8. KONGRES

ASOCIJACIJE LABORATORIJSKIH I SANITARNIH ZDRAVSTVENIH PROFESIONALACA U BOSNI I HERCEGOVINI S MEĐUNARODNIM UČEŠĆEM

Sarajevo, Bosna i Hercegovina, 16–19. maj 2024.

8th CONGRESS

ASSOCIATION OF LABORATORY AND SANITARY HEALTH PROFESSIONALS IN BOSNIA AND HERZEGOVINA WITH INTERNATIONAL PARTICIPATION

Sarajevo, Bosnia and Herzegovina, 16–19. May 2024.

KNJIGA SAŽETAKA

BOOK OF ABSTRACTS

EQA & QC – LABQUALITY PROGRAM OR UNIQUE PLATFORM TO PROVIDE REAL-TIME CONTROL IN A VARIETY OF FORMATS

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Invited speaker

Introduction: Laboratory medicine is a medical science pioneer in development and application of *EQA* of analytical procedures. An external quality control program consists in a systematic distribution of several control samples among a few laboratories and an evaluation of results obtained by an organization external to the participant laboratory. The generally accepted term for this activity is *EQA*. Another term used to refer to these activities is proficiency testing that is something practically identical to external *QC* that formally recognizes the attainment of good results by the participant.

Objectives/Content: An external *QC* program distributes same control samples to various laboratories and evaluates results obtained with a common criterion. The aim of this module is to summarize the evolution of various types of external programs, to point out the progresses to practical consequences of the participant laboratories. EQA programs were initiated at evidencing big discrepancies among laboratory results developed in various countries and some mechanisms to harmonize them were proposed to establish common performance specifications derived from biological variation and to use as educational tool to focus *EQA* to assure the adequate clinical use of laboratory tests, use commutable controls to harmonize the different *EQA* models by promoting a forum for co-operation and exchange of knowledge on quality-related matters.

Materials and methods: The material for this module is a brief revision of the different types of external programs that have been used for the last 20 years. The method is the critical analysis of the strong and weak points of each program model, from the light of our experience.

Results: The main objectives were to estimate the inaccuracy of results obtained by every participant laboratory, to verify the imprecision for schemes where the control material was analyzed several times, comparing to that obtained by the other participants, to evaluate acceptability of results, to define quality specifications for *EQA*, to promote use of homogeneous analytical systems (calibrator, reagents, and instrument from same manufacturer) and to select the best control material possible.

Conclusion: To participate in an *EQA* with commutable-reference method assigned values controls allows to know the real inaccuracy/accuracy of tests results and patient' impact, as well as calibrators traceability. Participation in *EQA* with commutable control material where the target value preferentially is set by a reference measurement procedure. To evaluate individual laboratory performance and participant methods performance using similar criteria among all *EQA* is to focus on *LQ* educational *EQA*, harmonization among *EQA* and *LQ* by Vigilance of the quality of the current available analytical methods.

Keywords: *external control; performance specifications; quality assurance*

IZAZOVI U ODREĐIVANJU I INTERPRETACIJI TUMORSKIH MARKERA

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Pozvani predavač

Tumor marker je biohemijski indikator prisustva tumora u organizmu. Markere proizvodi tumor ili domaćin kao odgovor na prisustvo malignog tkiva. Koriste se za diferencijaciju tumorskog od normalnog tkiva na osnovu njihovog određivanja u krvi. Markeri se mjere kvalitativno ili kvantitativno hemijskim, imunološkim metodama,te molekularno-dijagnostičkim metodama.

Ciljevi ovog preglednog rada su da se daju osnovne karakteristike tumor markera i ukaže na izazove pri njihovom određivanju i primjeni u kliničkoj praksi.

Tumor markeri uključuju različite supstance kao što su površni antigeni, citoplazmatski proteini, enzimi hormoni, onkofetalni antigeni, reveptori. Mogu se klasificirati bazirano na kliničkoj aplikaciji: skrining i rana detekcija, dijagnostika, odgovor na terapiju, prognoza i monitoring pacijenata. Najvažnije karakteristike tumorskih biomarkera je da su visoko specifični i osjetljivi. Ovakvi idealni tumor markeri ne postoje.

Neki markeri su specifični samo za jedan tip tumora, dok se drugi sreću kod više tumorskih tipova. Mnogi markeri se susreću u karcinomu ali i non-karcinomskim uslovima te nisu pouzdani za postavljanje dijagnoze karcinoma. Sa druge strane, koncentracija nekih tumorskih markera odražava tumorsku aktivnost i volumen istog.

Tumor markeri se ne mogu koristiti za skrining je nisu dovoljno specifični, ali su pojedini dobri alati za potvrdu dijagnoze, prognozu i praćenje pacijenta, izbor i monitoriranje terapije te otkrivanje rekurentne bolesti. Vrijednosti markera se tumače zajedno sa rezultatima kliničkih, drugih laboratorijskih i slikovnih pretraga ili se koriste paneli testova da bi im se povećala osjetljivost i specifičnost.

Ključne riječi: *tumorski marker; određivanje; klasifikacija; osjetljivost; specifičnost*

CHALLENGES IN DETERMINATION AND CLINICAL UTILITY OF TUMOR MARKERS

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Invited speaker

A tumor marker is a biochemical indicator of the tumor presence in the body. They are substances produced in tumor cells or by the host in response of tumor and secreted into body fluids in which they can be quantitated by non-invasive analyses. Their primary use is in differentiation of a tumor from normal tissue or to determine the presence of a tumor. Markers are measured qualitatively or quantitatively by chemical, immunological, or molecular diagnostic methods.

The aims of this review are to provide the basic characteristics of tumor markers and to underline the challenges in determination and application in clinical practice.

Tumor markers include a variety of substances like cell surface antigens, cytoplasmic proteins, enzymes, hormones, oncofetal antigens, receptors, oncogenes and their products. They can be classified based on clinical application: screening and early detection, aid in the diagnosis, determining response to therapy and follow-up of patients. The most important characteristics of an ideal tumor marker are to be highly specific to a given tumor type and to be highly sensitive to detect small tumors and avoid false positive results. So far, there is no ideal tumor marker in practice.

Some tumor markers are specific for only one type of cancer, the others are found in several cancer types. Many of the markers are seen in cancer but also in noncancerous conditions. Consequently, these tumor markers are not reliable as a cancer diagnostic tool. However, in some cases blood concentrations of tumor markers reflect active tumor mass and its volume.

Tumor biomarkers are not applicable for cancer screening, but ones that are accessible in laboratory and clinical practice for most cancer cases, are additional, valuable tools in estimating patient prognosis, assessing effectiveness of treatment modality, and detection of the disease recurrence. Determined marker values should be interpreted together with the results of clinical, laboratory and imaging tests, or use panels of test to increases their sensitivity and specificity.

Keywords: *tumor markers; determination; classification; sensitivity and specificity; clinical utility*

UTICAJ PREANALITIKE NA KVALITET LABORATORIJSKIH REZULTATA

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Pozvani predavač

Celokupan postupak laboratorijskog rada u svim njegovim fazama mora da bude definisan, standardizovan i kontrolisan. Kvalitet je kategorija od koje zavisi rad, uspeh i opstanak svake zdravstvene ustanove. Sistem kvaliteta laboratorijskog rada se ostvaruje poštujući nekoliko važnih principa: usmerenosti na korisnike, pružanjem kvalitetne i pravovremene usluge, usavršavanjem i informisanjem, praćenjem razvoja kliničko - biohemijske dijagnostike, uvođenjem savremenih i efikasnih metoda ispitivanja, tačnim i pravovremenim nalazima. Pored kvaliteta podjednako važan faktor je i etika zaposlenih. Osnovno načelo moderne etike je poštovanje života pacijenta. Medicinska etika ima za cilj da profiliše savremenog zdravstvenog radnika u kontekstu odnosa zdravstveni radnik - kolege, zdravstveni radnik - bolesnik, zdravstveni radnik - porodica pacijenta, zdravstveni radnik i zajednica. Sam proces rada u laboratorji protiče kroz tri faze laboratorijsko - dijagnostičkog ispitivanja: pre-analitika (57% rada u laboratoriji otpada na preanalitiku), analitika (25%) i post-analitika (17%). Najveći broj grešaka se dešava u pre-analitičkoj fazi (70%). Na rezultat laboratorijskih uzoraka mogu uticati razliciti faktori. Tako razlikujemo fizioloske varijable (starost, pol, rasa, cirkadijalni ritam, trudnoća, fizička aktivnost, nadmorska visina, pušenje), uzorkovanje krvi i rukovanje uzorcima (transport, stabilnost). Priprema pacijenta pre uzimanja uzorka je neophodna za ispravno određivanje traženih parametara, a podrazumeva stanje pacijenta pre uzimanja uzoraka kao i za vreme uzimanja uzorka. Pravilna priprema pacijenata, uzorkovanje i rukovanje uzorcima nakon venepunkcije je od velikog značaja za dobijanje ispravnog analita za laboratorijska ispitivanja. Ovaj rad ukazuje na značaj komunikacije i edukacije zdravstvenih radnika u cilju dobijanja kvalitetnog uzorka krvi, jer preanaliticka greška ima najveći uticaj na kvalitet laboratorijskih rezultata.

Ključne riječi: *kvalitet; kontrola; laboratorija*

INFLUENCE OF PREANALYTICS ON THE QUALITY OF LABORATORY RESULTS

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Invited speaker

The entire process of laboratory work in all its phases must be defined, standardized and controlled. Quality is a category on which the work, success and survival of any healthcare institution depend. The quality system of laboratory work is realized by adhering to several important principles: focusing on users, providing quality and timely services, training and information, monitoring the development of clinical and biochemical diagnostics, introducing modern and efficient testing methods, accurate and timely findings. In addition to quality, employee ethics is an equally important factor. The basic principle of modern ethics is respect for the life of the patient. Medical ethics aims to profile the modern healthcare worker in the context of the relationship between employee - colleague, employee - patient, employee - patient's family, employee and community.
The actual process of working in the laboratory goes through three phases of laboratory diagnostic testing: pre-analytical (57% of laboratory work is pre-analytical), analytical (25%) and post-analytical (17%). The largest number of errors occurs in the pre-analytical phase (70%). The results of laboratory samples can be influenced by various factors. For example, we distinguish between physiological variables (age, gender, race, circadian rhythm, pregnancy, physical activity, altitude, smoking), blood collection and sample handling (transportation, stability). Patient preparation prior to sample collection is necessary for the correct determination of the required parameters and includes both the patient's condition prior to sample collection and during sample collection. Proper preparation of the patient, collection of the sample and handling of the sample after venipuncture are of great importance for obtaining the correct analyte for laboratory testing. This article demonstrates the importance of communication and education of medical staff to obtain a high quality blood sample, as pre-analytical errors have the greatest impact on the quality of laboratory results.

Keywords: *quality; control; laboratory*

AKTUELNE PROMJENE LEGISLATIVE O VODI ZA PIĆE

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Pozvani predavač

U cilju osiguranja zdravstvene ispravnosti vode za ljudsku potrošnju, nedavno je u Europskoj Uniji, pa tako i u Hrvatskoj, temeljito izmijenjen pravni okvir koji regulira to područje. Promjene su proizašle iz potrebe za unaprjeđenjem zaštite javnog zdravlja, primjenom proširenih i pooštrenih kriterija kvalitete vode, uvođenjem novih obveza za javne isporučitelje i nadležna tijela te tehnološkim razvojem u procesu proizvodnje i obrade vode.

Stoga je 16. prosinca 2020. godine stupila na snagu nova Direktiva (EU) 2020/2184 Europskog parlamenta i Vijeća o kvaliteti vode namijenjene za ljudsku potrošnju (preinaka), što je rezultiralo ažuriranjem nacionalnog zakonodavstva zemalja članica, uključujući Hrvatsku. Ova Direktiva je transponirana u hrvatsko nacionalno zakonodavstvo Zakonom o vodi za ljudsku potrošnju (NN 30/2023), koji posebno ističe potrebu za učinkovitijim informiranjem javnosti.

Provedba zakon osigurana je kroz četiri provedbena akta. Jedan od tih akata definira uspostavu učinkovitog monitoringa parametara kvalitete vode, specificirajući vrstu i opseg analiza, dozvoljene granične vrijednosti te učestalost uzimanja uzoraka. Drugi pravilnik obvezuje isporučitelje vode na izradu i provedbu Planova sigurnosti vode - sustava samokontrole temeljenog na procjeni i upravljanju rizicima u cijelom lancu vodoopskrbe, od područja sliva, zahvaćanja, obrade, skladištenja i distribucije do krajnjeg potrošača. Treći pravilnik za vlasnike prioritetnih objekata uvodi obvezu izrade procjene rizika u kućnoj vodoopskrbnoj mreži, s fokusom na praćenje razine olova i Legionella. Prioritetni objekti uključuju velike javne ustanove poput zdravstvenih ustanova, škola, domova za starije, hotela, kampova, sportskih dvorana i trgovačkih centara. Pri procjeni rizika za ove objekte uzimaju se u obzir broj i osjetljivost izloženih osoba te tip izloženosti. Četvrti pravilnik prvi put u Republici Hrvatskoj uspostavlja minimalne higijenske zahtjeve za materijale koji dolaze u dodir s vodom namijenjenom za ljudsku potrošnju. Postavljeni su zahtjevi za kemikalije koje se koriste u obradi i medije za filtriranje koji dolaze u kontakt s vodom za ljudsku potrošnju.

Provedba navedenih pravnih akata ima za cilj osigurati dostupnost zdravstveno ispravne vode svima, u dovoljnim količinama.

Ključne riječi: *voda za ljudsku potrošnju; Plan sigurnosti vode; procjene rizika u kućnoj vodoopskrbnoj mreži; Legionella; olovo; minimalni higijenski zahtjevi za materijale*

CURRENT CHANGES IN DRINKING WATER LEGISLATION

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In order to ensure the safety of water for human consumption, the legal framework regulating this area has recently been thoroughly revised in the European Union, including Croatia. These changes arose from the need to enhance public health protection through the application of expanded and stricter water quality criteria, introducing new obligations for public water suppliers and competent authorities, and technological advancements in the production and treatment process of water.

Therefore, on December 16, 2020, the new Directive (EU) 2020/2184 of the European Parliament and of the Council on the quality of water intended for human consumption (amendment) came into force, resulting in the updating of the national legislation of member states, including Croatia. This Directive was transposed into Croatian national legislation by the Water Quality for Human Consumption Law no. 46 of 2023, which specifically emphasizes the need for more effective public information.

The implementation of the law is ensured through four implementing acts. One of these acts defines the establishment of an effective monitoring system for water quality parameters, specifying the type and scope of analyses, permissible limits, and the frequency of sample collection. The second regulation obliges water suppliers to develop and implement Water Safety Plans - a self-control system based on risk assessment and risk management throughout the entire water supply chain, from catchment areas, abstraction, treatment, storage, and distribution of water to the end consumer. The third regulation imposes an obligation on owners of priority facilities to conduct risk assessments in the domestic distribution systems, focusing on monitoring levels of lead and Legionella. Priority facilities include large public institutions such as healthcare facilities, schools, nursing homes, hotels, campsites, sports facilities, and shopping centers. When assessing risks for these facilities, the number and sensitivity of exposed individuals and the type of exposure are taken into account. The fourth regulation establishes hygiene requirements for products in contact with water intended for human consumption for the first time in the Republic of Croatia. Requirements are set for chemicals used in treatment and filtration media that come into contact with water intended for human consumption.

The implementation of these legal acts aims to ensure the availability of safe water for everyone in sufficient quantities.

Keywords: *water intended for human consumption, Water Safety Plan, risk assessment of the domestic distribution systems, Legionella, lead, hygiene requirements for products in contact with water intended for human consumption*

LABORATORIJSKA DIJAGNOSTIKA I MORFOLOŠKE KARAKTERISTIKE LIMFOCITA KOD PERTUSISA

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Uvod: Pertussis, poznat i kao veliki kašalj, je akutna zarazna bolest uzrokovana bakterijom *Bordetella pertussis*. Kod beba i male djece, hripavac je posebno opasan i može dovesti do potencijalno fatalnih komplikacija, poput upale pluća, apneje i encefalopatije. CDC preporučuje vakcinaciju protiv velikog kašlja za malu djecu, predtinejdžere, trudnice i nevakcinisane odrasle osobe. Rana dijagnoza i liječenje hripavca izuzetno je važno kako bi se ograničilo širenje bolesti. Laboratorijski testovi kao što su lančana reakcija polimeraze (PCR), kultura i serologija mogu otkriti prisustvo bakterije *B. pertussis*. Ovi testovi su veoma zavisni od vremena koje je prošlo od inicijalne infekcije, pa strategiju testiranja treba razviti u odnosu na vreme početka bolesti. Laboratorijski testovi za dijagnozu hripavca koje preporučuje CDC su hemokultura i PCR.

Cilj: Prikazati laboratorijske dijagnostičke metode za rano otkrivanje bolesti u cilju prevencije, liječenja i ograničavanja širenja bolesti, opis morfoloških karakteristika limfocita u perifernom razmazu, sa kojima se u kratkom vremenskom periodu mogu dobiti podaci o prisutnosti ove bolesti.

Materijal i metode: Bris nazofarinksa, kapilarna krv, Lančana reakcija polimeraze (PCR), diferencijalna krvna slika kapilarne krvi, mikroskopski pregled razmaza periferne krvi.

Rezultati: Apsolutna limfocitoza prisutna je kod >50% pacijenata. Karakteristični mali, zreli limfociti sa hiperkromatskim, rascjepanim jezgrima koji čine čak 56% (12%–56%; medijan, 31%) ukupnih limfocita.

Zaključak: Dobijeni rezultati naglašavaju važnost evaluacije razmaza periferne krvi kao dijagnostičkog alata dok drugi rezultati ne postanu dostupni.

Ključne riječi: *Bordetella pertussis; lančana reakcija polimeraze; limfociti; periferni razmaz*

LABORATORY DIAGNOSTICS AND MORPHOLOGICAL CHARACTERISTICS OF LYMPHOCYTES IN PERTUSSIS

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Introduction: Pertussis, known as whooping cough, is an acute infectious disease caused by the bacterium Bordetella pertussis. In infants and young children, whooping cough is particularly dangerous and can lead to potentially fatal complications such as pneumonia, respiratory failure and encephalopathy. The CDC recommends the pertussis vaccine for infants, adolescents, pregnant women and unvaccinated adults. Early diagnosis and treatment of whooping cough is extremely important to limit the spread of the disease. Laboratory tests such as polymerase chain reaction (PCR), culture and serology can detect the presence of B. pertussis. These tests are highly dependent on the time that has passed since the initial infection. The testing strategy should therefore be developed depending on the time of onset of the disease. The laboratory tests recommended by the CDC for the diagnosis of pertussis are blood cultures and PCR.

Objective: Laboratory diagnostic methods for early detection of the disease in order to prevent, treat and limit the spread of the disease, description of the morphological features of the lymphocytes characteristic of pertussis disease in the peripheral smear to obtain data on the presence of this disease in a short time.

Materials and methods: Nasopharyngeal swab, capillary blood, Polymerase chain reaction (PCR), differential blood count of capillary blood, microscopic examination of peripheral blood smear.

Results: Absolute lymphocytosis in >50% of patients, characteristic small, mature lymphocytes with hyperchromatic, cleft nuclei accounting for up to 56% (12%–56%; median, 31%) of total lymphocytes.

Conclusion: The results obtained emphasize the importance of evaluating the peripheral blood smear as a diagnostic tool until other results are available.

Keywords: *Bordetella pertussis; polymerase chain reaction; lymphocytes; peripheral smear*

DIJAGNOSTIČKI POTENCIJAL HEMATOLOŠKIH DISKRIMINATORNIH INDEKSA U SIDEROPENIČNOJ ANEMIJI I BETA TALESEMIJI

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Uvod: Uz sideropeničnu anemiju (SA), beta talasemija posljednjih decenija postaje sve učestaliji tip anemije na globalnom nivou. Dijagnostika ovih tipova anemija predstavlja značajan izazov u savremenoj laboratorijskoj dijagnostici zbog nedovoljno specifičnih kliničkih karakteristika i zahtjeva za složenim dijagnostičkim testovima. Potreba da se pronađu jednostavniji načini u njihovoj diferencijaciji datira od 1973. godine kada se razvijaju hematološki diskriminatorni indeksi (HDI) koji pokazuju varijabilne rezultate.

Cilj: Ispitati dijagnostički potencijal najčešće korištenih hematoloških diskriminatornih indeksa u sideropeničnoj anemiji i beta talasemiji.

Materijal i metode: Za potrebe ne-eksperimentalnog kvalitativnog tipa istraživanja pregledane su relevantne baze podataka kao što su PubMed, Google Scholar i Web of Science. Pretraživanje je izvršeno korištenjem ključnih riječi "*red blood cell parameters*", "*hematologic discriminatory indices*", "*iron deficiency anemia*" and "*beta-thalassemia*".

Rezultati: Danas je poznato preko 40 HDI baziranih na kombinaciji minimalno dva eritrocitna parametra s ciljem osiguranja veće jedinstvenosti i korisnosti u diferencijalnoj dijagnostici. Poseban akcenat je usmjeren na kombinacije eritrocitnih parametara i širine distribucije eritrocita (RDW), a prijavljene varijacije među rezultatima istraživanja posljedica su nedo-voljne standardizacije u hematološkoj praksi. Faktori koji utječu na interpretaciju rezultata su gegrafska heterogenost, populacione razlike, spol i starosna dob. U prilog navedenom, istraživanja provedena u europskim zemljama pokazuju da je najviši stepen osjetljivosti od 93% i specifičnosti od 90% HDI dobiven kombinacijom srednjeg volumena eritrocita (MCV) i RDW. Nešto niži stepen osjetljivosti i specifičnosti zabilježen u istraživanjima gdje je korištena vrijednost hemoglobina u HDI za diferencijaciju SA od beta talasemije. Iako je ispitana njihova korisnost u razlikovanju beta od alfa talasemije, njihov diskriminatorni potencijal potrebno temeljitije istražiti u slučaju ostalih hemoglobinopatija.

Zaključak: Prednost korištenja HDI je u skriningu suspektne populacije i smanjenju dodatnih zahtjeva za testiranjem, ali ne i u postavljanju definitivne dijagnoze. Imperativ za njihovu primjenu u redovnim praksama je odrediti stepen specifičnosti i osjetljivosti u ispitivanoj populaciji uvažavajući rezultate dosadašnjih istraživanja.

Ključne riječi: *eritrocitni parametri; hematološki diskriminatorni indeksi; sideropenična anemija; beta talasemija*

DIAGNOSTIC POTENTIAL OF HEMATOLOGIC DISCRIMINATORY INDICES IN IRON DEFICIENCY ANEMIA AND BETA–THALASSEMIA

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Introduction: In addition to iron deficiency anemia (IDA), beta-thalassemia has become an increasingly common form of anemia worldwide in recent decades. The diagnosis of these types of anemia represents a major challenge for modern laboratory diagnostics. The need to find simpler methods to differentiate them dates back to 1973, when hematologic discriminatory indices (HDI) were developed.

Objective: To investigate of the diagnostic potential of the most commonly used hematologic discriminatory indices iron deficiency anemia.

Methods and materials: For the purposes of non-experimental qualitative research, databases such as PubMed, Google Scholar and Web of Science were searched. The search was conducted using the keywords "red blood cell parameters", "hematologic discriminatory indices", "iron deficiency anemia" and "beta-thalassemia".

Results: Today, more than 40 HDIs are known based on the combination of at least two red blood cell parameters to provide greater clarity and usefulness in the differential diagnosis. Particular attention is paid to the combination of red cell parameters and red cell distribution width (RDW). The reported discrepancies between the research results are a consequence of insufficient standardization in hematological practice. Factors influencing the interpretation of results include geographical heterogeneity, population differences, gender and age. Studies in European countries show that the highest sensitivity of 93% and specificity of 90% HDI is achieved by tcombination of mean red cell volume (MCV) and RDW. A slightly lower sensitivity and specificity was found in studies that used the hemoglobin value in the HDI to differentiate between IDA and beta-thalassemia and other hemoglobinopathies.

Conclusion: The advantage of using the HDI is to screen the suspect population and reduce the need for additional testing, but not to make a definitive diagnosis. For use in regular practice, it is important to determine the degree of specificity and sensitivity in the population in accordance with the available research.

Keywords: *red blood cell parameters; hematologic discriminatory indices; iron deficiency anemia; beta-thalassemia*

PREDNOSTI I OGRANIČENJA KONVENCIONALNE I AUTOMATIZIRANE MIKROSKOPSKE TEHNIKE KOD LABORATORISKE ISPITIVANJA URINARNOG SEDIMENTA

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Uvod: Laboratorijska dijagnostika urina je u poslednje vreme postala visoko automatizirana, kao i sve druge oblasti laboratoriske analize. Imajući u vidu brzi razvitak tehnologije i laboratorijske dijagnostike, kvalitativna laboratorijska analiza sedimenta urina danas je u potpunosti automatizirana i ima poseban značaj u dijagnostici bubrežnih oboljenja i urinarnog trakta.

Cilj: Napraviti uporedbu prednosti i ograničenja automatizirane mikroskopske tehnike naspram konvencionalne, kao i uloge laboranata u celokupnom procesu pretrage i mikroskopske analize urinarnog sedimenta, posebno u procesu standardizacije celokupnog analitičkog postupaka.

Materijal i metode: Napravljena je mikroskopska analiza sedimenta urina prikupljenih od 50 pacijenata u prethodna tri meseca. Referentna metoda mikroskopske analize sedimenta mokra je akreditirana je prema normi ISO15189:2013 i sudjeluje u vanjskoj kontroli kvalitete - Labquality. Pararelno napravljena je analiza urinarnih sedimenata sa automatiziranom analizatoru: LabUMat 2 i UriSed 3 Pro. Sediment se analizira svjetlosnim mikroskopom i obrađuje digitalnom kamerom. Svaki sporni uzorak se dodatno pregleda manualnom mikroskopijom prema Europskim smjernicama za analizu urina.

Rezultati: Ukupno smo dobili 40 rezultata pretrage urina, od čega je 16 bilo negativno, mikrohematurija (<3 Erc/vid.polju) je pronađena u 10 uzoraka. Patološki elementi (cilindri, kristali, dismorfni eritrociti, bubrežne stanice, lipidi, gljivice) pronađeni su u 10, a bakterije u 14 uzoraka. Svih pozitivnih uzoraka dodatno je pregledano manuelnom mikroskopijom.

Zaključak: Automatizirane mikroskopske ispitivanja urinarnog sedimenta naspram konvencionalne mikroskopske tehnike omogućuju brže laboratoriske petrage i izdavanja rezultate, čime se postiže znatna ušteda vremena i rada, kao i smanjenje učinka subjektivnog rada svakog laboranata i minimaliziranja ljudske greške.

Ključne riječi: *eritrocitni parametri; hematološki diskriminatorni indeksi; sideropenična anemija; beta talasemija*

ADVANTAGES AND LIMITATIONS OF CONVENTIONAL AND AUTOMATED MICROSCOPIC TECHNIQUES

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Introduction: Laboratory diagnostics of urine has recently become highly automated, like all other areas of laboratory analysis. Bearing in mind the rapid development of technology and laboratory diagnostics, the qualitative laboratory analysis of urine sediment is now fully automated and has a special importance in the diagnosis of kidney and urinary tract diseases.

Objective: To compare the advantages and limitations of the automated microscopic technique vs. the conventional one, as well as the role of the laboratory technician in the entire process of investigation and microscopic analysis of urinary sediment, especially in the process of standardization of the entire analytical procedure.

Materials and methods: Microscopic analysis of urine sediment was performed on 50 patient samples in the previous 3 months. The reference method of microscopic analysis of wet sediment is accredited according to ISO15189:2013 and participates in external quality control - Labquality. Urinary sediments were analyzed in parallel with an automated analyzer: LabUMat 2 and UriSed 3 Pro. The sediment is analyzed with a light microscope and processed with a digital camera. Each questionable sample is additionally examined by manual microscopy according to the European guidelines for urine analysis.

Results: We received a total of 50 urine test results. Of them, 16 were negative, microhematuria (< 3 Erc/field of view) was found in 10 urine samples. Pathological elements (cylinders, crystals, dysmorphic erythrocytes, kidney cells, lipids, fungi) were found in 10 urine samples, and bacteria in 14 samples. All positive samples were additionally examined by manual microscopy.

Conclusion: Automated microscopic examinations of urinary sediment compared to conventional microscopic techniques enable fast laboratory tests and issuing results, which achieves significant savings in time and work, as well as reducing the subjective work of each laboratory worker and minimizing human error.

Keywords: *urine; sediment; microscopy; automated microscopic technique*

КУЛТУРА КРВИ КАО ЗЛАТНИ СТАНДАРД ЗА ДЕТЕКЦИЈУ И ИЗОЛАЦИЈУ МИКРООРГАНИЗАМА У КРВИ

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Циљ: Утврђивање динамике броја хемокултура утврђених одређеним индикацијама, као и заступљеност одређених микроорганизама у крви.

Материјал и методе: Узорак културе крви је венска крв. Један сет хемокултура се састоји од једне-Аеробне културе боце (АЕ) и анаеробне (и) културе инокулиране узорком венске крви узето са једног места са венецустер. Бацтец ФКС Аутоматизовани термостат са компатибилним комерцијалним флуидним флуинтским медијумом користи се у микробиолошкој лабораторији за метод изолације бактерија у крви.

Резултати: Из ретроспективне анализе компјутеризованог система који је саставни део. На уређају је забележено укупно 72 позитивних хемокултурала. Најозивишени микроорганизми су врста ентерокока у 91% случајева или у 65 хемокултурама, коагулазе стафилокока негативно у 85% или у 61 хемокултури, *Стафилококус ауреус* у 79% случајева или 57 од 57 произведених хемокултурама и 57% или 5.

Закључак: На основу резултата у истраживању, несумњиво је да се обрада хемокултурама увек мора пажљиво извршити и да се морају поштовати сви кораци. Прави приступ је праве важности који почиње од узимања узорака, као и његова одговарајућа обрада.

Кључне речи: *хемокултуре; микроорганизми; крв*

BLOOD CULTURE AS THE GOLD STANDARD FOR THE DETECTION AND ISOLATION OF MICROORGANISMS IN BLOOD

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Aim: To determine the dynamics of the number of blood cultures performed according to the established indication and the representation of certain microorganisms in the blood.

Material and method: The sample for blood culture is venous blood. One set for blood cultures consists of a vial for aerobic (AE) culture and a vial for anaerobic (AN) culture, which are inoculated with a sample of venous blood from a venipuncture. In the microbiology laboratory, the automated BACTEC FX thermostat is used with a compatible commercial liquid culture medium for methods to isolate bacteria from blood.

Results: From the retrospective analysis of the computerized system, which is an integral part, a total of 72 positive blood cultures were recorded on the device. The most frequently isolated microorganisms were *Enterococcus* species in 91% of the cases or in 65 blood cultures, *Staphylococcus* coagulase-negative in 85% or in 61 blood cultures, *Staphylococcus aureus* in 79% of the cases examined or in 57 prepared blood cultures and Gram-negative bacilli in 73% or in 53 blood cultures.

Conclusion: Based on the results of the study, there is no doubt that the processing of blood cultures must always be carried out with the utmost care and all steps must be followed from the first to the last moment. The correct procedure, starting with the collection of the sample, and its correct processing are of great importance.

Keywords: *blood cultures; microorganisms; blood*

MIKROKLIMATSKI USLOVI U VRTIĆIMA NA PODRUČJU KANTONA SARAJEVO – JAVNOZDRAVSTVENI ASPEKT

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Uvod: Nakon roditeljskog doma, vrtić je najvažnije mjesto boravka djece predškolske dobi. Procjenjuje se da djeca u vrtićima u prosjeku provedu 5 do 7 godina života, 5 do 10 sati dnevno. Poznato je da je to vrijeme intenzivnog psihičkog i fizičkog rasta i razvoja djece. Loša kvaliteta zraka u zatvorenom prostoru (IAQ) ima brojne negativne efekte na zdravlje općenito, utječući na dišni sistem zbog prisutnosti određenih zagađivača zraka iz različitih izvora.
Cilj: S obzirom na veličinu problema i karakteristike geografskog područja Kantona Sarajevo, istraživanje je imalo za cilj dobiti rezultate o kvaliteti zraka u predškolskim ustanovama.
Materijali i metode: Uključeno je pet dječjih vrtića u različitim općinama, sredinama i udaljenostima od glavnih saobraćajnica. Mjereni su nivoi zagađivača zraka i formaldehida. Za mjerenje čestica prašine (PM), formaldehida (HCHO) i ugljen monoksida (CO) korišten je Trotecov brojač čestica PC220 koji omogućuje praćenje i prikupljanje podataka o okolišu direktno na lokaciji. Ugljen dioksid (CO_2), temperatura i relativna vlažnost mjereni su mjeračem kvalitete unutrašnjeg zraka IAQ-Calc 7545. Za mjerenje buke korišten je profesionalni mjerač nivoa buke, Sound level meter PCE-322A sa ugrađenom funkcijom snimanja podataka i mjernim područjem od 30 do 130dB i greškom mjerenja ± 1,4 dB.
Rezultati: Utvrđeno je da su dnevne koncentracije čestica (PM) i nivo buke iznad preporučenih u svim vrtićima. Povišene koncentracije CO2 utvrđene su u četiri objekta, a povišene koncentracije formaldehida u jednom objektu.
Zaključak: Naši rezultati sugerišu da su zdravlje i opća dobrobit djece predškolske dobi ugroženi zbog lošeg IAQ-a. Postoji hitna potreba za donošenjem realnih strategija i akcijskih planova za poboljšanje životnih uslova djece predškolske dobi kako bi se smanjio rizik od štetnih efekata na zdravlje.

Ključne riječi: *kvaliteta zraka u zatvorenim prostorima; zagađivači zraka; predškolske ustanove; zdravlje*

MICROCLIMATE CONDITIONS IN KINDERGARTEN IN THE AREA OF SARAJEVO CANTON – PUBLIC HEALTH ASPECT

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Introduction: After the parental home, kindergarten is the most important place of residence for children of preschool age. It is estimated that children spend an average of 5 to 7 years of their lives in kindergartens, 5 to 10 hours a day. It is known that this is a time of children's intense psychological and physical growth and development. Poor indoor air quality (IAQ) has numerous negative effects on health in general, affecting the respiratory system due to the presence of certain air pollutants from various sources.
Objective: Considering the magnitude of the problem and characteristics of the geographic area of Sarajevo Canton, the study aimed to obtain results on IAQ in preschool institutions.
Materials and methods: Five kindergartens in different municipalities, environments, and distances from main roads were included. The levels of air pollutants and formaldehyde were measured. A Trotec Particle counter PC220 was used to measure dust particles (PM), formaldehyde (HCHO) and carbon monoxide (CO), which enables monitoring and collection of environmental data directly on location. Carbon dioxide (CO_2), temperature and relative humidity were measured with the Indoor Air Quality Meter IAQ-Calc 7545. A professional noise level meter, Sound level meter PCE-322A with a built-in data recording function and a measurement range of 30 to 130dB and a measurement error of ± 1.4 dB, was used to measure noise.
Results: Daily particulate matter (PM) concentrations and noise levels were found to be above recommended levels in all kindergartens. Higher CO_2 concentrations were found in four facilities and elevated formaldehyde concentrations in one facility.
Conclusion: Our results suggest that the health and general well-being of preschool-aged children are at risk from poor IAQ. There is an urgent need for the adoption of realistic strategies and action plans to improve the living conditions of preschool-aged children to reduce the risk of adverse health effects.

Keywords: *indoor air quality; air pollutant; preschool institutions; health*

POJAVA VELIKOG KAŠLJA U REPUBLICI SJEVERNA MAKEDONIJA – EPIDEMIJA UZROKOVANA SMANJENIM OBUHVATOM IMUNIZACIJE

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Uvod: Veliki kašalj (pertussis) je akutna, zarazna respiratorna bolest koju karakteriziraju napadi kašlja, uzrokovane bakterijom Bordetella pertussis. Novorođenčad i necijepljena odojčad su u najvećem riziku od bolesti i komplikacija, iako se ljudi svih uzrasta mogu razboljeti.

Cilj: Prikazati obim imunizacije u Republici Sjevernoj Makedoniji i pojavu epidemije velikog kašlja.

Rezultati: Pokrivenost primarnom vakcinacijom i revakcinacijom u Republici Sjeverna Makedonija u 2022., već treću godinu zaredom je ispod 90%. U proteklom periodu od 20 godina, do 2020. godine, nije registrovan obuhvat ispod 90% primarnom vakcinacijom (osim HPV vakcine). U RSM su zaključno sa 29.02.2024. godine registrovana su ukupno 173 slučaja velikog kašlja, sa incidencijom od 9,4/100.000 stanovnika. Od ukupnog broja registrovanih slučajeva (173), 102 slučajeva (ili 58,0%) nije vakcinisano. Od slučajeva koji su potpuno vakcinisani (n=56), prosječno proteklo vrijeme od posljednje doze vakcine do bolesti je 11,9 godina.

Zaključak: Trend smanjenja obuhvata obaveznom vakcinacijom povećava rizik od pojava epidemija vakcino-preventabilnih bolesti, kao što je porast broja slučajeva velikog kašlja i pojava morbila u prethodnom periodu.

Ključne riječi: *veliki kašalj; epidemija; Republika Sjeverna Makedonija*

EMERGENCE OF WHOOPING COUGH IN THE REPUBLIC OF NORTH MACEDONIA – EPIDEMIC CAUSED BY REDUCED IMMUNIZATION COVERAGE

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Introduction: Whooping cough (pertussis) is an acute, infectious respiratory disease characterized by coughing fits, caused by a type of bacteria called Bordetella pertussis. Newborns and unvaccinated infants are at the highest risk of disease and complications, although people of all ages can get sick

Objective: To show the scope of immunization in the Republic of North Macedonia and the occurrence of whooping cough epidemic.

Results: Primary vaccination and revaccination coverage in the Republic of North Macedonia in 2022 is below 90% for the third year in a row. In the past 20 years, until 2020, coverage below 90% by primary vaccination (except HPV vaccine) was not registered. They are in RSM as of February 29, 2024. A total of 173 cases of whooping cough were registered, with an incidence of 9.4/100,000 inhabitants. Out of the total number of registered cases (173), 102 cases (or 58.0%) were not vaccinated. Of the cases who were fully vaccinated (n=56), the average time elapsed from the last dose of vaccine to disease was 11.9 years.

Conclusion: The trend of reducing coverage by mandatory vaccination increases the risk of outbreaks of vaccine-preventable diseases, such as the increase in the number of cases of whooping cough and the occurrence of measles in the previous period.

Keywords: *whooping cough; epidemic; Republic of North Macedonia*

KOMUNIKACIJA I MEĐULJUDSKI ODNOSI

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Uvod: Komunikacija je vrlo složen proces razmjene informacija, najčešće putem jezika. Obično je opisana prema tri glavne dimenzije: sadržaju, formi i cilju. Zajedno, sadržaj komunikacije i forma kreiraju poruke koje se šalju prema cilju. Iako nisu toga svjesni, ljudi redovno unose prepreke u svoju komunikaciju s drugim ljudima. Procijenjeno je da ove prepreke čine oko 90% konverzacije kad jedna ili obje strane imaju problem koji treba riješiti ili neku potrebu koju žele zadovoljiti. Najčešće se dešava da se sagovornik ne sluša, što dovodi do problema kako u samoj komunikaciji tako i interpersonalnim odnosima. Umjeće slušanja podrazumijeva mnogo toga i zapravo je posebna tehnika koja ne uključuje samo naše uši, nego i aktivnu koncentraciju i razmišljanje.
Cilj: Unaprjeđenje komunikacijskih vještina sa pacijentima i kolegama.
Materijali i metode: Aktivnim slušanjem bolje ćemo razumjeti sagovornika, spoznajući ko je i kakva su mu očekivanja. Osnovni princip je stavljanje sagovornika u fokus i razumijevanje njegovih problema. Ukupnu komunikaciju čini 70% neverbalna, a samo 30% verbalna komunikacija. Ključ razumijevanja nečijeg autentičnog ponašanja često je upravo u neverbalnoj komunikaciji. Potrebno je posvetiti pažnju našem govoru tijela i onome što poručujemo osobi sa kojom komuniciramo. Vještina komunikacije je u tome da aktivno slušamo da bismo adekvatno odgovorili, dajemo povratne informacije koje su jasne i kratke, uzimamo odnos u obzir i razumijevamo o čemu se u odnosu radi, prilagođavamo se, vodimo računa o kontekstu, predmetu razgovora i imamo u vidu ono što je između rečenog i ono što treba razumije.
Rezultati: Aktivnim slušanjem i asertivnim načinom komunikacije mi postajemo sposobni da oslušnemo druge i uvidimo njihove stavove, želje i potrebe. Ne treba podrazumijevati šta je druga osoba htjela reći, dok to ne bude izrečeno.
Zaključak: Uspješna komunikacija predstavlja razumijevanje različitosti ljudi, a učinkovita asertivna komunikacija predstavlja umjetnost jasnog i iskrenog izražavanja, izražavanje vlastitog mišljenja te pozitivnih i/ili negativnih osjećaja.

Ključne riječi: *prepreke u komunikaciji; aktivno slušanje; asertivna komunikacija*

COMMUNICATION AND INTERPERSONAL RELATIONSHIPS

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Introduction: Communication is a very complex process of exchanging information, which usually takes place via language. It is usually described in terms of three main dimensions: Content, form and purpose. The content and form of communication together make up the messages that are sent to the target. Although they are not aware of it, people regularly build obstacles into their communication with other people. It is estimated that these obstacles make up about 90% of the conversation when one or both parties have a problem that needs to be solved or a need that they want to satisfy. The most common is not listening to the other party, which leads to problems both in the communication itself and in interpersonal relationships. The art of listening encompasses many things and is actually a special technique that involves not only our ears, but also our active concentration and thinking.
Objective: Improving communication skills with patients and colleagues.
Materials and methods: By actively listening, we can better understand the other person and find out who they are and what their expectations are. The basic principle is to put the other person at the center of the conversation and understand their problems. 70% of all communication is non-verbal and only 30% is verbal. The key to understanding a person's authentic behavior often lies precisely in non-verbal communication. It is necessary to pay attention to our body language and what we say to the person we are talking to. The art of communication consists of actively listening in order to respond appropriately, giving clear and brief feedback, considering the relationship and understanding what the relationship is about, adapting, paying attention to the context and topic of the conversation and keeping in mind what lies between what is said and what is intended to be understood.
Results: Active listening and a confident way of communicating will enable us to listen to others and recognize their attitudes, desires and needs. We should not assume what the other person means until they have said it.
Conclusion: Successful communication is an understanding of the diversity of people, and effective confident communication is the art of expressing oneself clearly and honestly and expressing one's opinion as well as positive and/or negative feelings.

Keywords: *obstacles in communication; active listening; assertive communication*

ИЗАЗОВИ У ИДЕНТИФИКАЦИЈИ МУЛТИПЛИХ АНТИТЕЛА

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Увод: Трансфузија крви је уобичајена медицинска процедура. Изводи се за лечење дуготрајних болести, током дате хоспитализације или у хитним случајевима, иако често спасавају живот, трансфузије нису без ризика. Неки можда нису забрињавајући, а други могу бити опасни по живот. Ретка компликација је изненадна имунолошка реакција која се јавља када имуни систем особе која прима крв нападне трансфузована крвна зрнца, са могућношћу развоја антитела на црвена крвна зрнца, посебно код вишеструких трансфузија, што може бити клинички значајно. Стога је заштита примаоца од нежељених реакција трансфузије услед сензибилизације на антиген црвених крвних зрнаца један од изазова за безбедну трансфузију крви.

Циљ: Представити нове могућности за идентификацију вишеструких антитела на црвеним крвним зрнцима код пацијената са политрансфузијом.

Резултати: Пацијент 1: 50-годишњи хематолошки пацијент, политрансфузиран са позитивним унакрсним подударањем са 30 јединица еритроцита и 1 негативним. Детекција и идентификација антитела је показала позитивну реакцију из серума и елуата. Урађена је типизација антигена. Истраживања су се односила на присуство топлих и хладних више антитела, једног анти-Фиа и вероватно анти-Е+ц, али ЦМ је и даље био позитиван. Пацијент 2: 66-годишњи мушки хематолошки пацијент, политрансфузован, са позитивним унакрсним подударањем са 20 јединица еритроцита и 2 негативна. Одређивање и идентификација антитела је показала позитивну реакцију, само је ДАТ негативан. Тестирање серума је показало присуство више антитела, једног анти-С, али друге специфичности нису могле бити идентификоване чак ни након типизације РБЦ антигена. Оба пацијента су регистрована у софтверу ИХ-АбИД (БиоРад) и добијени су различити резултати. За пацијента 1: анти-Фиа + Јка алоантитело, хладно алоанти-П1 и аутоантитело С из елуата, а за пацијента 2 су идентификована алоантитела С, Е и К.

Закључак: ИХ-АбИД софтвер, као помоћно средство, пружа кориснику упутства и информације за идентификацију антитела на антигене црвених крвних зрнаца. Овај софтвер олакшава идентификацију више антитела на црвена крвна зрнца код пацијената са политрансфузијом и омогућава брже решавање проблема код сензибилизованих пацијената, омогућавајући благовремену и квалитетну трансфузијску терапију.

Кључне речи: *трансфузија; антитела и антигени црвених крвних зрнаца*

CHALLENGES IN IDENTIFICATION OF MULTIPLY ANTIBODIES

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Introduction: Blood transfusion is a common medical procedure. It is performed to treat long-term illnesses, during a given hospitalization, or in medical emergencies. Although often life-saving, transfusions are not without risk. Some may not be worrisome and others may be life-threatening. A rare complication is a sudden immune reaction that occurs when the immune system of the person receiving the blood attacks the transfused blood cells, with the possibility of developing antibodies to the red blood cells, especially in multiples, which can be clinically significant. Therefore, protecting the recipient from adverse transfusion reactions due to sensitization against red blood cell antigen is one of the challenges of safe blood transfusion.

Objective: To present multiple possibilities in identification of multiple red blood cells antibodies in polytransfused patients.

Results: Patient 1: female 50 years old hematology patient, polytransfused with positive crossmatch (CM) in 30 RBC units and 1 negative. Detection and identification of antibodies showed positive reaction of serum from serum and eluate. Antigen typing was provided. Examinations associates on presence of warm and cold multiple antibodies, one anti-Fya and probably anti-E+s. But after all, the CM were still positive Patient 2: male 66 years old hematology patient, polytransfused, with positive cross match (CM) in 20 RBC units and 2 negative. Detection and identification of antibodies showed positive reaction, only DAT was negative. Testing the serum showed presence of multiple antibodies, one anti-S but no other specifity could be identified, even after the RBC antigen typing. We retested the both patients on software IH-AbID (BioRad) and we get different results for patient 1: alloantibody anti-Fya + Jka, cold aloanti-P1 and autoantibody S from eluate. For the patient 2 were identified alloantibody S, E and K.

Conclusion: The IH-AbID software, as a help tool, provides the user with guidance and information for the identification of antibodies to antigens on red blood cells. This software facilitates the identification of more antibodies to red blood cells in patients with polytransfusion and enables quick resolution of problems in sensitized patients, enabling timely and quality transfusion therapy.

Keywords: *transfusion; antibodies and antigens of red blood cells*

EVALUACIJA INDIREKTNIH INDEKSA U PROCJENI INZULINSKE REZISTENCIJE U OPĆOJ POPULACIJI

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Uvod: Iako se smatra "zlatnim standardom" za kvantifikaciju inzulinske osjetljivosti i procjenu inzulinske rezistencije (IR), tehnika hiperinzulinemijsko-euglikemijske kleme rijetko se koristi u rutinskoj kliničkoj praksi zbog komplicirane, dugotrajne i skupe tehničke izvedbe. Danas su u upotrebi dijagnostički pristupi koji uključuju različite laboratorijske parametre, ali se u praksi sve više koriste jednostavni i neinvazivni indeksi zasnovani na matematičkim modelima koji su primjenjivi za velika populaciona istraživanja.
Cilj: Utvrditi efikasnost različitih indirektnih indeksa u procjeni IR u općoj populaciji prema vrijednostima indeksa tjelesne mase (BMI).
Materijali i metode: U presječnu deskriptivno-analitičku studiju uključena su 123 ispitanika, od kojih je 91 ispitanik imao potvrđenu dijagnozu IR. Ova grupa je naknadno stratificirana na osnovu vrijednosti BMI u dvije podgrupe. Koristeći laboratorijske podatke, izračunali smo vrijednosti za šest kliničkih surogat markera: homeostatski model procjene IR (HOMA-IR), kvantitativni indeks provjere osjetljivosti na inzulin (QUICKI), McAuleyjev indeks (MCAi), metabolički rezultat za IR (METS-IR), indeks triglicerida i glukoze (TyG) i indeks TyG i BMI (TyG-BMI).
Rezultati: Uočene su značajne razlike u nivoima HOMA-IR između grupa (p <0,001). Sličan obrazac je pronađen za indeks TyG-BMI, sa statistički značajnim razlikama (p <0,001). Pretili ispitanici su imali najveće srednje vrijednosti za METS-IR i TyG indeks, dok je kontrolna grupa imala najveće srednje vrijednosti za QUICKI i MCAi indekse (p <0,001). Prema analizi, tri indeksa su pokazala statističku značajnost u predviđanju IR nezavisno od BMI (p <0,05).
Zaključak: Imajući u vidu da je IR složeno multifaktorsko stanje, vjerujemo da korištenje indeksa zasnovanih na kombinaciji lipidnih parametara i antropometrijskih pokazatelja kao što je BMI može značajno doprinijeti prognozi i smanjenju brojnih komplikacija što pokazuje TyG-BMI indeks u našoj studiji. U bliskoj budućnosti potrebno je istražiti i prilagoditi potencijal drugih antropometrijskih indikatora u kombinaciji sa izvedenim indeksima u većim populacionim istraživanjima.
Ključne riječi: *inzulinska rezistencija; HOMA-IR; TyG; TyG-BMI*

EVALUATION OF INDIRECT INDICES IN THE ASSESSMENT OF INSULIN RESISTANCE IN THE GENERAL POPULATION

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Introduction: Although it is considered the "golden standard" for quantifying insulin sensitivity and assessing insulin resistance (IR), the hyperinsulinemic-euglycemic clamp technique is rarely used in routine clinical practice due to complicated, time-consuming, and expensive technical implementation. Today, diagnostic approaches involving different laboratory parameters are available, but simple and non-invasive indices based on mathematical models are increasingly used in practice and applicable for large population research.
Objective: To determine the effectiveness of different indirect indices in assessing IR in the general population according to body mass index (BMI).
Materials and methods: In a cross-sectional descriptive-analytical study, 123 subjects were included, of which 91 had a confirmed diagnosis of IR. This group was subsequently stratified based on BMI scores into two subgroups. Using laboratory data, we calculated values for six widely used clinical surrogate markers: Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), Quantitative Insulin Sensitivity Check Index (QUICKI), McAuley index (MCAi), Metabolic Score for IR (METS-IR), Triglyceride-Glucose index (TyG) and TyG and BMI index (TyG-BMI).
Results: Significant differences in HOMA-IR levels were observed between groups (p <0.001). A similar pattern was found for the TyG-BMI index, with statistically significant differences (p <0.001). Obese subjects had the highest mean values for METS-IR and TyG index, while the control group had the highest mean values for QUICKI and MCAi indices (p <0.001). According to the analysis, three indices showed statistical significance in predicting IR independently of BMI (p <0.05).
Conclusion: Considering that IR is a complex multifactorial condition, we believe that the use of indices based on a combination of lipid parameters and anthropometric indicators such as BMI can significantly contribute to the prognosis and reduction of numerous complications. This was demonstrated by TyG-BMI in this study. Shortly, it is necessary to investigate and adjust the potential of other anthropometric indicators in combination with derived indices in larger population surveys.

Keywords: insulin resistance; HOMA-IR; TyG; TyG-BMI

INOVACIJE NASTAVNOG PLANA I PROGRAMA ODSEKA LABORATORIJSKIH TEHNIČARA U REPUBLICI SRBIJI

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Inovacije u nastavnom planu i programu predstavljaju ključni element u osiguravanju relevantnog obrazovanja koje prati potrebe tržišta rada i društva u celini. Na osnovu inoviranih standarda kvalifikacija, stručna znanja, veštine, sposobnosti i stavovi neophodni za laboratorijskog tehničara su sistematski integrisani u nastavni plan. Ovim pristupom omogućava se ne samo zapošljavanje već i dalji akademski napredak. Nastavni plan za obrazovni profil laboratorijskog tehničara razvijen je nakon pažljivog razvrstavanja ishoda na predmete i sačinjivanja odgovarajućeg fonda časova. Ovaj plan u skladu je sa zakonskim zahtevima, kao što je Član 6. Zakona o srednjem obrazovanju i vaspitanju, koji propisuje da plan i program nastave četvorogodišnjeg stručnog obrazovanja mora sadržati određeni procenat opštih i stručnih oblasti. Konkretno, ovaj plan podrazumeva 40% opšteg i najmanje 55% stručnog obrazovanja, osiguravajući tako balansiran pristup razvoju učenika. Ključne kompetencije koje se ističu prema Pravilniku o opštim standardima postignuća su vitalne za svakog srednjoškolca. Saradnja, digitalna kompetencija, preduzimljivost i preduzetnička kompetencija, odgovoran odnos prema zdravlju i okolini, sve su to veštine i stavovi koji se aktivno razvijaju kroz inovirani nastavni plan.
Ovim inovativnim pristupom, obrazovne institucije pružaju sveobuhvatan i relevantan program koji ne samo da oprema učenike sa potrebnim veštinama za uspeh u laboratorijskom okruženju, već ih takođe osnažuje da budu odgovorni članovi društva, spremni za buduće izazove i mogućnosti na tržištu rada.

Ključne riječi: *nastavni plan i program; laboratorijski tehničar; kompetencije*

INNOVATIONS OF THE CURRICULUM AND PROGRAM OF THE DEPARTMENT OF LABORATORY TECHNICIANS IN THE REPUBLIC OF SERBIA

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Innovation in curricula is a key element in ensuring relevant education that is aligned with the needs of the labor market and society as a whole. Based on innovative qualification standards, the professional knowledge, skills, abilities and attitudes required for a laboratory technician are systematically integrated into the curriculum. This approach enables not only employment, but also further academic progression. The curriculum for the laboratory technician training profile has been developed after a careful division into subjects and the creation of an appropriate pool of lessons. This plan is in line with legal requirements, such as Article 6 of the Law on Secondary Education, which stipulates that the four-year vocational training curriculum must include a certain percentage of general and vocational areas. Specifically, this plan includes 40% general education and at least 55% vocational education, thus ensuring a balanced approach to student development. The key competencies highlighted in the General Achievement Standards framework are essential for every high school student. Collaboration, digital literacy, entrepreneurship and business skills, a responsible approach to health and the environment - these are all skills and attitudes that are actively developed through the innovative curriculum.
With this innovative approach, the educational institutions provide a comprehensive and relevant program that not only equips students with the necessary skills to succeed in a laboratory environment, but also empowers them to be responsible members of society ready for future challenges and opportunities in the job market.

Keywords: c*urriculum; laboratory technician; competencies*

KOMPARACIJA SERUMSKOG TESTOSTERONA I ANDROSTENDIONA KOD ŽENA SA I BEZ SINDROMA POLICISTIČNIH JAJNIKA

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Uvod: Sindrom policističnih jajnika (PCOS) je uobičajeno hormonsko stanje koje pogađa žene u reproduktivnom dobu, karakterizirano hormonskom neravnotežom, neredovnim menstruacijama, viškom androgena i cistama na jajnicima. Iako uzrok nije potpuno razumljiv, rizik od PCOS-a povezan je s porodičnom anamnezom i dijabetesom tipa 2. Simptomi mogu uključivati nepravilne menstruacije, neplodnost, akne, pojačanu dlakavost, gubitak kose i prekomjerno debljanje, te povećan rizik od drugih zdravstvenih problema poput dijabetesa, visokog krvnog pritiska i srčanih bolesti.

Cilj: Prikazati i komparirati razliku u razini serumskog testosterona i androstendiona kod žena s sindromom policističnih jajnika i žena bez sindroma policističnih jajnika.

Materijali i metode: Ovaj rad predstavlja neekperimentalno – kvalitativno istraživanje, odnosno naučni pregled literature.

Rezultati: Rezultati pregleda literature ukazuju na nekoliko važnih saznanja o PCOS. Povećani omjer testosterona i androstendiona u serumu kod žena sa PCOS normalne težine može biti marker za metaboličku funkciju. Androstendion se pokazao kao značajan biomarker za hiperandrogenizam kod pacijenata sa PCOS. Hiperandrogenizam je bio dominantna biohemijska abnormalnost kod žena sa PCOS, pri čemu su nivoi testosterona ostali visoki.Testosteron i androstendion su bili značajno viši kod žena sa PCOS u poređenju s kontrolnom grupom. Povišeni nivoi slobodnog testosterona bili su povezani sa dijabetesom tipa 2 kod žena. Omjer androstendiona prema slobodnom testosteronu bio je povezan s povoljnim metaboličkim profilom kod žena sa PCOS. Visoka prevalenca akni bila je primijećena kod žena sa PCOS, što naglašava važnost dermatološke evaluacije. Ovi rezultati naglašavaju raznolikost manifestacija PCOS i potrebu za holističkim pristupom u dijagnostici i upravljanju ovim stanjem.

Zaključak: Istraživanja su pokazala da žene sa PCOS imaju statistički značajno povećane nivoe testosterona i androstendiona u serumu u poređenju sa ženama koje nemaju ovaj sindrom. S druge strane, žene koje nemaju PCOS imaju normalne ili niže nivoe testosterona i androstendiona u serumu, što je u skladu s njihovim normalnim reproduktivnim funkcijama.

Ključne riječi: *sindrom policističnih jajnika; testosteron; androstendion*

COMPARISON OF SERUM TESTOSTERONE AND ANDROSTENEDIONE IN WOMEN WITH AND WITHOUT POLYCYSTIC OVARY SYNDROME

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Introduction: Polycystic ovary syndrome (PCOS) is a common hormonal condition affecting women of reproductive age, characterized by hormonal imbalance, irregular periods, androgen excess, and ovarian cysts. Although the cause is not fully understood, the risk of PCOS is associated with a family history and type 2 diabetes. Symptoms can include irregular periods, infertility, acne, increased hairiness, hair loss and excessive weight gain, and an increased risk of other health problems such as diabetes, high blood pressure and heart disease.

Objective: To show and compare the difference in the level of serum testosterone and androstenedione in women with polycystic ovary syndromE and women without polycystic ovary syndrome.

Materials and methods: This work represents a non-experimental - qualitative research, that is, a scientific review of the literature.

Results: The results of this literature review indicate several important findings about PCOS. An increased ratio of serum testosterone to androstenedione in women with PCOS of normal weight may be a marker for metabolic function. Androstenedione has been shown to be a significant biomarker for hyperandrogenism in PCOS patients. Hyperandrogenism was the dominant biochemical abnormality in women with PCOS, with testosterone levels remaining high. Testosterone and androstenedione were significantly higher in women with PCOS compared to the control group. Elevated free testosterone levels were associated with type 2 diabetes in women. The ratio of androstenedione to free testosterone was associated with a favorable metabolic profile in women with PCOS. A high prevalence of acne was observed in women with PCOS, which emphasizes the importance of dermatological evaluation. These results highlight the diversity of PCOS manifestations and the need for a holistic approach in the diagnosis and management of this condition.

Conclusion: Studies have shown that women with PCOS have statistically significantly increased levels of testosterone and androstenedione in serum compared to women without this syndrome. On the other hand, women without PCOS have normal or lower serum levels of testosterone and androstenedione, which is consistent with their normal reproductive functions.

Keywords: *polycystic ovary syndrome; testosterone; androstenedione*

PROCJENA RIZIKA RADNIH MJESTA – BIOLOŠKE ŠTETNOSTI

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Procjena rizika je ključni instument za provođenje sigurnosti i zaštite zdravlja na radu. Kvalitet zraka u zatvorenom prostoru je kvalitet zraka unutar i oko same zgrade kao i objekta. Poznato je da IAQ utiče na zdravlje, udobnost i dobrobit osobe koja u njima borave. Loš kvalitet vazduha u zatvorenom prostoru povezan je sa sindromom bolesne zgrade, smanjenom produktivnošću i oštećenim učenjem u obrazovnim ustanovama. SZO je 1986. godine definisala sindrom bolesne zgrade kao skup bolesti izazvanih ili stimulisanih zagađenjem vazduha u zatvorenim prostorima. U slučaju prisustva bolesti koje se javljaju nakon ili u toku boravka u zgradama sa pristunim kontaminantima u vazduhu radi se o tzv.oboljenjima povezanih sa zgradama (eng. *Buliding related Ilness*- BRL). Loš kvalitet zraka povezan je sa simptomima poput glavobolje, umora, problema s koncentracijom i iritacija očiju, nosa, grla i pluća. S obzirom da zaposleno osoblje tokom radnog vremena boravi u zatvorenom prostoru, cilj istraživanja bio je pratiti vrijednosti i prisutnost mikrobioloških pokazatelja u radnom okolišu (zraku) te odrediti mikrobiološki kvalitet zraka unutar radnih prostorija. Mjerenjem bioloških štetnosti radnog prostora ciljano se dolazi do utvrđenog broja i vrste mikroorganizama, te njihovog direktnog ili indirektnog opasnog djelovanja na zdravlje radnika. Za određivanje nivoa prisutnosti mikroorganizama sa bilo koje radne površine upotrebljava se Metoda brisa - BAS EN ISO 18593:2019, Horizontalna metoda za detekciju i određivanje broja Enterobacteriaceae - BAS EN ISO 21528-2:2018, Detekcija i brojanje plijesni - Uzorkovanje udarima - BAS ISO 16000-18:2013, Prema Sanitarnim standardima Europske komisije za neindustrijske prostore, prema smjernicama American Conference of Govermental Industrial Hygienists, Pravilnik o učestalosti kontrole i normativima mikrobiološke čistoće u objektima pod sanitarnim nadzorom (nn.hr). Iako je prevencija rizika uvijek najvažniji cilj, u praksi to nije uvijek moguće ostvariti u punom obimu. Kada rizik nije moguće eliminisati, treba ga što je moguće više smanjiti, a preostali rizik staviti pod kontrolu.

Ključne riječi: *procjena rizika; zaštita zdravlja; kvalitet zraka; biološke štetnosti; radni prostor; mikroorganizmi*

RISK ASSESSMENT OF WORKPLACES – BIOLOGICAL HAZARDS

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Risk assessment is a key instrument for implementing safety and health protection at work. Indoor air quality is the air quality inside and around the building itself as well as the facility. It is known that IAQ affects the health, comfort and well-being of the people who stay in them. Poor indoor air quality is associated with sick building syndrome, reduced productivity and impaired learning in educational institutions. In 1986, WHO defined sick building syndrome as a set of diseases caused or stimulated by air pollution in closed spaces. In the case of the presence of diseases that occur after or during a stay in buildings with contaminants in the air, these are also called building-related illnesses (BRL). Poor air quality is associated with symptoms such as headaches, fatigue, concentration problems and irritation of the eyes, nose, throat and lungs. Given that the employed staff stays indoors during working hours, the goal of the research was to monitor the values and presence of microbiological indicators in the working environment (air) and to determine the microbiological quality of the air inside the working premises. By measuring the biological hazards of the workplace, the determined number and type of microorganisms, as well as their direct or indirect dangerous effect on the health of the workers, is determined. To determine the level of the presence of microorganisms from any work surface, the swab method is used - BAS EN ISO 18593:2019, Horizontal method for detection and determination of the number of Enterobacteriaceae - BAS EN ISO 21528-2:2018, Detection and counting of molds - Impact sampling - BAS ISO 16000-18:2013, According to the Sanitary Standards of the European Commission for non-industrial premises, according to the guidelines of the American Conference of Governmental Industrial Hygienists (ACGIH), Rulebook on the frequency of control and norms of microbiological cleanliness in facilities under sanitary supervision (nn.hr). Although risk prevention is always the most important goal, in practice it is not always possible to achieve it in full. When the risk cannot be eliminated, it should be reduced as much as possible, and the remaining risk should be brought under control.

Keywords: *risk assessment; health protection; air quality; biological hazards; work space; microorganisms*

PLAZMOCITNA LEUKEMIJA KAO IZAZOV U LABORATORIJSKOJ DIJAGNOSTICI

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Uvod: Plazmocitna leukemija (PL), predstavlja rijedak, ali izuzetno agresivan oblik proliferativnog oboljenja plazma ćelija. U 70% slučajeva, bolest se manifestira kao primarni tip, dok se sekundarni tip pojavljuje u 40% slučajeva kao posljedica leukemijske transformacije multiplog mijeloma. Originalni dijagnostički kriteriji postavljeni 1974. godine nisu se značajnije mijenjali, što je tokom vremena rezultiralo brojnim dilemama u kliničkoj praksi i naučnoj zajednici. Kao posljedica nedovoljno specifičnih kliničkih pokazatelja, PL predstavlja jedan od najozbiljnijih izazova u laboratorijskoj hematologiji.

Cilj: Predstaviti trenutni pristup u laboratorijskoj dijagnostici plazmocitne leukemije.

Materijal i metode: Za potrebe ne-eksperimentalnog kvalitativnog tipa istraživanja pregledane su relevantne baze podataka kao što su PubMed (Medline) i Google Scholar. Pretraživanje je izvršeno uz pomoć ključnih riječi na engleskom jeziku „*plasma leukemia*", „*plasma cell dyscrasia*", "*laboratory diagnostics*".

Rezultati: Brojna istraživanja potvrđuju da ograničenja u dijagnostici PL proizilaze iz niza faktora kao posljedica heterogene prirode oboljenja. Dijagnoza PL se primarno postavlja na osnovu morfološke dijagnostike kojom se procjenjuje prisutnost neoplastičnih plazma ćelija u krvi i koštanoj srži. Međutim, rezulati istraživanja ističu da ne postoji jasan konsenzus za postavljanje dijagnoze PL. Uočeno je da postotak cirkulirajućih plazma ćelija u perifernoj krvi varira između 10% do 79% ovisno o kliničkom slučaju. Zbog toga, uočena je potreba za kreiranjem jedinstvenog dijagnostičkog algoritma koji će se bazirati na integraciji većeg broja savremenih metoda kao što su imunofenotipizacija, citogenetička analiza i molekularna dijagnostika.

Zaključak: Sveobuhvatan pristup dijagnostici, koji uključuje širok spektar različitih metoda ključan je za dijagnozu PL. Iako morfološka dijagnostika predstavlja primarni pristup u dijagnostici PL, implementacija savremenih dijagnostičkih metoda može pružiti dodatna saznanja o patogenezi bolesti i potencijalno imati implikacije na prognozu i razvoj personalizirane medicine.

Ključne riječi: *plazmocitna leukemija; plazma ćelije; diskrazija plazma ćelija; laboratorijska dijagnostika*

PLASMA CELL LEUKEMIA AS A CHALLENGE FOR LABORATORY DIAGNOSTICS

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Introduction: Plasma cell leukemia (PCL) is a rare but extremely aggressive form of proliferative plasma cell disease. The disease manifests as a primary type in 70% of cases, with the secondary type arising from a leukemic transformation of multiple myeloma in 40% of cases. The original diagnostic criteria from 1974 have not changed significantly, which has led to numerous dilemmas in clinical practice and in the scientific community over time. Due to insufficiently specific clinical indicators, PL represents one of the greatest challenges in laboratory hematology.

Objective: To present the current approach for laboratory diagnosis of plasma cell leukemia.

Methods and materials: As part of a non-experimental qualitative research, the available literature was reviewed in relevant databases such as PubMed (Medline) and Google Scholar using the keywords „*plasma leukemia*", „*plasma cell dyscrasia*", "*laboratory diagnostics*".

Results: Numerous studies confirm that the diagnosis of PCL is limited by various factors due to the heterogeneous nature of the disease. The diagnosis of PCL is primarily made on the basis of morphologic diagnosis, which evaluates the presence of neoplastic plasma cells in the blood and bone marrow. The percentage of circulating plasma cells in the peripheral blood varies between 10% and 79% depending on the clinical case. Therefore, the need to develop a unique diagnostic algorithm based on the integration of a number of modern methods such as immunophenotyping, cytogenetic analysis and molecular diagnostics has been recognized in recent years.

Conclusion: A comprehensive diagnostic approach encompassing a broad spectrum of different methods is crucial for the diagnosis of PCL. Although morphological diagnosis is the primary approach in the diagnosis of PL, the application of modern diagnostic methods may provide additional knowledge about the pathogenesis of the disease and have implications for prognosis and the development of personalized medicine.

Keywords: *plasma cell leukemia; plasma cells; plasma cell dyscrasia; laboratory diagnostics*

MIKROBIOLOŠKA ISPRAVNOST LEDA U UGOSTITELJSKIM OBJEKTIMA NA PODRUČJU KANTONA SARAJEVO

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Uvod: Svjetska zdravstvena organizacije navodi da led koji je namijenjen za konzumaciju ili je u neposrednom kontaktu s hranom, treba biti jednake kvalitete i jednako siguran za ljude kao i voda za piće. Zbog široke upotrebe u ugostiteljstvu, led ima veliki javnozdravstveni značaj i potrebno je osigurati njegovu mikrobiološku ispravnost. Konzumacija namirnica koje su bile u kontaktu s kontaminiranim ledom može rezultirati prenosom patogenih mikroorganizama na ljude, što može dovesti do pojave hranom prenosivih bolesti.

Cilj: Prikazati javnozdravstveni značaj ispravnosti leda i njegovu mikrobiološku ispravnost u odabranim subjektima u poslovanju s hranom na području Kantona Sarajevo kroz presječno, pilot istraživanje provedeno u Zavodu za javno zdravstvo Federacije Bosne i Hercegovine.

Materijal i metode: Istraživanje je provedena u Kantonu Sarajevo u razdoblju juni 2021 – august 2022. U istraživanju je učestvovalo ukupno 25 subjekata u poslovanju s hranom, gdje je uzorkovan led, te su uzeti brisevi lopatica za led i ledomata. Prilikom uzorkovanja očitavana je i trenutna temperatura spremnika za led. Nakon urađenih mikrobioloških analiza, urađena je deskriptivna analiza i interpretacija dobivenih rezultata. Brisevi su uzorkovani u skladu sa smjernicama standardne metode BAS EN ISO 18593:2019. Mikrobiološka analiza ciljanih mikrobioloških parametara je provedena u skladu sa standardnim metodama BAS EN ISO 9308-1:2015, BAS EN ISO 7899-2:2003, BAS EN ISO 26461-2:2003, BAS EN ISO 16266:2009, BAS EN ISO 4833-1:2014 i BAS EN ISO 21528-2:2018.

Rezultati: Rezultati su pokazali da više od polovine (51%) uzroka leda ne odgovara parametrima Smjernica za mikrobiološke kriterije za hranu. Kod čak 39% analiziranih uzoraka je izolovana Escherichia coli, dok je Pseudomonas aeruginosa izolovan u četvrtini (26%) ispitanih uzoraka leda. U petini (20%) ugostiteljskih objekata na uzorkovanim brisevima površina su izolovane *Enterobacteriaceae*, kod njih 12% *Staphylococcus aureus*, dok ih je skoro četvrtina (24%) sadržavala aerobne bakterije u vrijednostima iznad preporučenih.

Zaključak: Ovim istraživanjem je ustanovljeno da postoji rizik od pojave bolesti uzrokovanih konzumacijom leda neodgovarajuće mikrobiološke ispravnosti, te da je potrebno usmjeriti inspekcijske nadzore u ovu oblast, kako bi se u ugostiteljskim objektima obezbjedilo provođenje dobrih higijenskih praksi.

Ključne riječi: *led; ugostiteljski objekti; mikrobiološka ispravnost; hranom prenosive bolesti*

MICROBIOLOGICAL CORRECTNESS OF ICE IN CATERING FACILITES IN SARAJEVO CANTON

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Introduction: The World Health Organization states that ice intended for consumption or in direct contact with food should be the same quality and as safe for humans as drinking water. Due to its wide use in catering, ice has great public health significance and it is necessary to ensure its microbiological correctness. Eating foods that have been in contact with contaminated ice can result in the transmission of pathogenic microorganisms to humans, which can lead to foodborne illnesses.

Objective: To present the public health significance of the correctness of ice, and its microbiological correctness in selected subjects in the food business in the area of Sarajevo Canton, through a review, of pilot research conducted by the Institute of Public Health of the Federation of Bosnia and Herzegovina.

Methods and materials: The type of research is a cross- sectional, descriptive-analytical study, conducted in Sarajevo Canton in the period June 2021-August 2022. 25 subjects in the food business participated in the research, where ice was sampled and swabs taken from ice scoops and ice machines. In each facility, the current temperature of the ice storage tank was measured. After the microbiological analyses,a descriptive analysis and interpretation of the obtained research results was performed.

Results: Our research consisted of ice sampling in catering facilities in the Sarajevo Canton area, and microbiological analysis of the samples according to the parameters of the Guidelines for Microbiological Criteria for Food. The results showed that more than half (51%) of the causes of ice do not correspond to the parameters of the Microbiological Guidelines for Food. Escherichia coli was isolated in as many as 39% of the analyzed samples, while Pseudomonas aeruginosa was isolated in a quarter (26%) of the tested ice samples. *Enterobacteriaceae* were isolated from sampled surface swabs in a fifth (20%) of catering establishments, *Staphylococcus aureus* in 12% of them, while almost a quarter (24%) contained aerobic bacteria in values above the recommended values.

Conclusion: This research determined that there is a risk of diseases caused by the consumption of ice of inadequate microbiological correctness, and that it is necessary to direct inspection supervision in this area, in order to ensure the implementation of good hygiene practices in catering facilities.

Keywords: *ice; catering facilities; microbiological correctness; food-borne diseases*

PREDNOST I SPECIFIČNOST TEKUĆINSKE CITOLOGIJE

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Uvod: PAPA test je skrining test na karcinom grlića maternice i zahvaljujući njemu smrtnost od navedenog je značajno smanjena. Nacionalni skrining programi širom svijeta koji su bazirani na konvencionalnim PAPA testovima dali su odlične rezultate, a razvoj novih dijagnostičkih metoda poput tekućinske citologije (eng. *liqiud based cytology*, LBC) i molekularne dijagnostike humanog papilomavirusa (HPV) mogu značajano ubrzati i poboljšati testove probira.
Cilj: Istražiti dijagnostičke prednosti tekućinske citologije u usporedbi s konvencionalnim PAPA testom.
Materijal i metode: Pretražene su sljedeće znanstvene baze podataka: MEDLINE/PubMed i Google Scholar za relevantna randomizirana kontrolirana ispitivanja i opservacijske studije s usporednim skupinama u razdoblju od 2002. do 2024. godine. Prihvatljive studije uključivale su žene u dobi od 15 do 70 godina koje su pregledane korištenjem konvencionalne citologije i citologije na bazi tekućine. Provedena je meta-analiza 30 studija koje su zadovoljavale kriterije za uključivanje u istraživanje.
Rezultati: Zbirni dokazi 16 studija ističu da je tekućinska citologija jednako senzitivan i specifičan kao i konvencionalni PAPA test, dok dokazi 14 studija ističu da LBC pokazuje bolju specifičnost ili je na osnovu nekog drugog parametra bolja metoda u odnosu na konvencionalnu.
Zaključak: Tekućinska citologija je ekvivalentna po specifičnosti i osjetljivosti konvencionalnim PAPA testovima, a njena najveća prednost se ogleda kroz smanjen broj nezadovoljavajućih briseva, te povećan broj pregledanih briseva u kraćem vremenskom razdoblju. Konvencionalne metode se smatraju prihvatljivijim za zemlje u razvoju. Iako se konvencionalni PAPA test još uvijek ne može proglasiti za zastarjelu metodu, tekućinska citologija je dosta lakša za izvedbu, brža i dijagnostički ekvivalentna metoda. Dakle, LBC predstavlja atraktivnu opciju za poboljšanje skrininga na karcinom grlića maternice.

Ključne riječi: *papa test; citologija; tekućinska citologija*

ADVANTAGE AND SPECIFICITY OF LIQUID CYTOLOGY

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Introduction: Pap smear is a screening test for cervical cancer and because of it mortality from the above is significantly reduced. National screening programs around the world based on conventional PAP tests have yielded excellent results, and the development of new diagnostic methods such as liquid based cytology (LBC) and molecular diagnostics of human papillomavirus (HPV) can significantly accelerate and improve screening tests.
Objective: To investigate the diagnostic advantages of liqiud based cytology compared to conventional Pap smear.
Methods and materials: The following scientific databases were searched: MEDLINE/PubMed and Google Scholar for relevant randomized controlled trials and observational studies with comparative groups in 2002-2024. Acceptable studies included women between the ages of 15 and 70 who were reviewed using conventional cytology and liquid based cytology. A meta-analysis of 30 studies that met the criteria for inclusion in the study was conducted.
Results: Aggregate evidence from 16 studies indicates that liquid based cytology is equally sensitive and specific as conventional PAP test, while evidence from 14 studies suggests that LBC shows better specificity or is a superior method based on some other parameter compared to conventional methods.
Conclusion: Liqud based cytology is equivalent in specificity and sensitivity to conventional PAP tests, with its greatest advantage being a reduced number of unsatisfactory samples and an increased number of samples examined in a shorter time period. Conventional methods are considered more acceptable for developing countries. Although a conventional Pap smear can still not be declared as an outdated method, fluid cytology is much easier to perform, a faster and diagnostic equivalent method. Thus, LBC represents an attractive option to improve screening for cervical cancer.

Keywords: *pap smear; cytology; liquid based cytology*

KRISTALI SMRTI: FENOMEN U MORFOLOŠKOJ DIJAGNOSTICI

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Uvod: Povezanost morfološki karakterističnih plavo-zelenih citoplazmatskih inkluzija s letalnim ishodom pacijenata tokom 48 sati od njihove identifikacije, rezultirala je pojavom termina "kristali smrti" u naučnoj literaturi. Morfološki poremećaji nalaze se isključivo u ćelijama s fagocitnom aktivnošću, kao što su neutrofili i monociti, dok njihovo prisustvo nije dokazano u limfocitima. Iako razlog pojave kristala smrti u citoplazmi leukocita u potpunosti nije jasan, posljednjih godina postali su predmet brojnih istraživanja.

Cilj: Predstaviti značaj i potencijal morfološke dijagnostike u razumijevanju i prepoznavanju kristala smrti.

Materijal i metode: Odabrani naučni članci za potrebe ne-eksperimentalnog kvalitativnog tipa istraživanja pregledani su elektroničkim putem uz pomoć dostupnih relevantnih baza podataka kao što su PubMed (Medline) i Google Scholar korištenjem ključnih riječi na engleskom jeziku „*crystals of death*", "*blue-green inclusions*", i "*green crystals*".

Rezultati: Analizirane studije slučaja pokazuju da su kristali smrti uočeni kod pacijenata starijih od 40 godina s nekrozom jetre, multisistemskim zatajenjem organa, laktatnom acidozom, ali i SARS-CoV-2 infekcijom (engl. *Severe Acute Respiratory Syndrome Coronavirus 2*). Kao posljedica složene strukture i zastupljenosti u manje od 5% neutrofila i monocita njihova pojava u morfološkoj dijagnostici često ostaje neprepoznata i zanemarena primjenom rutinskog bojenja. Iako tačan sastav kristala smrti ostaje nepoznat, pojedina istraživanja objašnjavaju da se sastoje od lipofuscina ili biliverdina koji se posljedično nakupljaju u oštećenom i nekrotičnom tkivu. Primjenom specijalnog bojenja kao što su PAS (engl. *Periodic Acid-Schiff*), *Zeihl-Neelsen* i *Oil Red O* uočeno je da su ove heterogene strukture produkti lizosomske degradacije, dok prijavljena pozitivnost u rijetkim neutrofilima sugeriše na visok sadržaj lipida.

Zaključak: Kao posljedica nedovoljnog znanja i svjesnosti o ovom fenomenu, u eri razvoja tehnologije koja se sve više implementira u hematopatologiji, raste potreba za njihovom detaljnom procjenom i provjerom primjenom specijalnih metoda kako bi se objasnio patofiziološki mehanizam njihovog nastanka, kao i dijagnostički i prognostički značaj.

Ključne riječi: *kristali smrti; plavo-zelene inkluzije; zeleni kristali*

CRYSTALS OF DEATH: PHENOMENA IN MORPHOLOGY DIAGNOSIS

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Introduction: The association of morphologically characteristic blue-green cytoplasmic inclusions with the fatal outcome of patients within 48 hours of their identification led to the appearance of the term "death crystals". The morphological abnormalities are found exclusively in cells with phagocytic activity. Although the reason for the occurrence of death crystals is not entirely clear, they have been the subject of numerous studies in recent years.

Objective: To illustrate the importance and potential of morphological diagnostics for the understanding and detection of death crystals.

Methods and materials: A selection of scientific papers was made using relevant databases such as PubMed (Medline) and Google Scholar and the keywords „*crystals of death*", „*blue-green inclusions*", "*green crystals*" to conduct a non-experimental, qualitative study.

Results: The analyzed studies have shown that death crystals occur in patients over 40 years of age who have been diagnosed with liver necrosis, multisystem organ failure, lactic acidosis and severe acute respiratory syndrome coronavirus 2 infection. Due to their complex structure and their occurrence in less than 5% of neutrophils and monocytes, their presence is often not recognized in morphological diagnostics. Some studies explain that they are composed of lipofuscin or biliverdin, which consequently accumulate in damaged and necrotic tissue. Using special stains such as PAS (Periodic Acid-Schiff), Zeihl-Neelsen and Oil Red O, it has been established that these heterogeneous structures are products of lysosomal degradation, while the reported positivity in rare neutrophils indicates a high lipid content.

Conclusion: As a result of insufficient knowledge and awareness of this phenomenon, in the era of technological development increasingly used in hematopathology, there is an increasing need for its detailed evaluation and verification with specialized methods to explain the pathophysiological mechanism of its occurrence as well as its diagnostic and prognostic significance.

Keywords: *crystals of death; blue-green inclusions; green crystals*

AUTOLOGNA TRANSPLANTACIJA HEMATOPOETSKIH MATIČNIH ĆELIJA DESETOGODIŠNJE ISKUSTVO U RADU TIMA ZA TRANSPLANTACIJU ZAVODA ZA TRANSFUZIJSKU MEDICINU FEDERACIJE BOSNE I HERCEGOVINE

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Uvod: Transplantacija hematopoetskih matičnih ćelija (HMC) predstavlja terapijski pristup liječenju različitih vrsta urođenih i stečenih malignih bolesti hematopoetskog i imunološkog sistema, kao i nekih solidnih tumora. Uvođenjem u rutinsku praksu značajno su poboljšani ishodi liječenja, stopa preživljavanja i produžen životni vijek pacijenta. Postupkom leukofereze, HMC se prikupljaju iz venske krvi pacijenta pomoću aferezног separatora, a nakon prikupljanja željenog broja stanica, iste se obrađuju postupkom krioprezervacije, pohranjuju i čuvaju na niskim temperaturama u tečnom azotu do upotrebe.

Cilj: Predstaviti desetogodišnje rezultate tima za transplataciju u autolognoj transplantaciji hematopoetskih matičnih ćelija.

Materijal i metode: Retrospektivna analiza podataka pacijenta uključenih u proces autologne transplantacije prema važećim terapijskim kriterijumima i standardima u posljednjoj dekadi.

Rezultati: Provedeno je 279 procedura prikupljanja autolognih perifernih HMC kod 198 pacijenata, čiji su proizvodi afereze kriokonzervirani u 736 vrećica. U prosjeku, broj kriokonzerviranih vrećica po pacijentu iznosio je 3,72 (raspon 2-15 vrećica). Analizom je obuhvaćeno 97 pacijenata (49%) i 101 pacijentkinja (51%) starosti od 1 do 65 godina, oboljelih od multiplog mijeloma, NHL, HL i drugih onkoloških bolesti. Ciljani broj ćelija prikupljenih jednom procedurom afereze uspješno je izveden kod 129 pacijenata (65%), dok je za 69 pacijenata (35%) provedeno dva ili više procedura. Efikasnost sakupljanja je procenjena na osnovu broja CD34+ ćelija po kilogramu telesne težine pacijenta u finalnom produktu leukofereze. Prosječan broj sakupljenih ćelija bio je 4,03x10e6/kgTT (raspon 2,30-7,22x10e6/kg). Kod svih pacijenata sakupljen je minimalni broj ćelija ≥2x10e6/kgTT CD34+ ćelija, dok je kod većine sakupljen poželjan ili čak optimalan broj ćelija ≥2,5x10e6/kgTT, odnosno 3-5x10e6/kgTT CD34+ potreban za jednu transplantacija. U istom periodu urađeno je i 214 reinfuzija ćelija iz 544 vrećice proizvoda afereze.

Zaključak: Rezultati našeg dosadašnjeg rada ukazuju na uspješnost primjenjih protokola u autolognoj transplantaciji hematopoetskih matičnih ćelija i ne odstupanju od ostalih centara. Minimalna terapijska doza ciljnih stanica prikupljena je kod svih pacijenata.

Ključne riječi: *afereza; krioprezervacija; CD34+*

AUTOLOGOUS TRANSPLANTATION OF HEMATOPOIETIC STEM CELLS TEN YEARS OF EXPERIENCE IN THE WORK OF THE TRANSPLANTATION TEAM OF THE INSTITUTE FOR TRANSFUSION MEDICINE OF THE FEDERATION OF BOSNIA AND HERZEGOVINA

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Introduction: Hematopoietic stem cell (HSC) transplantation represents a therapeutic approach to treating various types of congenital and acquired malignant diseases of the hematopoietic and immune systems, as well as some solid tumors. By introducing it into routine practice, the outcomes of treatment, survival rates, and the patient's lifespan have been significantly improved. Through the process of leukapheresis, HSCs are collected from the patient's venous blood using an apheresis separator, and after collecting the desired number of cells, they are processed by cryopreservation, stored, and kept at low temperatures in liquid nitrogen until use.

Objective: To present the ten-year results of the transplantation team in autologous transplantation of hematopoietic stem cells.

Methods and materials: Retrospective analysis of patient data involved in the process of autologous transplantation according to valid therapeutic criteria and standards in the last decade.

Results: A total of 279 procedures for collecting autologous peripheral HSCs were performed on 198 patients, whose apheresis products were cryopreserved in 736 bags. On average, the number of cryopreserved bags per patient was 3.72 (range 2-15 bags). The analysis included 97 patients (49%) and 101 female patients (51%) aged 1 to 65 years, suffering from multiple myeloma, NHL, HL, and other oncological diseases. The targeted number of cells collected in one apheresis procedure was successfully achieved in 129 patients (65%), while for 69 patients (35%), two or more procedures were conducted. The efficiency of collection was assessed based on the number of CD34+ cells per kilogram of the patient's body weight in the final leukapheresis product. The average number of collected cells was 4.03x10e6/kgBW (range 2.30-7.22x10e6/kg). All patients had a minimum number of cells ≥2x10e6/kgBW CD34+ cells collected, while most had the desired or even optimal number of cells ≥2.5x10e6/kgBW, or 3-5x10e6/kgBW CD34+ necessary for one transplantation. In the same period, 214 cell reinfusions were also performed from 544 bags of apheresis products.

Conclusion: Our work so far indicate the success of the applied protocols in autologous transplantation of hematopoietic stem cells and our results do not deviate from other centers. The minimum therapeutic dose of target cells was collected in all patients.

Keywords: *apheresis, cryopreservation, CD34+*

SMRTNOST OD KARDIOVASKULARNIH BOLESTI U REPUBLICI SJEVERNA MAKEDONIJA

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Uvod: Kardiovaskularne bolesti zajedno sa malignim bolestima su uzrok skoro tri četvrtine smrtnosti u evropskom regionu. Procjene pokazuju da najmanje 80% svih srčanih bolesti, srčanog udara i dijabetesa tipa 2 se može spriječiti.

Cilj: Prikazati mortalitet od kardiovaskularnih bolesti u Republici Sjevernoj Makedoniji u periodu od 2010-2022.

Materijal i metode: Korišćeni su podaci Državnog zavoda za statistiku i Instituta za javno zdravlje Republike Sjeverne Makedonije, kao i izvještaji Svjetske zdravstvene organizacije. Primijenjena je deskriptivna epidemiološka metoda rada.

Rezultati: Stopa mortaliteta od ishemijske bolesti srca u periodu 2010-2022. godine veći je kod muške populacije. Smrtnost od ishemijske bolesti srca značajno je veća u populaciji starijoj od 65 godina u odnosu na smrtnost u populaciji mlađoj od 64 godine. U 2022. godini u Republici Makedoniji, akutni infarkt miokarda činio je 94,7% ishemijskih bolesti srca.

Zaključak: Kardiovaskularne bolesti su vodeći uzrok smrti u svijetu i uzrokuju više smrtnih slučajeva nego svi drugi uzroci zajedno. Uglavnom su pogođene zemlje sa niskim i srednjim prihodima.

Ključne riječi: *mortalitet; kardiovaskularne bolesti; faktori rizika*

MORTALITY FROM CARDIOVASCULAR DISEASES IN THE REPUBLIC OF NORTH MACEDONIA

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Introduction: Cardiovascular diseases together with malignant diseases are the cause of almost three quarters of mortality in the European region. Estimates show that at least 80% of all heart disease, heart attack and type 2 diabetes can be prevented.

Objective: To present mortality from cardiovascular diseases in the Republic of North Macedonia in the period from 2010-2022.

Methods and materials: Data from the State Statistical Office and the Institute for Public Health of the Republic of North Macedonia, as well as WHO reports, were used. A descriptive epidemiological work method was applied.

Results: The mortality rate from ischemic heart disease in the period 2010-2022 is higher in the male population. Mortality from ischemic heart disease is significantly higher in the population older than 65 years compared to mortality in the population younger than 64 years. In 2022 in the Republic of Macedonia, acute myocardial infarction accounted for 94.7% of ischemic heart diseases.

Conclusion: Cardiovascular diseases are the leading cause of death worldwide and cause more deaths than all other causes combined. Mostly low- and middle-income countries are affected.

Keywords: *mortality, cardiovascular diseases, risk factors*

UMJETNA INTELIGENCIJA U HEMATOLOGIJI

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Umjetna inteligencija (engl. *artificial intelligence*; AI) zasniva se na simulaciji ljudske inteligencije i sposobnosti rješavanja problema primjenom različitih algoritama i kompjuterskih sistema. Ova tehnologija u medicini ima primarnu svrhu da prepozna i izdvoji podatke od kliničkog značaja. Iako trenutno nema široku praktičnu primjenu u hematologiji, istraživanja ukazuju na veliki potencijal njene implementacije. Sa ciljem evaluacije značaja primjene AI u navedenoj oblasti, proveden je pregled relevantnih baza podataka (MEDLINE i ScienceDirect) upotrebom ključnih riječi poput "*artificial intelligence*", "*hematology*" i "*hematopathology*".

U oblasti hematologije, AI se koristi u probiranju, predikciji, dijagnostici i klasifikaciji različitih hematoloških bolesti poput anemija, hemoglobinopatija, talasemija i hematoloških maligniteta. Najčešće primjenjivani modeli AI u osnovi imaju neuralne mreže čiji rad se temelji na prepoznavanju određenih uzoraka u skupu podataka. U hematologiji, AI se najviše koristi u automatizovanoj analizi slika gdje se kao ulazni podaci koriste slike razmaza perferne krvi ili koštane srži. Ovakav pristup omogućava kvantifikaciju krvnih ćelija, ali i njihovu diferencijaciju prema citomorfološkim karakteristikama u jako kratkom vremenu. Poseban značaj navedenog ogleda se u diferencijaciji blasta i leukocitnih prekursora te njihovoj klasifikaciji prema ćelijskoj lozi, što značajno doprinosi dijagnostici akutnih i hroničnih leukemija. Kao ulazni podaci koriste se i vrijednosti hematoloških i drugih parametara, važnih u diferencijalnoj dijagnostici i prognozi bolesti. Među najvećim prednostima AI izdvajaju se visoka specifičnost, osjetljivost, tačnost i preciznost, iako potreba za specijalizovanim softverima i hardverima, te adaptacija i cijena istih mogu biti problem u njenoj implementaciji. Kao ograničenja primjene AI u hematologiji navode se i potreba za velikom količinom podataka, te način pripreme preparata i razlike u rezoluciji slika. Međutim, softveri i algoritmi kreirani na odgovarajući način, te prilagodba ulaznih podataka istima, mogu značajno doprinijeti unaprijeđenju dijagnostičkih postupaka u hematologiji, ali i smanjiti opterećenje laboratorijskih stručnjaka što će imati pozitivan utjecaj na njihov kvalitet rada.

Ključne riječi: *umjetna inteligencija; hematologija; hematološke neoplazme; dijagnostika; krvne ćelije*

ARTIFICIAL INTELLIGENCE IN HEMATOLOGY

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Artificial intelligence (AI) is based on simulating human intelligence and problem-solving abilities using various algorithms and computer systems. This technology is utilized in various disciplines, including medicine, where its goal is to identify and extract clinically significant data. While its widespread application in hematology is currently limited, research suggests considerable potential for the practical implementation. To asses the importance of implementing AI in this field, a review of relevant databases (MEDLINE and ScienceDirect) was concluded using keywords such as „*artificial intelligence*", „*hematology*" and „*hematopathology*".

In hematology, AI is employed for screening, prediction, diagnosis and classification of various hematological diseases such as anemias, hemoglobinopathies, thalassemias and hematological malignanicies. The most commonly used AI models are based on neural networks which rely on recognizing specific patterns in the dataset. In hematology, AI is primarily used in automated image analysis, where the input data consists of images of blood and bone marrow smears. This approach enables quantification of blood cells and differentiation based on cytomorphological characteristics in short periods of time. Of particular importance is the differentiation of blasts and leukocyte precursors and their classification according to cellular lineage, significantly contributing to the diagnosis of acute and chronic leukemias. Input data also include values of hematological and other parameters important in differential diagnosis and disease prognosis. Among the major advantages of AI are high specificity, sensitivity, accuracy and precision, although the need for specialized software and hardware, as well as their adaptation and costs can be an issue in its implementation. Limitations of AI application in hematology include the requirement for large datasets, preparation of blood smears and image resolution. However, appropriately designed software and algorithms, along with adaptation of input data, can significantly improve diagnostic procedures in hematology and reduce the workload of laboratory professionals, positively impacting the quality of their work.

Keywords: *artificial intelligence; hematology; hematologic neoplasms; diagnostics; blood cells*

ZNAČAJ ODREĐIVANJA HEPCIDINA U ANEMIJI HRONIČNE BOLESTI

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Uvod: Hepcidin kao antimikrobni peptidni hormon predstavlja homeostatski regulator metabolizma željeza čija je ekspresija pod utjecajem brojnih faktora kao što su inflamacija i hipoksija. Tokom inflamacije aktivirani makrofagi otpuštaju širok spektar citokina što pojačava ekspresiju hepcidina i pridonosi razvoju anemije hroničnih bolesti (AHB) koju karakteriše zadržavanje željeza u makrofagima i smanjena intestinalna reapsorpcija. Uz to, procjena nedostatka željeza u deficitarnim anemijama postaje sve veći izazov zbog direktnog utjecaja inflamacije na parametre koji opisuju status željeza u organizmu.
Cilj: Ispitati značaj određivanja hepcidina u diferencijalnoj dijagnostici anemija.
Materijal i metode: Za potrebe ne-eksperimentalnog kvalitativnog istraživanja pregledana dostupna literatura kroz relevantne baze kao što su Medline i Google Scholar koristeći ključne riječi na engleskom jeziku „hepcidin", "*anemia chronic disease*" i „*iron metabolism*".
Rezultati: Istraživanja naglašavaju značaj serumskog određivanja hepcidina u AHB, pri čemu je prijavljena visoka stopa osjetljivosti i specifičnosti od 94% i 85%, ali i njegova uloga u terapijskom pristupu. U diferencijalnoj dijagnostici sideropenične anemije (SA) i AHB, uočeno je da su vrijednosti hepcidina niže kod SA u odnosu na AHB. S ciljem pravilne procjene inflamacije, prijavljena je pozitivna korelacija između hepcidina, feritina i C-reaktivnog proteina kod AHB u odnosu na SA. Međutim, autori naglašavaju veliki potencijal hepcidina u isključivanju SA kod pacijenata s mješovitom etiologijom. Hepcidin reaguje u roku od nekoliko sati na promjene u hematološkom statusu, te se osim u krvi može odrediti u uzorku urina, što ga čini veoma korisnim u pedijatrijskoj populaciji. Za njegovo određivanje u laboratorijskoj praksi najčešće se koristi imunološki test s antihepcidinskim antitijelima, iako je poznat veliki broj metoda, njihova primjena je ograničena kao posljedica prisustva brojnih faktora u uzorcima koje je teško eliminirati.
Zaključak: Određivanje hepcidina osigurava osjetljivu i specifičnu diferencijalnu dijagnozu SA i AHB, čime se smanjuje dijagnostičko vrijeme i omogućava razvoj odgovarajućeg terapijskog pristupa kod anemija s pravim deficitom željeza.

Ključne riječi: *hepcidin; anemija hroničnih bolesti; metabolizam željeza; hepcidin regulator željeza*

SIGNIFICANCE OF HEPCIDIN DETERMINATION IN ANEMIA OF CHRONIC DISEASE

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Introduction: Hepcidin, an antimicrobial peptide hormone, plays a crucial role as a homeostatic regulator of iron metabolism. Its expression is influenced by various factors, including inflammation and hypoxia. During inflammation, activated macrophages release a plethora of cytokines that enhance the expression of hepcidin. This contributes to the development of Anemia of Chronic Diseases (ACD), characterized by iron retention in macrophages and diminished intestinal reabsorption. The assessment of iron deficiency in anemias is increasingly challenging due to inflammation's direct impact on parameters describing the body's iron status.
Objective: To examine the significance of hepcidin determination in the differential diagnosis of anemia.
Methods and materials: For the purposes of non-experimental qualitative research, the available literature was reviewed through relevant databases such as Medline and Google Scholar using the English keywords "*hepcidin*", "*anemia chronic disease*" and "*iron metabolism*".
Results: Studies underscores the importance of serum hepcidin determination in ACD, reporting a high sensitivity and specificity rate of 94% and 85%, respectively. It also highlights its role in therapeutic approaches. In the differential diagnosis of Sideropenic Anemia (SA) and ACD, it was observed that hepcidin levels are lower in SA compared to ACD. To accurately assess inflammation, a positive correlation was reported between hepcidin, ferritin, and C-reactive protein in ACD compared to SA. However, the authors emphasize hepcidin's potential in excluding SA in patients with mixed etiology. Hepcidin responds within a few hours to changes in hematological status and can be determined in a urine sample, making it particularly useful in the pediatric population. Although numerous methods for its determination in laboratory practice are known, their application is limited due to the presence of numerous factors in the samples that are difficult to eliminate.
Conclusion: Determining hepcidin levels offers a sensitive and specific differential diagnosis of SA and ACD. This reduces diagnostic time and facilitates the development of an appropriate therapeutic approach in true iron deficiency anemia.

Keywords: *hepcidin; anemia of chronic diseases; iron metabolism; hepcidin iron regulator*

MOGUĆNOSTI HEMATOLOŠKOG ANALIZATORA SYSMEX HN–3100 U IDENTIFIKACIJI ERITROBLASTA – PRIKAZ SLUČAJA

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Uvod: Normalno se u perifernoj krvi ne nalaze eritroblasti, izuzev kod novorođenčadi. Njihova pojava može biti rezultat ubrzane eritropoeze i narušene arhitekture koštane srži upalnim oštećenjima i hipoksijom. Eritroblasti se u perifernoj krvi javljaju u sklopu teških bolesti sa lošom prognozom, te ih je bitno na vrijeme otkrititi. Prisutvo eritroblasta u perifernoj krvi može predstavljati problem prilikom određivanja kompletne krvne slike sa diferencijalnom na hematološkim analizatorima, zbog morfologije eritroblasta koji sadrže jedro. Hematološki analizatori ih mogu ubrojati u leukocite i tako lažno povećati broj leukocita, što posljedično može negativno uticati na dijagnosticiranje oboljenja.

Cilj: Uporediti rezultate dobijene primjenom Sysmex XN-3100 hematološkog analizatora u odnosu na svjetlosnu mikroskopiju kao referentnu metodu.

Materijal i metode: U radu je korišten automatski hematološki analizator Sysmex XN-3100, koji se sastoji od dva brojača XN-10 i XN-20, te posjeduje automatsku pripremu i bojenje razmaza krvi, kao i digitalnu mikroskopiju. S druge strane, korištena je standardna priprema krvnog razmaza sa *May-Grunwald-Giemsa* bojom za svjetlosnu mikroskopiju.

Rezultati: Pacijent starosti 47 godina sa dijagnozom hepatosplenomegalije. Ukupan broj leukocita je bio unutar referentnog intervala, iznosio je 3,72x10e9/L, uz izraženu trombocitopeniju sa brojem trombocita 49x10e9/L. Uz to crvena krvna loza pokazala je anemiju sa brojem eritrocita 2,83x10e12/L, hemoglobinom 74g/L i hematokritom 24,6%. Broj eritroblasta na hematološkom analizatoru je bio 3,16x10e9/L (84,9%). Automatska digitalna mikroskopija u preklasifikaciji pokazala je prisustvo 140,9% eritroblasta. Nakon reklasifikacije procenat eritroblasta je iznosio 169,8% (103,8% acidofilnh, 64,8% polihromatofilnih i 1,0% bazofilnih eritroblasta). Manuelnim pregledom krvnog razmaza nađeno je 101% eritroblasta (46% acidofilnih, 64% polihromatofilnih i 1,0% bazofilnih eritroblasta).

Zaključak: Primjena savremenih hematoloških analizatora u dijagnostici ima veliki broj prednosti u svakodnevnom radu, posebno u zdravstvenim ustanovama tercijarnog nivoa. Uvidom u dobijene rezultate nameće se potreba dodatne evaluacije na velikom broju uzoraka, kako bi se jasno utvrdila tačnost analizatora u odnosu na referentnu metodu.

Ključne riječi: *eritroblasti; hematologija; savremeni hematološki analizator*

POSSIBILITIES OF THE SYSMEX HN–3100 HEMATOLOGY ANALYZER IN ERYTHROBLAST IDENTIFICATION – CASE REPORT

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Introduction: Normally, erythroblasts are not found in the peripheral blood, except in newborns. Their appearance can be the result of accelerated erythropoiesis and impaired bone marrow architecture due to inflammatory damage and hypoxia. Erythroblasts in the peripheral blood occur as part of severe diseases with a poor prognosis and it is important to detect them in time. The presence of erythroblasts in peripheral blood can be a problem when determining the complete blood count with the differential on hematological analyzers, due to the morphology of erythroblasts that contain a nucleus. Hematological analyzers can count them as leukocytes and thus falsely increase the number of leukocytes, which can consequently negatively affect the diagnosis of the disease.

Objective: To compare the results obtained using the Sysmex XN-3100 hematology analyzer in relation to light microscopy as a reference method.

Methods and materials: The work used an automatic hematology analyzer Sysmex XN-3100, which consists of two counters XN-10 and HN-20, and has automatic blood smear preparation and staining, as well as digital microscopy. On the other hand, a standard blood smear preparation with May-Grunwald-Giemsa stain was used for light microscopy.

Results: 47-year-old patient diagnosed with hepatosplenomegaly. The total number of leukocytes was within the reference interval, it was 3.72x109/L, with marked thrombocytopenia with a platelet count of 49x109/L. In addition, the red blood line showed anemia with the number of erythrocytes 2.83x1012/L, hemoglobin 74g/L and hematocrit 24.6%. The number of erythroblasts on the hematology analyzer was 3.16x109/L (84.9%). Automatic digital microscopy in reclassification showed the presence of 140.9% erythroblasts. After reclassification, the percentage of erythroblasts was 169.8% (acidophilic erythroblasts 103.8%, polychromatophilic erythroblasts 64.8% and basophilic erythroblasts 1.0%). Manual examination of the blood smear revealed 101% erythroblasts (46% acidophilic, 64% polychromatophilic and 1.0% basophilic erythroblasts).

Conclusion: The use of modern hematology analyzers in diagnostics has a large number of advantages in everyday work, especially in tertiary level healthcare institutions. An insight into the obtained results imposes the need for additional evaluation on a large number of samples, in order to clearly establish the accuracy of the

CONTROL OF THE WASTE-WATER IN THE FOOD INDUSTRY

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Introduction: Waste-waters are the ones that are brought to waste station or are brought to the point of releasing (surface or underground waters). Releasing of the waste water in the industry (with no treatment) is being released in certain recipient. Soil, sewage, water streams, accumulations lakes are counted as recipients of the waste water. Pollution of the environment from the food capacities represents a serious problem in the production in the food industry.

Objective: To make an effect for reducing the pollution of the surface and underground waters with various polluting materials from the waste-waters through the industrial processes.

Methods and materials: The monitoring of the waste water is controlled during the entire year through a 5-year period (2019-2023). All the results were conducted in the laboratories in Centre for Public Health – Veles. The main samples that had been taken for consideration for this presentation are from the food industry (non-alcohol drink and water factory) and the results that are taken for comparation are from the metallurgic industry. The location of the sampling place is at the exit point of the waste-water station located outside the factory. The key parameters for the testing of the waste water are: Biological usage of oxygen-5, chemical usage of oxygen and pH level of the waste-water. The materials that we use for picking up samples of waste water are 1l bottles and Winkler bottles.

Results: Average results (during the observations period) for Biological usage of oxygen-5 is 1.39; Average results (during the observations period) for chemical usage of oxygen is 0.28 and Average results (during the observations period) for pH level of the waste water is 8.05 Based from the results there are no deviations in the perimeters and all the results are according to the state laws.

Conclusion: According to the state laws and the water law it can be concluded that the waste water samples are fitted to the conditions and regulations for waste waters and protection zones.

Keywords: *control; waste waters; food industry*

FIZIOLOŠKA ULOGA GRELINA, LEPTINA I ADIPONEKTINA U METABOLIČKIM PROCESIMA

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Uvod: Grelin, leptin i adiponektin su hormoni uključeni u regulaciju metabolizma, metaboličkih procesa i energetske homeostaze. Ključni su za održavanje ravnoteže između unosa hrane i energetske potrošnje, a njihova disfunkcija može doprinijeti razvoju metaboličkih poremećaja. Grelin ili "hormon gladi" je cirkulirajući peptidni hormon kojeg u najvećem obimu proizvode stanice fundusa želuca i stanice gušterače. Njegova uloga se ogleda kroz stimulaciju apetita i regulaciju, odnosno smanjenje energetske potrošnje. Istraživanja pokazuju da utjecajem na povećanje unosa hrane i poticanjem sinteze lipida u jetri, grelin doprinosi povećanju tjelesne mase i razvoju pretilosti. Leptin je proizvod lučenja adipocita, a djeluje kao supresor apetita i regulator neuroendokrinih funkcija i energetske homeostaze, utječući na niz drugih fizioloških procesa kao što su metabolizam, endokrina regulacija i imunološka funkcija, te se povezuje sa raznim metaboličkim sindromima, posebno gojaznošću. Adiponektin je hormon koji se također izlučuje iz adipocita, a njegova uloga se ogleda kroz regulaciju metabolizma i osjetljivosti na inzulin, odnosno regulaciju glukoze i lipida.
Cilj: Istražiti značaj i kompleksne mehanizme djelovanja hormona grelina, leptina i adiponektina na metaboličke procese, kao i njihovu međusobnu interakciju.
Materijal i metode: Za potrebe neeksperimentalnog kvalitativnog istraživanja provedena je analiza rezultata dostupnih naučnoistraživačkih radova, baziranih na kombinaciji kliničkih istraživanja i in vitro eksperimenata usmjerenih na istraživanje utjecaja grelina, leptina i adiponektina na gojaznost, dijabetes i druge metaboličke poremećaje.
Rezultati: Rezultati dobijeni pregledom postojećih istraživanja ukazuju na važnost ovih hormona u patofiziologiji metaboličkih poremećaja, ukazujući da promjene u nivou i funkciji ovih hormona mogu doprinijeti razvoju gojaznosti, inzulinske rezistencije i drugih metaboličkih stanja. Integracija laboratorijskih tehnika poput ELISA-e za kvantifikaciju nivoa hormona u krvi i PCR za analizu genske ekspresije omogućava dublje razumijevanje djelovanja ovih hormona i njihovog utjecaja na metabolizam.
Zaključak: Razumijevanje mehanizama djelovanja grelina, leptina i adiponektina može imati značajne implifikacije za terapiju i prevenciju metaboličkih bolesti. Identifikacija ciljanih terapijskih strategija koje regulišu aktivnost ovih hormona može pružiti nove mogućnosti za tretiranje metaboličkih poremećaja i poboljšanja zdravlja pacijenata.

Ključne riječi: *leptin; grelin; adiponektin; metabolički poremećaji*

THE PHYSIOLOGICAL ROLE OF GHRELIN, LEPTIN, AND ADIPONECTIN IN METABOLIC PROCESSES

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Introduction: Ghrelin, leptin, and adiponectin are hormones involved in the regulation of metabolism, metabolic processes, and energy homeostasis. They are crucial for maintaining the balance between food intake and energy expenditure, and their dysfunction can contribute to the development of metabolic disorders. Ghrelin, or the "hunger hormone," is a circulating peptide hormone produced by fundus cells of the stomach and pancreatic cells. The role of ghrelin is manifested through appetite stimulation and regulation, as well as reduction of energy expenditure. Research indicates that by increasing food intake and promoting lipid synthesis in the liver, ghrelin contributes to weight gain and obesity development. Leptin is secreted by adipocytes and acts as an appetite suppressant and regulator of neuroendocrine functions and energy homeostasis, influencing various physiological processes such as metabolism, endocrine regulation, and immune function, and it is associated with various metabolic syndromes, especially obesity. Adiponectin is also secreted by adipocytes, and its role is in the regulation of metabolism and insulin sensitivity, specifically regulating glucose and lipid metabolism.
Objective: To explore the significance and complex mechanisms of ghrelin, leptin, and adiponectin hormones on metabolic processes, as well as their mutual interaction.
Methods and materials: For the purposes of non-experimental qualitative research, an analysis of results from available scientific research papers, based on a combination of clinical studies and in vitro experiments aimed at investigating the impact of ghrelin, leptin, and adiponectin on obesity, diabetes, and other metabolic disorders, was conducted.
Results: The results obtained from the review of existing studies indicate the importance of these hormones in the pathophysiology of metabolic disorders, suggesting that changes in the level and function of these hormones may contribute to the development of obesity, insulin resistance, and other metabolic conditions. The integration of laboratory techniques such as ELISA for hormone level quantification in blood and PCR for gene expression analysis enables a deeper understanding of the action of these hormones and their impact on metabolism.
Conclusion: Understanding the mechanisms of action of ghrelin, leptin, and adiponectin can have significant implications for the therapy and prevention of metabolic diseases. Identification of targeted therapeutic strategies that regulate the activity of these hormones can provide new opportunities for the treatment of metabolic disorders and improvement of patient health.

Keywords: *leptin; ghrelin; adiponectin; metabolic disorders*

IDENTIFIKACIJA RIZIKOFAKTORA I LABORATORIJSKI MONITORING KARCINOMA DOJKE KOD ŽENA

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Uvod: Osim genetske podloge odnosno postojanja historije karcinoma dojke u porodici i nošenja mutacija na BRCA 1 i BRCA 2 genu postoje i drugi rizikofaktori kao što su: gojaznost kao posljedica nezdravog života sa manjkom fizičke aktivnosti nakon menopauze, pušenje i konzumiranje alkohola, ali i starenje, nerađanje ili kasno prvo rađanje djeteta iza 30. godine života, nedojenje, menstruacija prije 12. godine života i menopauza iza 55. godine života, korištenje hormonske nadomjesne terapije i korištenje oralnih kontraceptiva.
Cilj: Ispitati povezanost starenja, hormonskog uticaja i stilova života sa povećanim rizikom za razvoj karcinoma dojke. Ispitati koja je najzastupljenija vrsta karcinoma dojke u Kantonu Sarajevo. Ispitati efikasnost korištenja CA 15-3, CEA, CA 19-9 i CA 125 u prevenciji, dijagnostici, praćenju i otkrivanju recidiva karcinoma dojke kod žena, kao i osjetljivost i specifičnost kombinacije tumorskih markera CA 15-3 i CEA u otkrivanju recidiva karcinoma dojke.
Materijal i metode: Istraživanje je provedeno sa alatom za prikupljanje podataka o rizikofaktorima i tumorskim markerima iz kartona pacijentica na Odjelu porodične medicine u OJ Dom zdravlja Novi Grad Sarajevo. Korišteni su Kolmogorov-Smirnov i Shapiro-Wilk test i podaci o rizikofaktorima nisu imali normalnu raspodjelu za čiju analizu su primijenjeni neparametrijski testovi kao što su Hi-kvadrat test i Fisherov egzaktni test, a tumorski markeri su imali normalnu raspodjelu i korišteni su parametrijski testovi kao što su One Sample T-test i Paired Samples T-test. Osjetljivost i specifičnost tumorskih markera je određena pomoću ROC krive.
Rezultati: Najčešće dijagnostikovan tip karcinoma dojke kod žena u Kantonu Sarajevo je invazivni duktalni karcinom. Nakon testiranja statističkim testovima dokazana je signifikatna povezanost između starenja, hormonskog uticaja i stilova života sa povećanim rizikom za razvoj karcinoma dojke kod žena.
Zaključak: Povišeni nivoi CA 15-3 za praćenje recidiva su imali osjetljivost koja je iznosila 81,8% sa specifičnošću koja je iznosila 100%.

Ključne riječi: *karcinom dojke; tumorski markeri; rizikofaktori*

IDENTIFICATION OF RISK FACTORS AND LABORATORY MANAGMENT OF FEMALE BREAST CANCER

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Introduction: Except for genetic background or existence of history of breast cancer in the family and carrying mutations on BRCA 1 and BRCA 2 gene there are other risk factors: obesity as consequence of unhealthy life with lack of physical activity after menopause, smoking and drinking alcohol, aging, non-birth or late first birth after 30th year, no breastfeeding, menstruation before 12th year and menopause after 55th year, using hormonal replacement therapy and oral contraceptives.
Objective: Examine if there is a higher risk for development of breast cancer in regards to age, hormonal influence and lifestyle factors. Examine which type of breast cancer is the most diagnosed among women in Kanton Sarajevo. Examine efficiency of se of CA 15-3, CEA, CA 19-9 and CA 125 in prevention, diagnostics, screening and detecting of reccurence of female breast cancer, but also make an assesment of sensitivity and specificity for CA 15-3 and CEA combination of tumor markers in screening of relapse of female breast cancer.
Methods and materials: Research is conducted with tool for gathering data of risk factors and tumor markers from family medicine record on Department of Family medicine in Organizational unit Primary Healthcare Unit Novi Grad Sarajevo. We have used the Kolmogorov-Smirnov and Shapiro-Wilk test and data about risk factors didn't have normal distribution and for which we used non-parametrical tests like Chi-Square test and Fisher's exact test, and tumor markers had normal distribution and we used parametrical tests like One-Sample T-test and Paired Samples T-test. Sensitivity and specificity of tumor markers have been got with the use of ROC curve.
Results: The most diagnosed type of female breast cancer in Kanton Sarajevo is invasive ductal cancer. After use of stastical tests we have proven the significant correlation between aging, hormonal influence and lifestyles with higher risk of developing breast cancer among women.
Conclusion: Elevated levels of CA 15-3 used for screening of relapse had sensitivity of 81.8% with specificity of 100%.

Keywords: *breast cancer; tumor markers; risk factors*