and tilting of the pelvis to the left during verticalization. **Conclusion.** Rhabdomyolysis caused by influenza-A is on the increase, and given the degree of morbidity and mortality, thorough assessment of patients is necessary.

**Key words:** Rhabdomyolysis; Influenza A Virus, H3N2 Subtype; Polyneuropathies; Risk Factors; Signs and Symptoms; Disease Progression; Treatment Outcome

#### Introduction

Influenza causes respiratory tract diseases with acute respiratory distress syndrome (ARDS) as the leading and most severe life threatening complication. In terms of early diagnosis, extrapulmonary complications are less common, but clinically a significant problem [1]. In the territory of Vojvodina, influenza occurs in epidemic forms, usually in the winter months. The most common cause is the virus Influenza A. In the season 2014/2015, the dominant type was A/H3N2. Pulmonary complications were the most common complications, and also the most common cause of death [2, 3]. However, we are witnessing the appearance of

#### Sažetak

**Uvod.** Ekstrapulmonalne komplikacije influenza virusne infekcije su često neprepoznate. Cilj ovog rada je da se ukaže na rhabdmiolizu kao potencijalnu vitalno ugrožavajuću komplikaciju gripa. **Prikaz slučaja.** Mesec dana nakon početka gripa komplikovane bronhopneumonijom, kod devetnaestogodišnje devojke došlo je do pogoršanja opšteg stanja razvojem progresivne mišićne slabosti, uz pojavu tamne prebojenosti urina. Na sprovedenu intenzivnu rehidraciju i antibiotsku terapiju, opšte stanje se i dalje pogoršava, a u laboratorijskim nalazima se zapaža pancitopenija, hypoalbuminemija i oko 1 000 puta povišena aktivnost kreatin fosfokinaze. Analizom polimerazne lančane reakcije uzorka brisa grla dokazana je *Influenza A H3N2*. Elektromioneurografijom se verifikuje akutna teška polineuropatija muskulature koju inerviše *n. peroneus* i znaci polimiozitisa, a patohistološki pregled biopata levog *m. gastrocnemius* potvrđuje *myositis chronica cum atrophia neurogenes cum necrosis*. Kako i pored obilne hidratacije nije došlo do očekivanog poboljšanja stanja bolesnice, ordiniran je metilprednizolon. Nakon šest nedelja lečenja, pacijentkinja je otpuštena dobrog opšteg stanja, urednih laboratorijskih nalaza, sa slabosću dorzifleksora stopala i naginjanjem karlice na levu stranu tokom vertikalizacije. **Zaključak.** Rhabdmioliza uzrokovani influencom-A se sve češće beleži u praksi, a s obzirom na stepen morbiditeta i mortaliteta iziskuje pažljiv pristup proceni stanja pacijenta.

**Ključne reči:** rhabdmioliza; influenza A virus, podtip H3N2; polineuropatije; faktori rizika; znaci i simptomi; progresija bolesti; ishod lečenja

other rare and often unrecognized, life threatening complications.

Rhabdomyolysis (RM) is the destruction of skeletal muscle followed by the release of intracellular myofibrils into the bloodstream and extracellular fluid. Clinical manifestations vary, from asymptomatic to life threatening conditions, such as acute renal failure and disseminated intravascular coagulation [4]. Although myositis is the most common symptom of the flu syndrome, the development of RM is rare, and it is more likely to occur in individuals with a genetic predisposition.

The aim of this paper is to highlight RM as a potentially life threatening complication of influenza.

### Abbreviations

ARDS	– acute respiratory distress syndrome
RM	– rhabdomyolysis
CRP	– C-reactive protein
AST	– aspartate aminotransferase
LDH	– lactate dehydrogenase
ALT	– alanine transaminase
PCR	– polymerase chain reaction
CPK	– creatine phosphokinase
NaHCO <sub>3</sub>	– sodium bicarbonate

### Case Report

At the beginning of January 2015, a seventeen year old girl presented with Influenza syndrome (dry cough, elevated body temperature up to 38°C). She was under regular medical supervision due to asthma therapy in the past two years (budesonide and formoterol as needed). Five days after the onset, bronchopneumonia was detected by auscultation, and cefpodoxime (200 mg per 12 hours) was initiated. The respiratory symptoms have resolved, but at the same time muscle weakness with intense pain and inability to move started. The patient presented with dark discoloration of the urine, and was admitted to a regional hospital in the second week of February with the diagnosis of suspected infectious myositis.

On admission, the patient was afebrile, hypotensive, tachycardic, cyanotic with generalized skeletal muscle pain, and with paresis of all extremities and hyporeflexia. The laboratory findings showed the following: C-reactive protein (CRP) 21.7 (below 5 mg/l), aspartate aminotransferase (AST) 572 (below 37 U/l), alanine transaminase (ALT) 130 (below 40 U/l), lactate dehydrogenase (LDH) 1684 (460 U/L and creatine phosphokinase (CPK) 19344 (below 171 U/l), and after basic diagnostic procedures were performed, intravenous hydration and antibiotic therapy (ceftriaxone, amikacin) were initiated. Despite the administered therapy, the laboratory findings got worse: an increase of leukocytes, anemia, thrombocytopenia, hypoalbuminemia, CPK 176 421 (below 168 U/l), AST 3080 (below 37 U/l), ALT 467 (below 40 U/l), LDH 3209 (below 460 U/l) and after 24 hours the patient was transferred to the Clinic of Infectious Diseases for suspected sepsis and infectious myositis.

Intensive intravenous hydration with mannitol and correction of metabolic acidosis were performed. Immunological tests (anti nuclear antibodies - ANA, anti neurotrophic cytoplasmatic antibody virus - ANCA, anti-double-stranded deoxyribonucleid acid At) were negative. Assessments were done for Adeno, Coxsackie A and B, Influenza A and B, Parainfluenza, Varicella Zoster, Herpes Simplex, Respiratory Syncytial Virus, Epstein Barr Virus, Parvo B19, Cytomegalovirus infections, Mycoplasma pneumonia, Hepatitis B Virus surface antigen (HBsAg), anti Hepatitis C Virus antibody (AntiHCV), which proved negative. However, polymerase chain reaction (PCR) microbiological analysis of the throat swab was Influenza A H3N2 positive. As there was no satisfactory response, corticosteroids (methylprednisolone 120 mg) was initiated, that resulted in moderate clinical and laboratory improvements.

During further treatment at the Clinic of Infectious Diseases the patient was gradually recovering. Electromyoneurography (EMNG) indicated a severe acute polyneuropathy of muscles innervated by perineal nerve and signs of polymyositis. Histopathological examination of the left gastrocnemius confirmed chronic myositis with necrotic neurogenic atrophy. After six weeks of treatment, the patient was discharged recovered, with blood results within reference ranges, with weakness of foot dorsiflexor, tilting of the pelvis to the left during verticalization. Eighteen months later, there were mild sequelae - occasional pain in the muscles of the lower extremities and difficulty doing squats.

### Discussion

Myositis is a well-known manifestation of numerous infectious diseases, viral infections being the most common (Influenza A and B, Coxsackie Virus, Epstein Barr Virus, Herpes Simplex Virus, Parainfluenza, Adenovirus, Echovirus, Human Immunodeficiency Virus (HIV) and Cytomegalovirus (CMV). In general, myositis is not the main symptom and rarely progresses to life threatening RM.

Presented Influenza A virus infection was confirmed by detection with PCR isolation from the pharynx swab and serology test - detection of IgM Influenza A antibodies by the ELISA method. Prolonged duration of viral shedding, unusual for Influenza A virus, can be explained by the application of corticosteroid therapy in the treatment of asthma [5, 6].

Although there are indications of direct viral myotoxic effect (EBV), RM is most often the result of T-cell hyperactivity [7, 8].

A number of exogenous and endogenous factors may accelerate destructive immune response to the muscle tissue [4]. The most common concomitant factors, which may contribute to the development of RM in viral infections, are alcohol abuse and use of certain drugs, which was excluded by toxicological analyses. Cytochrome P450 inhibitors (statins, acetaminophen) are described as the most provoking factors of RM; although the pathogenesis is still not proven, it is believed that they reduce production of adenosine triphosphate (ATP) within the muscle cells which destabilizes the membrane [8]. However, our patient denied taking drugs from this group. Genetic predisposition for the development of RM should also be taken into consideration.

According to recent studies, people with virus induced RM are often carriers of mutations of RYR1 gene that creates defective ryanodine receptor 1 on myocytes, thus creating susceptibility to malignant hyperthermia, which leads to RM. We could not perform genetic analysis, but we considered genetic predisposition unlikely to be the cause of RM due to the long latent period (one month), and absence of high body temperatures (up to 38°C). A number of metabolic, genetically determined RM can also occur, but they are usually recurrent and occur after intense physical activity, regardless of the infection. The patient regularly practiced folklore and never complained of myalgia, nor reported darker urine color.

Progression of symptoms in terms of difficulty of movement, inability of verticalization and dark urine, immediately pointed to RM, especially when blood results showed five times elevated CPK levels and acidosis, with pathological urine [9]. Myoglobinuria is the last of three classical RM symptoms (nausea, myalgia, dark urine) that appeared. It is present in less than 10% of patients with RM, and most patients do not have weakness or myalgia, but do have systemic manifestations such as tachycardia, fever, nausea and vomiting [3]. Myoglobinuria does not occur without RM, but RM is not a mandatory result in myoglobinuria. It occurs when the threshold of renal filtration from 0.5 to 1.5 mg/dl is exceeded, and it is macroscopically visible only when the quantities reach 100 mg/dl [10]. Myoglobin in the urine of our patients was not determined, since this analysis is not included in the standard diagnostic procedure.

The main complications of RM are acute kidney failure, electrolyte imbalance, especially hyperkalemia which leads to arrhythmia, hypophosphatemia and hypocalcaemia. In order to prevent this, quick and adequate therapy is needed. Intense i.v. hydration with saline 300 – 500 ml/h should be given. Since our patient was hemodynamically stable, these quantities of fluid were not exceeded. Although there is no protocol in the literature to define duration of intense hydration, it is considered that it should be applied until the level of serum CPK decreases to 1000 U/l or less [4]. Alkalinization of urine with sodium bicarbonate ( $\text{NaHCO}_3$ ) is beneficial in three ways: it reduces precipitation of Tamm-Horsfall protein-myoglobin complex, it inhibits oxidation-reductive process of myoglobin and lipid peroxidase reducing the damage to the tubules, and it reduces vasoconstriction caused by metmyoglobin in acidic environment [11, 12]. It is recommended to apply infusion of one ampoule of  $\text{NaHCO}_3$  (20 ml, 1 ml contains 84  $\text{NaHCO}_3$ ) in one saline bottle or 2 – 3 ampoules

in one 5% glucose bottle at 100 ml/h rate, in order to maintain urine pH above 6.5 preventing acute kidney failure. Hemodialysis is considered in cases with excessive hyperkalemia and metabolic acidosis [13, 14]. Given the small amount of data on the efficacy of corticosteroids in the treatment of RM, and bearing in mind they are used in recurrent RM with chronic myositis of autoimmune etiology, they were not administered during hospitalization in our clinic [15].

Delayed development of RM (one month after the first symptoms) and good therapeutic response to corticosteroids, despite negative immunological test results, may point to autoimmune diseases in the background (dermatomyositis, polymyositis). Biopsy of m. gastrocnemius has been done according to the recommendations - 8 weeks after the first symptoms and four weeks after completion of corticosteroid therapy. The result was chronic myositis with necrotic neurogenic atrophy, reactive inflammation with no signs of immune or dystrophy myositis. Considering good recovery and minimal sequelae, with no signs of recurrence, we concluded that RM was caused by Influenza A virus (H3N2).

## Conclusion

Complications of Influenza A are a global problem, so it is of crucial importance to take into consideration the range of clinical manifestations, beyond the typical symptoms of respiratory infections. Reports on rhabdomyolysis caused by influenza-A are increasing and given the degree of morbidity and mortality, assessment of patients suspected for the development of rhabdomyolysis should be done carefully, especially those with general weakness and muscle pain.

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## SEMINAR FOR PHISICIANS *SEMINAR ZA LEKARE U PRAKSI*

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### DIETARY REGIMENS FOR PERSONS WITH TYPE 2 DIABETES: RECOMMENDATIONS, ISSUES AND POTENTIAL SOLUTIONS

*ISHRANA OSOBA SA DIJABETESOM TIP 2: PREPORUKE, PROBLEMI I MOGUĆA REŠENJA*

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#### Summary

**Introduction.** Type 2 diabetes mellitus is a global public health problem. Altered dietary habits and modern lifestyle lead to obesity and insulin resistance, the main factors in the pathogenesis of this disease. **Dietary Regimens for Patients with Type 2 Diabetes.** There is no consensus on the most appropriate dietary therapy for glycemic control and long-term weight loss. Individualized approach, based on metabolic needs and goals of each patient, is recommended. Because of the relationship between the body mass and insulin resistance, permanent weight loss is the strategy recommended to obese patients with diabetes. Permanent weight loss is achieved by reducing caloric intake and increased physical activity. **Issues.** Although careful nutrition is an essential control element of this disease, most patients with type 2 diabetes mellitus consider dietary recommendations too restrictive and reject them, leading to poor glycemic control in over 60% of patients. The feeling of frustration and hopelessness, fear that they will be deprived of their favourite foods, fear that treatment of diabetes will negatively affect their social life, lead to escapism into forbidden foods. **Potential solutions.** Understanding, knowledge, attitudes and beliefs of patients about the importance of dietary regimens in the treatment of type 2 diabetes mellitus are crucial in the new approach of education and public health policies that will support wider acceptance of dietary habits and lead to a better control of the disease. Providing more quality time between doctors and patients for better communication is part of this comprehensive approach, which is the only way to stop the global epidemic of type 2 diabetes. **Key words:** Diabetes Mellitus, Type 2; Diet, Diabetic; Weight Loss; Life Style; Nutrition Therapy; Health Knowledge, Attitudes, Practice; Motivation; Energy Intake; Recommended Dietary Allowances

#### Introduction

##### *Public health aspects*

Type 2 diabetes mellitus (T2DM) is a global public health problem, and the number of patients in the

#### Sažetak

**Uvod.** Dijabetes melitus tipa 2 je globalna epidemija savremenog sveta i veliki javnozdravstveni problem. Izmenjene dijetetske navike i stil života savremenog čoveka doveli su do ogromnog porasta gojaznosti u populaciji koja dovodi do insulinorezistencije, dominantnog faktora u patogenezi ove bolesti. **Ishrana osoba sa dijabetesom tipa 2.** Ne postoji konsenzus o dijetetskom tretmanu koji najviše odgovara kontroli glikemije i dugoročnom gubitku težine. Preporučuje se individualizovani pristup koji odgovara metaboličkim ciljevima svakog pojedinca. Zbog odnosa telesne mase i insulinorezistencije, trajni gubitak težine jeste strategija koja se preporučuje gojaznim osobama sa dijabetesom kroz smanjen ukupni kalorijski unos i povećanu fizičku aktivnost. **Problemi.** Iako je pažljiva dijetetska praksa esencijalni element kontrole ove bolesti, većina pacijenata smatra dijetetske preporuke preterano restriktivnim i odbija da ih se pridržava, dovodeći do loše kontrole bolesti u preko 60% slučajeva. Osećaj frustracije i beznada; strah da će im omiljena hrana biti oduzeta; da će biti hendikepirani neučestvovanjem u društvenom životu i da su promene potrebne za uspešan tretman dijabetesa nedostižne vode čestim „bekstvima u zabranjenu hranu“. **Moguća rešenja.** Upućenost pacijenta, njegova znanja, shvatanja i verovanja o ulozi ishrane u tretmanu ove bolesti od ključnog su značaja u novom pristupu edukaciji i javnozdravstvenim politikama koje bi išle u prilog prihvatanju dijetetskih navika i postizanju bolje kontrole bolesti. Dovoljno kvalitetnog vremena koje lekar može da posveti svakom pacijentu deo je ovog sveobuhvatnog pristupa kojim se jedino može zaustaviti globalna epidemija dijabetesa tipa 2.

**Ključne reči:** dijabetes melitus, tip 2; dijabetesna dijeta; smanjenje težine; stil života; nutritivna terapija; znanje o zdravlju stavovi, praksa; motivacija; energetski unos; dijetetske preporuke

world is reaching epidemic proportions [1]. The World Health Organization (WHO) estimated that, globally, 422 million adults aged over 18 years were living with diabetes in 2014, out of which over 95% with T2DM [2]. The number of patients worldwide is constantly

### Abbreviations

T2DM	– type 2 diabetes mellitus
WHO	– World Health Organization
ADA	– American Diabetes Association
HbA1c	– glycosylated hemoglobin

rising, and 80% live in low- and middle-income countries [3], Serbia being among them. According to data from 2012, 1.5 million deaths were caused directly by diabetes, and 2.2 million were the result of cardiovascular and renal complications caused by diabetes; thus, diabetes is on the high eighth place among the leading causes of death in both sexes, and 43% of all deaths caused by elevated values of serum glucose that occur in the age group of 20 – 69 years [2]. It has been estimated that the direct annual cost of diabetes to the world is more than 827 billion dollars [4]. According to data from the Institute of Public Health of Serbia, in 2014 there were 710.000 registered persons with diabetes or 12.4% of the adult population, which corresponds to the prevalence rate of 9.9% [5] and represents the highest rate in the region [6].

### Pathogenesis of T2DM and lifestyle changes

Type 2 diabetes mellitus represents a potential end of a long and extremely complicated path that starts with insulin resistance, caused by chemical substances from adipose tissue, reducing the sensitivity of liver cells and skeletal muscles to insulin effects [7]. Most patients with T2DM are overweight, obese or have predominantly abdominal distribution of visceral fat, and the body composition in T2DM patients is the main cause of insulin resistance [8]. Due to insulin resistance, the level of glycemia is kept within normal ranges, but at the cost of overloading the pancreas and secretion of large quantities of insulin [7]. This temporary equilibrium is called prediabetes, and the American Diabetes Association (ADA) defines it as fasting glucose of 5.6 – 6.9 mmol/l and values of glycosylated hemoglobin (HbA1c) of 5.7 – 6.4% [8, 9]. Prediabetes is a potentially reversible condition. The reduction in body weight will unload the pancreas of excessive insulin secretion and thus the development of T2DM will be avoided. Otherwise, over time, pancreas loses the ability to maintain fasting glycemia within normal limits causing excessive secretion of insulin that leads to diabetes [7].

Global epidemic of T2DM can be attributed to changes in dietary habits, lifestyle changes, and aging population [7, 10]. The traditional dietary patterns have disappeared, while foods with high energy density, large portions with highly refined carbohydrates, unhealthy fats and sugary drinks are becoming the dominant model [10, 11]. These eating habits lead to obesity, that is the driving force of this global disease [11]. According to statistics from 2014, an astonishing 43% of population older than 18 years is overweight or obese. Changing patterns of everyday life and reduced energy consumption contribute to the patho-

genesis of obesity [10, 11]. The “thrifty gene” hypothesis is an excellent interpretation of the impact of lifestyle transition on the T2DM epidemics. “Thrifty genes” are genes, which enable individuals to efficiently collect and process food to deposit fat during periods of food abundance in order to provide for periods of food shortage. The same genes, in conditions of food abundance, make the population vulnerable and prone to diabetes. The adaptive genetic response has become maladaptive, contributing to obesity that is a base for insulin resistance and development of T2DM [7]. On the other side, if a person manages eating habits and physical activity properly, in spite of genetic risk, it is unlikely that the disease will develop [2, 7].

### Dietary regimens for persons with T2DM

#### *Diet and management of diabetes*

For many people with diabetes, the most challenging aspect of the treatment is determining what to eat [12]. Although careful dietary regimen is one of the essential elements of controlling diabetes, WHO data indicate that approximately 80% of patients with T2DM refuse or avoid dietary recommendations [13]. Researches indicate that eating habits contribute with 51% to overall variations of HbA1c in the population of diabetic patients [14], whereas non-adherence of patients with T2DM to dietary recommendations remains high and ranges from 48% to 74% [15]. Negative attitudes of patients with T2DM towards dietary recommendations inevitably lead to poor management of the disease. The results of the international prospective study conducted in 28 countries show that almost 60% of patients with T2DM have poor management of the disease [16], that is HbA1c  $\geq 7\%$ , which is the recommended limit for avoiding micro-vascular complications of this type of diabetes [17]. In the neighbouring Croatia, only 21.6% of people with T2DM have good control of glycemia, while 87% of patients are obese or overweight [18].

#### *Dietary recommendations for persons with T2DM*

Although medical nutrition therapy and lifestyle modifications are considered cornerstones in the treatment of T2DM, there is still no consensus on the most appropriate dietary treatment for glycemic control and long-term weight loss [19]. The primary goals of dietary intervention in T2DM is adoption of eating habits to achieve long-term energy balance, optimize body weight, reduce cardiovascular risk factors and prevent complications [1, 12]. Therefore, 2017 recommendations of ADA emphasize individualized approach based on metabolic needs and goals of each patient [12]. However, individualized approach means there are also some general principles to follow.

The key dietary approach in the management of T2DM is limited intake of calories in general, not of specific foods [1]. Since almost three out of four

persons with T2DM are overweight, and over 50% are obese, and due to the relationship between the body mass and insulin resistance, the ADA recommends a weight loss strategy to obese patients with diabetes [12]. Reduced intake of calories and increased physical activities decrease blood sugar even before the body weight loss, thus relieving the pancreas and reducing insulin resistance [7]. Significant weight loss is associated to T2DM remission. The risk of developing T2DM after a significant loss of body weight remains reduced even if lost weight is partially regained under the influence of psychosocial factors and physiological changes (compensatory hormonal changes that influence weight gain) [20]. Current nutrition recommendations do not support any particular dietary approach for reducing excess weight, but different dietary patterns with overall quality diet, resulting in reduced energy intake [10, 12].

The total amount of carbohydrates is a key strategy in achieving glycemic control in T2DM [1]. Although carbohydrates with lower glycemic index further improve glycemic control [1, 19], the choice of carbohydrates should be seen primarily in terms of direct impact on energy balance and body weight [12]. Consequently, sucrose and other sugars should not be strictly avoided, but seen from the perspective of overall energy balance and replaced with other carbohydrate sources [1]. Although fibers of plant origin slow down the absorption of carbohydrates, consumption of whole grains is not associated with improved glycemic control in T2DM patients, and in its latest guidelines ADA does not recommend increased fiber intake i. e. more than in general population [12]. Fructose ("free fructose"), potentially is not harmful, unless exceeds 10% of the total caloric intake due to the relatively slow digestion and absorption [10]. The intake of "sweets for diabetics" must also be limited, because they almost always contain a large amount of fructose which turns into lipids in the liver, leading to dyslipidemia, visceral obesity and insulin resistance [11]. Low calorie sweeteners reduce the total caloric intake, do not have glycemic effect whatsoever, but there is not enough evidence of their effects on the reduction of body weight and metabolic risk factors [10, 12].

Data on the ideal amount of fat in the diet of persons with diabetes are still controversial. Type of fat that is consumed, from the viewpoint of the objectives of the metabolic control and cardiovascular risk, is much more important than the total amount of fat. A large number of randomized controlled studies of patients with T2DM suggest that a diet rich in monounsaturated fats can improve the glycemic control and lipids in serum [12]. In the cohort study of women with diabetes, higher intake of fish and omega-3 fatty acids with a long chain was associated with a lower incidence rate of coronary artery disease [21]. A large study including 12.536 people with diabetes or at potential risk of diabetes has shown that omega-3 polyunsaturated

fatty acids used as a supplement did not lead to a reduction of mortality and rate of cardiovascular accidents [22]. Therefore, the ADA does not recommend omega-3 polyunsaturated fatty acids as a supplement neither in patients with diabetes, nor in general population; the ADA recommends their higher intake through foods [10, 12].

### **Dietary barriers perceived by patients with T2DM**

Studies show that patients with T2DM prefer pharmacological treatment rather than strict dietary modifications that lead to weight loss [19, 23]. Reasons for this are complex and include:

#### *Lack of knowledge and understanding*

Patients feel they cannot keep in mind all the information they receive and feel adrift [19]. Embracing the information may be reduced, especially at the time of diagnosis [24]. Repeating the information given during the first visit may be necessary, so patients would not make wrong choices of food [19]. Some of the most common problems that patients are facing include [1, 19]:

- lack of understand the concept of carbohydrates (carbohydrates are just sugar and starchy foods, but biscuits, snacks and corn rolls are free to consume; brown bread (not necessarily whole grain) is better for glycemic control and its intake is allowed in larger quantities;
- issue of portion size (especially the quantity of bread);
- should fruits be consumed, which ones and how many per day;
- should patients be more concerned about sugars than fats (diet should have low level of carbohydrates, while the quantity and ingredients of fats are irrelevant).

All aforementioned indicates that effective and useful dietary guidelines are necessary for patients with T2DM, with developed cultural directions and involvement of patients [25]. The health professionals recommend the term "blood sugar" to be replaced by the term "blood glucose" in order to avoid visualization of sugar in food that is directly transferred into the bloodstream, which contributes to poor conceptual understanding of carbohydrates [1].

#### *Negative perception towards the new dietary regimens*

The feeling that some foods are limited, but tempting sometimes, in patients with T2DM cause negative emotions like frustration and hopelessness. There is a fear that they will be deprived of their favourite foods [14], and that successful treatment of diabetes requires unattainable lifestyle changes (7). The sense of deprivation, often accompanied by a sense of loss of control (21) leads to an increased tendency towards uncontrolled consumption of "forbidden foods", emotional overeating, and self decep-



tion, later followed by increased stress [1]. Therefore, a new dietary regimen should be presented as an opportunity to improve health, without associating it with deprivation and dietary restraint [1, 25].

#### *Obstacles associated with motivation factors*

Results of dietary changes are not immediately visible; therefore, compliance with new dietary regimens can be difficult. Motivation is influenced by the objectives and priorities: evaluation of good glycemic control versus freedom from everyday burdens of T2DM is a question of personal choice [24]. Although knowledge of the risk that the disease brings can act as a motivating factor, individuals perceive these risks differently (believing that they personally will not be affected) [24]. Lack of short-term consequences, that is characteristic of T2DM, acts as a demotivating factor. Individuals have no symptoms, so they are not motivated to change [19]. Losing the illusions, due to the lack of change and the abandonment of the dietary regimen is evident especially in patients who see blood glucose control as the primary therapeutic target. A high level of blood glucose, despite dietary changes is the reason for giving up [1, 19]. Some patients do not consider T2DM a serious disease, so they do not see the need to change their diet, believing that taking prescription medications is sufficient and that “they do not have to starve themselves” [7, 19]. Responsibility towards family is considered a motivational factor [25].

#### *Psychosocial obstacles*

Food plays an important role in maintaining social relations and there is a considerable pressure to eat with too many temptations and often with inadequate offer for patients with T2DM which is a major challenge for adherence to certain dietary requirements [19]. In these situations, family members and friends have different, positive and/or negative, impact on behavior related to the dietary regimen [1, 19]. Although family support is generally considered a significant factor that influences changes in lifestyle, only 13% of diabetic patients stated that their family has made any change beneficial for them [24]. Very often the needs of people with T2DM are secondary in relation to the preferences of other family members, so their food choices at home can be challenging [19, 25]. On the other hand, overprotective families show that they have little confidence in the abilities [24] of patient and increase their sense of stigma [26].

A significant problem exists among the elderly population, who make half of the patients with T2DM. Memory loss and cognitive problems reduce the compliance to dietary advices [3]. Older people with long-established dietary habits frequently discard dietary recommendations with limited food choices. Food can be one of the greatest pleasures of their daily routine [27]. With the increasing duration of disease, adherence towards dietary recommendations declines which can be explained by the

fact that these patients simply grow tired complying to dietary regimens [3].

#### **Solution must be comprehensive**

Diet significantly contributes to the control of glycemia and body weight in diabetic patients. A reduced intake of carbohydrates, especially simple sugars, as well as replacing saturated fat with unsaturated, represents great advantage in improving these parameters, thus reducing the risk of cardiovascular complications and mortality.

Subjective knowledge, attitudes and beliefs which patients adhere, in regard to importance of dietary regimen in treatment of T2DM, are influenced by many factors, including dietary advice patients receive from health professionals, other patients, literature and media. Unfortunately, modus operandi in everyday life is often different. The study conducted in 2011, by the American Academy of Nutrition and Dietetics, reveals that the most popular sources of information on nutrition are television, newspapers and the internet; however, information obtained from the dieticians, doctors and nurses are considered more credible [28].

#### *Necessities for organizational changes in the healthcare system*

Moving away from fragmented healthcare and using an integrated management of diabetes in primary health care, assures health promotion, prevention and treatment of this disease [2]. Population-based screening for T2DM in Serbia, as an important strategic decision, was not accompanied by analysis of existing resources able to carry the increased workload caused by screening itself or new cases. Thus, due to the workload of doctors and short time they really spend “face to face” with their patients, the messages about healthy eating and physical activity are often left unsaid. Recommendations of health professionals are highly valued, considered credible, and even the smallest advices that patients receive are of great importance [28].

#### *A new approach to patient education*

It has been proven that patients appreciate more the visual experience of food model and portion sizes, which are much easier to adopt, opposed to approaches that include discussions about healthy food [1]. Training in groups also turned out to be a cost-effective strategy [2]. Successful education, beside changes related to knowledge, needs to introduce a change in beliefs, understanding and way of thinking about diabetes [1]. In order to achieve that, it is necessary to introduce research about the experiences, problems and obstacles that people with T2DM encounter while managing the disease. Many attitudes about dietary regimens are geographically, culturally, religiously, traditionally, and otherwise specific. Most of the attitudes, knowledge and recommendations that we use originate from research done

within Western countries and are specific for that given area. Unfortunately, researches on knowledge, attitudes and problems that patients suffering from T2DM in Serbia encounter, almost do not exist. Dietary choices must be individual, but patients must be familiar with all moderators, specific to this given area, which affect these choices.

### *Changes in public health policy*

Public health policy should create a healthy food environment, through favoring the production and distribution of healthy foods, promoting socially responsible business as well as additional taxation of highly refined food products.

### **Conclusion**

Type 2 diabetes mellitus represents a global epidemic of the modern world that can be attrib-

uted to altered dietary habits and lifestyle of the modern man leading to obesity as the main cause of this disease. It is known that a careful diet practice represents an essential control element of this disease. Despite the knowledge, most patients with type 2 diabetes mellitus continue to be non-adherent towards dietary recommendations, which leads to poor control of the disease in over 60% of patients. Understanding, knowledge, attitudes and beliefs of patients about the importance of dietary regimen in the treatment of type 2 diabetes mellitus are crucial in the new approach of education and public health policies that should support wider acceptance of dietary habits and lead to a better control of the disease. Providing doctors enough quality time with their patients is part of this comprehensive approach, which is the only way to stop the global epidemic of type 2 diabetes.

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## HISTORY OF MEDICINE *ISTORIJA MEDICINE*

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### BRANISLAV NUŠIĆ AND X-RAYS IN THE STORY "ROENTGEN'S PHOTOGRAPHY"

*BRANISLAV NUŠIĆ I X-ZRACI U PRIČI "RENTGENOVA FOTOGRAFIJA"*

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Strahinja R. BABIĆ<sup>3</sup> and Nevena R. BABIĆ<sup>3</sup>

#### Summary

**Introduction.** Shortly after the discovery of X-rays, their practical application in the clinical practice became the object of interest of many non-medical individuals. One of them was the famous Serbian writer, Branislav Nušić. This paper presents the life and work of Branislav Nušić, as well as his article: "Roentgen's Photography" which was published in the journal "Politics" (July 8, 1906; N° 892, p. 3), under the alias Ben Akiba, in the Cyrillic script. **The life and work of Branislav Nušić.** Alchiviadi Nuša, later Branislav Nušić (1864 - 1938) was a great Serbian literate, playwright, journalist, photographer, politician, diplomat, member of the Serbian Royal Academy, President of the Association of Yugoslav Playwrights, manager of the theaters in Belgrade, Novi Sad, Skopje and Sarajevo, and a military volunteer in the Serbian - Bulgarian war (1885). **"Roentgen's Photography"**. The author wrote this text in his own way, the only way he could and knew, vividly and wittily. He knew about the great power and strength of X-ray radiation, and he wrote of his knowledge in this short story. Without Branislav Nušić, the history of Serbian radiology would be poorer for not seeing the X-rays by the eyes of an educated, intelligent and, above all, humorous writer. **Conclusion.** Branislav Nušić, alongside Nikola Tesla, Mihajlo Pupin Idvorski, Dr. Abraham Vinaver, and all past and present Serbian radiologists, has become an essential and memorable link in the chain of the history of the Serbian radiology.

**Key words:** Famous Persons; History of Medicine; Radiology; Radiography; X-Rays; Medicine in Literature

#### Introduction

Branislav Nušić (October 20, 1864, Belgrade, the Principality of Serbia – January 19, 1938, Belgrade, Yugoslavia) (**Figure 1**) was a Serbian writer, playwright, comedian, journalist, photographer, politician, diplomat, member of the Serbian Royal Academy, President of the Association of Yugoslav Playwrights, manager of the theaters in Belgrade, Novi Sad, Skopje and Sarajevo, member of the Radical party, a military volunteer in the Serbian - Bulgarian

#### Sažetak

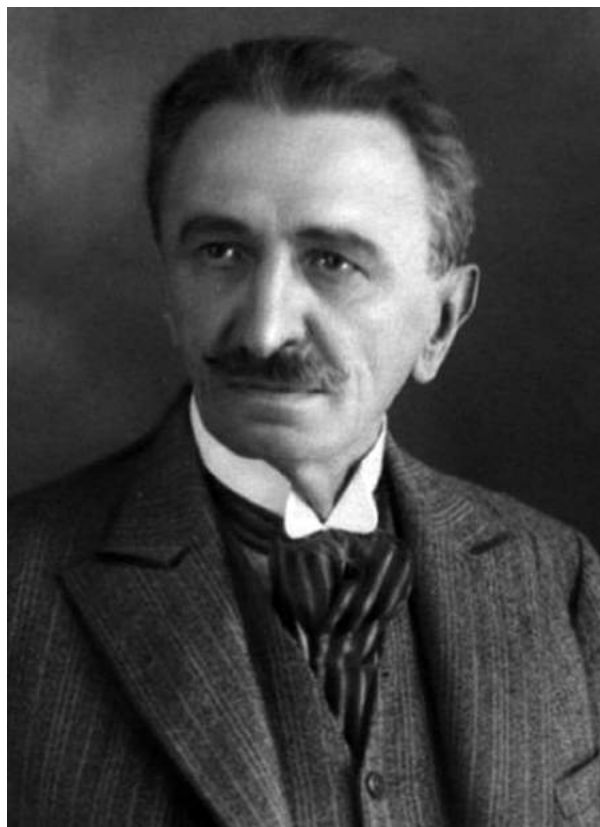
**Uvod.** Rendgenski zraci, vrlo brzo posle otkrivanja i praktične primene u kliničkoj praksi, postaju predmet interesovanja i nemedicinskih poslenika. Jedan od njih je i čuveni srpski književnik Branislav Nušić. Radom se predstavlja život i delo Branislava Nušića kao i njegov tekst pod naslovom "Rentgenova fotografija", objavljen u listu "Politika" (8. jul 1906; N° 892, str. 3) pod pseudonimom Ben Akiba, na ćirilicom pismu. **Život i rad Branislava Nušića.** Alchibiad Nuša (*Alchiviadi Nuša*), kasnije Branislav Nušić (1864–1938) bio je veliki srpski književnik, dramski pisac, novinar, fotograf, političar, diplomata, član Srpske kraljevske akademije, predsednik Udruženja jugoslovenskih dramskih pisaca, upravnik pozorišta u Beogradu, Novom Sadu, Skoplju i Sarajevu, ratnik dobrovoljac u Srpsko-bugarskom ratu (1885). **"Rentgenova fotografija"**. Autor je napisao tekst na svoj način, kako je samo on mogao i znao, projektovano i duhovito. Znao je za veliku moć i snagu rendgenskog zračenja, te znanje pretočio u ovu kratku priču. Bez Branislava Nušića istorija srpske radiologije bila bi siromašnija za viđenje X-zračenja očima obrazovanog, pronicljivog i nadasve, duhovitog književnika. **Zaključak.** Rame uz rame sa Nikolom Teslom, Mihajlom Idvorskim Pupinom, dr Avramom Vinaverom i svim srpskim radiolozima prošlosti i sadašnjosti, Nušić je postao bitna i neizbrisiva alka u lancu istorije srpske radiologije.

**Ključne reči:** poznate osobe; istorija medicine; radiologija; radiografija; X-zraci; medicina u literaturi

ian war (1885) (**Figure 2**) and a convict sentenced to two years of prison in Požarevac, because of using "filthy language" (1888) (**Figure 3**) [1–6].

In 2010, the Post of Serbia issued an edition of postage stamps "Giants of Serbian Literature" and in honor of Branislav Nušić a post stamp with his image. The Post of Yugoslavia has also issued a post stamp with the image of Branislav Nušić (**Figure 4**).

Also, in honor of the 150<sup>th</sup> birthday anniversary of the great Serbian writer Branislav Nušić, the National Library of Serbia digitized the greatest achievements



**Figure 1.** Branislav Nušić, alias Alchiviadi Nuša, alias Ben Akiba

*Slika 1.* Branislav Nušić, alias Alkibijad Nuša (Alchiviadi Nuša), alias Ben Akiba

of this distinguished playwright. Digital editions of twenty-five Nušić’s books published by Geca Kon, are part of the Digital Library of the National Library of Serbia. Four titles have a searchable text, and audio recordings are being prepared, so that Nušić’s books will be available to blind and visually impaired persons for the first time. Digital copies of Nušić are available at: [www.digitalna.nb.rs/sf/NBS/Knjige/II\\_4042](http://www.digitalna.nb.rs/sf/NBS/Knjige/II_4042) [6].

### The life and work of Branislav Nušić

Branislav Nušić was born in a Cincar family. His father Đorđe, who was a cereal merchant, and his mother Ljubica, named him Alkibijad Nuša (Alchiviadi Nuša). When he was eighteen, he changed his name into Branislav Nušić. He spent his childhood in Smederevo, where his family moved after the bankruptcy of his father. He finished his elementary school and two grades of high school in Smederevo, and graduated in Belgrade. Nušić started his law studies in Graz, and continued in Belgrade, where he graduated from the Law School of the University of Belgrade in 1886 [1–3].

He wrote his first comedy “A Member of Parliament” at the age of nineteen.

Apart from writing under his real name, he also wrote under an alias - Ben Akiba.



**Figure 2.** Corporal Branislav Nušić in the Serbian-Bulgarian War

*Slika 2.* Desetar Branislav Nušić u Srpsko-bugarskom ratu

After publishing his controversial poem “Two Slaves” (1887) in the Daily Gazette, King Milan ordered his arrest in 1888. Branislav Nušić was sentenced to two years of prison, but after spending one year in Požarevac, at the request of his father, he was pardoned. After imprisonment, King Milan and the Minister of Foreign Affairs awarded him with a position in civil service, where he spent ten years as a clerk of Serbian consulates in Bitola, Skopje, Thessaloniki, Serres and Priština, then part of the Ottoman Empire [1–3].

In 1900, Nušić was appointed as a Secretary of the Ministry of Education, Head of the Art Department of the Ministry of Education (1918), Head Dramaturge of the National Theatre in Belgrade (1902), Head of the Serbian National Theatre in Novi Sad (1904), Head of the Sarajevo National Theatre (1927). He was the founder of the Theatre in Skopje (1913), Children’s Theatre in Novi Sad (1904) and “Stork Theatre” in Belgrade, today the theatre “Boško Buha”. He became a full member of the Serbian Royal Academy on February 10, 1933 [1–6].

Branislav Nušić made a great contribution to the beginnings and development of Serbian photography. His knowledge and work in photography was truly a work of a pioneer, cultural, theoretical, innovative and creative.

His major works are:



**Figure 3.** Branislav Nušić serving a prison sentence in Požarevac

*Slika 3. Branislav Nušić na odsluženju zatvorske kazne u Požarevcu*

Comedies: A Member of the Parliament (1883), A Suspicious Person (1887), Favoritism (1889), An Ordinary Man (1899), The Publicity (1906), Travel Around the World (1910), The Cabinet Minister's Wife (1929), Mister Dollar (1932), SYEW - Society of Yugoslav Emancipated Women (1933), Bereaved Family (1935), PhD (1936), The Deceased (1938), Never Despair, Authority (unfinished), Dole Kermit (unfinished);

– Novels: County's Child (1902), The Outlaws (1933), The 1915<sup>th</sup> (1920), Autobiography (1924);

– Dramas: Offing (1901), It Had to Be This Way, Autumn Rain (1907), Behind God's Back (1910), Rental Fee, Ignoramus;

– Short stories: Political Rival, Eulogy, Class, The Corporal's Stories; **Photography** (1906), **Roentgen's Photography** (1906);

– Tragedies: Prince Ivo of Semberia, Hodža-Loja, Foundling;

– Textbook: A Discourse on Rhetorics;

– Travelogue: Kosovo, Description of the Country and People [1–6];

– Poems: Two Slaves.

Branislav Nušić was a holder of the Order of St. Sava - I grade (Kingdom of Serbs, Croats and Slovenes), Order of Prince Danilo I - IV degree (Kingdom of Montenegro), Order of St. Sava - IV grade (Kingdom of Serbia), and the Order of the White Eagle - V class (Kingdom of Serbs, Croats and Slovenes) (**Figure 5**) [5].

### “Roentgen's Photography” by Branislav Nušić

Shortly after the discovery of X-rays, their practical application in the clinical practice became the object of interest of many non-medical individuals. One of them was the famous Serbian writer Branislav Nušić. His article: “Roentgen's Photography”, was published in the journal “Politics” (July 8, 1906, No 892, p. 3) under the alias Ben Akiba, in the Cyrillic script, in a column From Belgrade Life (**Figure 6**) [8].

Not much is known how Branislav Nušić wrote and published the story about X-ray radiation. His godfather, a photographer Milan Jovanović, made a photo of Branislav Nušić. Branislav Nušić signed his name at the beginning and at the end of the story “Roentgen's Photography” and wrote his saying: “My humor provokes laughter and softens the hardships of life”.

Branislav Nušić wrote this text in his own way, the only way he could and knew, vividly and wittily. He begins the story “Roentgen's Photography”:



**Figure 4.** Branislav Nušić on a postage stamp of the Post Office of Yugoslavia

*Slika 4. Branislav Nušić na poštanskoj marki koju je izdala Pošta Jugoslavije*



**Figure 5.** Branislav Nušić is a holder of the Order of St. Sava - I grade (Kingdom of Serbs, Croats and Slovenes), Order of Prince Danilo I - IV degree (Kingdom of Montenegro), Order of St. Sava - IV grade (Kingdom of Serbia) and the Order of the White Eagle - V class (Kingdom of Serbs, Croats and Slovenes)

**Slika 5.** Branislav Nušić je nosilac Ordena Svetog Save - I reda (Kraljevine Srba, Hrvata i Slovenaca), Ordena Kneza Danila I - IV stepena (Kraljevine Crne Gore), Ordena Svetog Save - IV reda (Kraljevina Srbija) i Ordena belog orla - V klase (Kraljevina Srba, Hrvata i Slovenaca)

“So now even we have installed a roentgen photography in Belgrade. This is the novelty that newspapers reported about a few days ago. It was about time we got an X-ray machine, because we took enough pictures of our looks, and it is time we began taking pictures of our inner selves” [8].

It was an excellent beginning for a story. A few sentences in the first paragraph reveal everything and he says:

– Belgrade got the first X-ray machine in July 1906;

– The news was published in all newspapers in the city, including “Politics”;

– Roentgen’s Photography is the name for a radiograph. Branislav Nušić was not far from the true name, because he was the one of the first Serbian photographers and a press photographer of that time;

– Capture - Branislav Nušić’s word for radiography, the word “radio-paint” that we radiologists often use in jargon;

– Of course, Branislav Nušić would not be true to himself, if he did not use the power of this scientific discovery to ridicule the society - “it is time we began taking pictures of our inner selves”.

We can see that he knew the power and strength of X-ray radiation well, and that this scientific discovery was a great novelty for Serbs from the following: “It will have endless practical consequences. Imagine this: ....” [8].

As the story develops, Nušić is describing several persons from the urban environment, trying to ridicule human weaknesses, greed, love, and to

make things even funnier, he tries to visualize and show them on “roentgen photography”.

Nušić begins with a description of love between Mr. Živko and Ms. Stanka, arranged by the match-maker Savka, which is confirmed, magnified, and visualized by a “roentgen photo”. Thus, Ms. Stanka says to Ms. Savka - I would like to have the gentleman’s roentgen images...just to see if his heart is empty” [8].

The story continues: “Imagine now if X-rays were used during proposals and falling in love...and lovers could take X-rays...for example, Ms. Dana takes a heart X-ray and the roentgen photography shows the entire 25<sup>th</sup> Class of Military Academy, in her heart...” And concludes: “If we now start “taking pictures”, who knows what we will find in everyone of us under the roentgen rays” [8].

The text continues: “... if Mr. Jova Ždravković takes an X-ray, just his stomach will be visible. Everything else, the heart and the soul, will be transparent and will not appear on the image, and only the stomach will be seen, beautifully painted”. Or, for



**Figure 6.** “Roentgen’s Photography” by Ben Akiba. The beginning and the end of the story published in the Journal Politics, No. 892, page 3

**Slika 6.** „Rentgenova fotografija”, pisac: Ben Akiba. Početak i kraj priče objavljene u dnevnom listu „Politika“, broj 892, str. 3.

example, Ms. Olga takes an X-ray, and the image does not show a single drop of blood, and then you can see why she never blushes when someone declares love to her” [8].

So, for transparency Nušić uses the word “transparent”, of course, to describe a translucent and empty soul of Mr. Jovan Zdravković, who is probably obese and who thinks only of food and insensitivity of Ms Olga. At the same time, in this part of the story Nušić shows the importance of centering the object in radiography: “only the stomach will be seen, beautifully painted”; in this way Nušić enters the sphere of the “Fundamentals of roentgenography”.

Nušić further wrote: “Or, for example, master Pera, who complains of some stomach cramps since his youth, takes an X-ray. The image of master Pera is transparent, but in one corner of his stomach a coin can be seen... since 1875, everything becomes clear. While he was an apprentice of master Sava... he took it and put into his mouth as in a cashbox... saving like that three of four dinars per month” [8].

Nušić continues the story: “... Let’s say, Ms. Nata, a young girl who has just turned seventeen, has stomach ache. She is cured in different ways... and someone counsels her to take an X-ray. An X-ray is taken ... she is all transparent like every little girl at sixteen should be... There is nothing to be seen in the image, just one little love letter:

*My dearest,  
I received your letter  
Receive my heart  
I love you immensely  
I love you strongly, faithfully  
Yours, Mita.*

The thing becomes immediately clear... her father came in ... and she swallowed it. As an experienced doctor for the soul, Nušić concludes: “She always knew the cause for her stomach cramps, and now it is clear to her father, clear that the child is not only suffering from stomach ache, but also from heart ache” [8].

The last paragraph of the article particularly stands out, and is the final word of Branislav Nušić: “It is a good thing, the X-ray photography, but I would rather not take a photo. What I am, and what I had to swallow during my life, and what I carried in my heart all my life; well, thank you very much, but I’d rather not show it all in one picture” [8].

We will add to this Nušić’s article the great accomplishments of our doctors and scientists:

– Nikola Tesla published ten papers on X-radiation from March 11, 1896 to August 11, 1897, and laid the basic principles of radiology and first proved the harmfulness of X-radiation on human body [7, 9];

– Mihajlo Pupin began his research on X-rays right after their discovery; he studied X-fluoroscopy and shortening the exposure to X-rays in February 1896 [7, 10].

– In 1899, at the initiative of the engineer Đorđe Stojanović, the first X-rays were applied in the High School in Belgrade.

– In 1900, Dr. Avram Vinaver installed the first X-ray machine in Šabac, at the time when many developed countries of the world did not have X-ray machines, and wrote the first papers on the application of X-rays [7, 11];

– Dr. Nikola Krstić (1905) made the first roentgenogram; it was the roentgenogram of the king Petar I Karađorđević’s hand [12].

These are the works, assembled and blended like puzzles into the first Serbian X-ray image, which is the first and real foundation of radiology in Serbia.

## Conclusion

In this paper, the authors showed the life and work of Branislav Nušić, as well as his short story entitled “Roentgen’s Photography”, published in the journal “Politics” (July 8, 1906, No 892, p. 3), under the alias Ben Akiba. The story is written in the Cyrillic script. At that time, such a story could not have been written by any other playwright and writer of the world than Branislav Nušić himself.

The story “Roentgen’s Photography” reveals Branislav Nušić to our and world public as a great promoter of world scientific discovery of roentgen radiation. Branislav Nušić, alongside Nikola Tesla, Mihajlo Pupin Idvorski, Dr. Abraham Vinaver, and all past and present Serbian radiologists, has become an essential and memorable link in the chain of the history of the Serbian of radiology.

We brought the story “Roentgen’s Photography” from oblivion to the light; we were also the first to include Branislav Nušić into the Serbian history of radiology.

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Zaključci moraju proisteći isključivo iz rezultata istraživanja rada; treba izbegavati uopštene i nepotrebne zaključke. Zaključci koji su navedeni u tekstu rada moraju biti u saglasnosti sa zaključcima iz Sažetka.

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Potrebno je da se literatura numeriče arapskim brojevima redosledom kojim je u tekstu navedena u parentezama; izbegavati nepotrebno velik broj navoda literature. Časopise bi trebalo navoditi u skraćenom obliku koji se koristi u *Index Medicus* (<http://www.nlm.nih.gov/tsd/serials/lji.html>). Pri citiranju literature koristiti Vankuverski sistem. Potrebno je da se navedu svi autori rada, osim ukoliko je broj autora veći od šest. U tom slučaju napisati imena prvih šest autora praćeno sa *et al.*

Primeri pravilnog navođenja literature nalaze se u nastavku.

#### Radovi u časopisima

##### \* Standardni rad

Ginsberg JS, Bates SM. Management of venous thromboembolism during pregnancy. *J Thromb Haemost* 2003;1:1435-42.

##### \* Organizacija kao autor

Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002;40(5):679-86.

##### \* Bez autora

21st century heart solution may have a sting in the tail. *BMJ*. 2002;325(7357):184.

##### \* Volumen sa suplementom

Magni F, Rossoni G, Berti F. BN-52021 protects guinea pig from heart anaphylaxis. *Pharmacol Res Commun* 1988;20 Suppl 5:75-8.

##### \* Sveska sa suplementom

Gardos G, Cole JO, Haskell D, Marby D, Pame SS, Moore P. The natural history of tardive dyskinesia. *J Clin Psychopharmacol* 1988;8(4 Suppl):31S-37S.

##### \* Sažetak u časopisu

Fuhrman SA, Joiner KA. Binding of the third component of complement C3 by *Toxoplasma gondi* [abstract]. *Clin Res* 1987;35:475A.

#### Knjige i druge monografije

##### \* Jedan ili više autora

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. *Medical microbiology*. 4th ed. St. Louis: Mosby; 2002.

##### \* Urednik (urednici) kao autor (autori)

Danset J, Colombani J, eds. *Histocompatibility testing 1972*. Copenhagen: Munksgaard, 1973:12-8.

##### \* Poglavlje u knjizi

Weinstein L, Shwartz MN. Pathologic properties of invading microorganisms. In: Soderman WA Jr, Soderman WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: Saunders; 1974. p. 457-72.

##### \* Zbornik radova sa kongresa

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. *Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming*; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. p. 182-91.

##### \* Disertacija

Borkowski MM. *Infant sleep and feeding: a telephone survey of Hispanic Americans* [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

#### Elektronski materijal

##### \* Članak iz časopisa u elektronskom formatu

Aboud S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. *Am J Nurs* [Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: <http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle>

##### \* Monografija u elektronskom formatu

CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reeves JRT, Maibach H. CMEA Multimedia Group, producers. 2nd ed. Version 2.0. San Diego:CMEA;1995.

##### \* Kompjuterska datoteka

Hemodynamics III: the ups and downs of hemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems; 1993.

#### 5. Prilozi (tabele, grafikoni, sheme i slike)

##### BROJ PRILOGA NE SME BITI VEĆI OD ŠEST!

Tabele, grafikoni, sheme i slike se postavljaju kao posebni dokumenti.

– Tabele i grafikone bi trebalo pripremiti u formatu koji je kompatibilan programu u kojem je napisan tekst rada. Slike bi trebalo poslati u jednom od sledećih oblika: *JPG, GIF, TIFF, EPS*.

– Svaki prilog mora biti obeležen arapskim brojem prema redosledu po kojem se navodi u tekstu rada.

– Naslovi, tekst u tabelama, grafikonima, shemama i legende slika bi trebalo da budu napisani na srpskom i engleskom jeziku.

– Nestandardne priloge označiti u fusnoti uz korišćenje sledećih simbola: \*, †, ‡, §, ||, ¶, \*\*, † †, ‡ ‡.

– U legendi slika trebalo bi napisati korišćeno uveličanje okulara i objektivna mikroskopa. Svaka fotografija treba da ima vidljivu skalu.

– Ako su tabele, grafikoni, sheme ili slike već objavljene, navesti originalni izvor i priložiti pisano odobrenje autora za njihovo korišćenje.

– Svi prilozi će biti štampani kao crno-bele slike. Ukoliko autori žele da se prilozi štampaju u boji, obavezno treba da plate dodatne troškove.

#### 6. Dodatne obaveze

AUTORI I SVI KOAUTORI RADA OBAVEZNO TREBA DA PLATE GODIŠNJU PRETPLATU ZA ČASOPIS *MEDICINSKI PREGLED*. U PROTIVNOM, RAD NEĆE BITI ŠTAMPAN U ČASOPISU.

## INFORMATION FOR AUTHORS

**Medical Review** publishes papers (previously neither published in nor submitted to any other journals) from various fields of biomedicine intended for broad circles of doctors.

Since January 1<sup>st</sup>, 2013 the Medical Review has been using the service e-Ur: Electronic Journal Editing. All users of the Registration system, i.e. authors, reviewers, and editors have to be registered users with only one e-mail address. Registration should be made on the web address:

<http://aseestant.ceon.rs/index.php/medpreg/user/register>.

Manuscript submission should be made on the web address:

<http://aseestant.ceon.rs/index.php/medpreg/>

A SUPPLEMENTARY FILE, WITH THE STATEMENT THAT THE PAPER HAS NOT BEEN SUBMITTED OR ACCEPTED FOR PUBLICATION ELSEWHERE AND A CONSENT SIGNED BY ALL AUTHORS, HAVE TO BE ENCLOSED WITH THE MANUSCRIPT.

Authors may not send the same manuscript to more than one journal concurrently. If this occurs, the Editor may return the paper without reviewing it, reject the paper, contact the Editor of the other journal(s) in question and/or contact the author's employers.

Papers should be written in English language, with an abstract and title page in English, as well as in Serbian language.

All papers submitted to **Medical Review** are seen by one or more members of the Editorial Board. Suitable articles are sent to at least two experts to be reviewed, their reports are returned to the assigned member of the Editorial Board and the Editor. Revision of an article gives no guarantee of acceptance and in some cases revised articles are rejected if the improvements are not sufficient or new issues have arisen. Material submitted to *the Journal* remains confidential while being reviewed and peer-reviewers' identities are protected unless they elect to lose anonymity.

**Medical Review** publishes the following types of articles: editorials, original studies, preliminary reports, review articles, professional articles, case reports, articles from history of medicine and other types of publications.

**1. Editorials** – up to 5 pages – convey opinions or discussions on a subject relevant for the Journal. Editorials are commonly written by one author by invitation.

**2. Original studies** – up to 12 pages – present the authors' own investigations and their interpretations. They should contain data which could be the basis to check the obtained results and reproduce the investigative procedure.

**3. Review articles** – up to 10 pages – provide a condensed, comprehensive and critical review of a problem on the basis of the published material being analyzed and discussed, reflecting the current situation in one area of research. Papers of this type will be accepted for publication provided that the authors confirm their expertise in the relevant area by citing at least 5 self-citations.

**4. Preliminary reports** – up to 4 pages – contain scientific results of significant importance requiring urgent publishing; however, it need not provide detailed description for repeating the obtained results. It presents new scientific data without a detailed explanation of methods and results. It contains all parts of an original study in an abridged form.

**5. Professional articles** – up to 10 pages – examine or reproduce previous investigation and represent a valuable source of knowledge and adaption of original investigations for the needs of current science and practice.

**6. Case reports** – up to 6 pages – deal with rare casuistry from practice important for doctors in direct charge of patients and are similar to professional articles. They emphasize unusual characteristics and course of a disease, unexpected reactions to a therapy, application of new diagnostic procedures and describe a rare or new disease.

**7. History of medicine** – up to 10 pages – deals with history with the aim of providing continuity of medical and health care culture. They have the character of professional articles.

**8. Other types of publications** – The journal also publishes feuilletons, book reviews, extracts from foreign literature, reports from congresses and professional meetings, communications on activities of certain medical institutions, branches and sections, announcements of the Editorial Board, letters to the Editorial Board, novelties in medicine, questions and answers, professional and vocational news and In memoriam.

### Preparation of the manuscript

The complete manuscript, including the text, all supplementary material and covering letter, is to be sent to the web address above.

### The covering letter:

– It must contain the proof given by the author that the paper represents an original work that it has neither been previously published in other journals nor is under consideration to be published in other journals.

– It must confirm that all the authors meet criteria set for the authorship of the paper, that they agree completely with the text and that there is no conflict of interest.

– It must state the type of the paper submitted (an original study, a review article, a preliminary report, a professional article, a case report, history of medicine).

### The manuscript:

#### General instructions.

Use Microsoft Word for Windows to type the text. The text must be typed in font *Times New Roman*, page format A4, space 1.5 (for tables as well), margins set to 2.5 cm and font size 12pt. All measurements should be reported in the metric system of the International System of Units – SI. Temperature should be expressed in Celsius degrees (°C) and pressure in mmHg.

The manuscript should contain the following elements:

#### 1. The title page.

The title page should contain a concise and clear title of the paper, without abbreviations, then a short title (up to 40 characters), full names and surnames of the authors (not more than 6) indexed by numbers corresponding to those given in the heading along with the full name and place of the institutions they work for. Contact information including the academic degree(s), full address, e-mail and number of phone or fax of the corresponding author (the author responsible for correspondence) are to be given at the bottom of this page.

#### 2. Summary.

The summary should contain up to 250 words, without abbreviations, with the precise review of problems, objectives, methods, important results and conclusions. It should be structured into the paragraphs as follows:

– Original and professional papers should have the introduction (with the objective of the paper), materials and methods, results and conclusion

– Case reports should have the introduction, case report and conclusion

– Review papers should have the introduction, subtitles corresponding to those in the paper and conclusion.

The authors should provide up to 10 keywords below the summary. These keywords will assist indexers in cross-indexing the article and will be published with the summary, but the authors' keywords could be changed in accordance with the list of Medical Subject Headings, MeSH of the American National Medical Library.

The summary should be written in both languages, English as well as Serbian. The summary in Serbian language should be the translation of the summary in English; therefore, it has to contain the same paragraphs.

### 3. The text of the paper.

The text of original studies must contain the following: introduction (with the clearly defined objective of the study), materials and methods, results, discussion, conclusion, list of abbreviations (if used in the text) and not necessarily, the acknowledgment mentioning those who have helped in the investigation and preparation of the paper.

The text of a case report should contain the following: introduction (with clearly defined objective of the study), case report, discussion and conclusion.

**Introduction** contains clearly defined problem dealt with in the study (its nature and importance), with the relevant references and clearly defined objective of the investigation and hypothesis.

**Materials and methods** should contain data on design of the study (prospective/retrospective, eligibility and exclusion criteria, duration, demographic data, follow-up period). Statistical methods applied should be clear and described in details.

**Results** give a detailed review of data obtained during the study. All tables, graphs, schemes and figures must be cited in the text and numbered consecutively in the order of their first citation in the text.

**Discussion** should be concise and clear, interpreting the basic findings of the study in comparison with the results of relevant studies published in international and national literature. It should be stated whether the hypothesis has been confirmed or denied. Merits and demerits of the study should be mentioned.

**Conclusion** must deny or confirm the attitude towards the Obased solely on the author's own results, corroborating them. Avoid generalized and unnecessary conclusions. Conclusions in the text must be in accordance with those given in the summary.

**4. References** are to be given in the text under Arabic numerals in parentheses consecutively in the order of their first citation. Avoid a large number of citations in the text. The title of journals should be abbreviated according to the style used in Index Medicus (<http://www.nlm.nih.gov/tsd/serials/lji.html>). Apply Vancouver Group's Criteria, which define the order of data and punctuation marks separating them. Examples of correct forms of references are given below. List all authors, but if the number exceeds six, give the names of six authors followed by 'et al'.

#### Articles in journals

##### *\* A standard article*

Ginsberg JS, Bates SM. Management of venous thromboembolism during pregnancy. *J Thromb Haemost* 2003;1:1435-42.

##### *\* An organization as the author*

Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002;40(5):679-86.

##### *\* No author given*

21st century heart solution may have a sting in the tail. *BMJ*. 2002;325(7357):184.

##### *\* A volume with supplement*

Magni F, Rossoni G, Berti F. BN-52021 protects guinea pig from heart anaphylaxis. *Pharmacol Res Commun* 1988;20 Suppl 5:75-8.

##### *\* An issue with supplement*

Gardos G, Cole JO, Haskell D, Marby D, Pame SS, Moore P. The natural history of tardive dyskinesia. *J Clin Psychopharmacol* 1988;8(4 Suppl):31S-37S.

##### *\* A summary in a journal*

Fuhrman SA, Joiner KA. Binding of the third component of complement C3 by *Toxoplasma gondii* [abstract]. *Clin Res* 1987;35:475A.

#### Books and other monographs

##### *\* One or more authors*

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. *Medical microbiology*. 4th ed. St. Louis: Mosby; 2002.

##### *\* Editor(s) as author(s)*

Danset J, Colombani J, eds. *Histocompatibility testing 1972*. Copenhagen: Munksgaard, 1973:12-8.

##### *\* A chapter in a book*

Weinstein L, Shwartz MN. Pathologic properties of invading microorganisms. In: Soderman WA Jr, Soderman WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: Saunders; 1974. p. 457-72.

##### *\* A conference paper*

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. *Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming*; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. p. 182-91.

##### *\* A dissertation and theses*

Borkowski MM. *Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]*. Mount Pleasant (MI): Central Michigan University; 2002.

#### Electronic material

##### *\* A journal article in electronic format*

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. *Am J Nurs* [Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: <http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle>

##### *\* Monographs in electronic format*

CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reeves JRT, Maibach H. CMEA Multimedia Group, producers. 2nd ed. Version 2.0. San Diego:CMEA;1995.

##### *\* A computer file*

Hemodynamics III: the ups and downs of hemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems; 1993.

### 5. Attachments (tables, graphs, schemes and photographs).

THE MAXIMUM NUMBER OF ATTACHMENTS ALLOWED IS SIX!

– Tables, graphs, schemes and photographs are to be submitted as separate documents, on separate pages.

– Tables and graphs are to be prepared in the format compatible with Microsoft Word for Windows programme. Photographs are to be prepared in JPG, GIF, TIFF, EPS or similar format.

– Each attachment must be numbered by Arabic numerals consecutively in the order of their appearance in the text

– The title, text in tables, graphs, schemes and legends must be given in both Serbian and English languages.

– Explain all non-standard abbreviations in footnotes using the following symbols \*, †, ‡, §, ||, ¶, \*\*, † †, ‡ ‡.

– State the type of color used and microscope magnification in the legends of photomicrographs. Photomicrographs should have internal scale markers.

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– All attachments will be printed in black and white. If the authors wish to have the attachments in color, they will have to pay additional cost.

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SHOULD THE AUTHOR AND ALL CO-AUTHORS FAIL TO PAY THE SUBSCRIPTION FOR MEDICAL REVIEW, THEIR PAPER WILL NOT BE PUBLISHED.