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# 1. Key note speaker

## ■ Ima li obiteljska medicina budućnost?



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**Ključne riječi:** Obiteljska medicina, temeljna načela, održivost, razvoj

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Obiteljska medicina suočava se s nizom izazova koji ugrožavaju njezinu budućnost. Politička nestabilnost, ekološki problemi, komercijalizacija zdravstva, tehnološke promjene i smanjenje autonomije struke samo su neki od razloga za zabrinutost. Sve veći zahtjevi sustava, uz sve manji broj liječnika, dodatno opterećuju profesiju i smanjuju privlačnost specijalizacije iz obiteljske medicine među mladim liječnicima.

Unatoč tome, postoji razlog za optimizam. Obiteljska medicina ostaje temelj zdravstvenog sustava, a njezin akademski razvoj otvara nove mogućnosti. Ključno pitanje nije hoće li opstati, već kako će izgledati u budućnosti. Putokazi za njezin razvoj uključuju usmjerenost na pacijenta, jednakost u pristupu zdravstvenoj skrbi, kontinuitet, znanstvenu utemeljenost, interdisciplinarnu suradnju te visoke etičke i profesionalne standarde.

Uloga edukatora u ovom procesu je ključna. Oni moraju biti svjesni svih dimenzija obiteljske medicine, prepoznati i izbjeći pogrešne smjerove te mladima služiti kao uzor. Samo kroz sustavnu edukaciju, suradnju i predanost temeljnim načelima obiteljske medicine moguće je osigurati njezinu održivost i razvoj.

## ■ Does Family Medicine Have a Future?



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**Keywords:** Family medicine, core values, sustainability, development

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Family medicine faces numerous challenges that threaten its future. Political instability, environmental crises, commercialization of healthcare, technological shifts, and the diminishing autonomy of the profession contribute to growing concerns. Increasing system demands and a declining number of family physicians make the field less attractive to young doctors.

Despite these difficulties, there are reasons for optimism. Family medicine remains the cornerstone of healthcare, and its academic development creates new opportunities. The key question is not whether it will survive, but what form it will take in the future. Its guiding principles include patient-centered care, health equity, continuity, scientific advancement, interdisciplinary collaboration, and strong ethical and professional standards.

Educators play a vital role in shaping this future. They must understand the field in all its dimensions, recognize and avoid pitfalls, and serve as role models for young professionals. Through continuous education, collaboration, and dedication to the core values of family medicine, we can ensure its sustainability and development.

## ■ Vitamin D



**Nenad  
Bogdanovic**

**Ključne riječi:** Vitamin D, kognicija, VDR, Alzheimerova bolest, cerebrospinalna tekućina, APOE

Vitamin D, prvenstveno poznat po svojoj ulozi u metabolizmu kostiju, također je povezan s kognitivnim funkcijama i neuroprotekcijom. Prisutnost receptora za vitamin D (VDR) u moždanim regijama osjetljivim na neurodegenerativne bolesti, poput Alzheimerove bolesti (AD), ukazuje na njegovu širu ulogu izvan regulacije homeostaze kalcija. Istraživanja sugeriraju da vitamin D utječe na kogniciju putem genomskih i negenomskih puteva, uključujući modulaciju neuroinflamacije, oksidativnog stresa i metabolizma amiloida.

Nedavne studije pokazale su povezanost između razine vitamina D u cerebrospinalnoj tekućini (CSF) i tau patologije, dok jasna povezanost s nakupljanjem amiloid- $\beta$  još nije utvrđena. Povišene razine vitamina D u CSF također su povezane s povećanim razinama IL-8, što ukazuje na njegovu moguću ulogu u neuroinflamatornim procesima. Međutim, dokazi koji podupiru vitamin D kao zaštitni faktor u AD-u ostaju neuvjerljivi.

Čini se da nedostatak vitamina D nerazmjerno utječe na izvršne funkcije i pažnju, više nego na pamćenje, što bi moglo biti povezano s promjenama u volumenu korteksa. S obzirom na široko rasprostranjenu učestalost nedostatka vitamina D, potrebna su daljnja istraživanja kako bi se razjasnila njegova uloga u zdravlju mozga i moguća primjena u kognitivnom probiru.

## Vitamin D



**Nenad  
Bogdanovic**

**Ključne riječi:** Vitamin D, cognition, VDR, Alzheimer's disease, cerebrospinal fluid, APOE

Vitamin D, primarily recognized for its role in bone metabolism, has also been implicated in cognitive function and neuroprotection. The presence of vitamin D receptors (VDR) in brain regions vulnerable to neurodegenerative diseases, such as Alzheimer's disease (AD), suggests a broader role beyond calcium homeostasis. Research indicates that vitamin D influences cognition through both genomic and non-genomic pathways, including modulation of neuroinflammation, oxidative stress, and amyloid metabolism.

Recent studies have identified associations between cerebrospinal fluid (CSF) vitamin D levels and tau pathology, though no clear link has been found with amyloid- $\beta$  accumulation. Elevated CSF vitamin D has also been correlated with increased IL-8 levels, highlighting its potential involvement in neuroinflammatory processes. However, evidence supporting vitamin D as a protective factor in AD remains inconclusive.

Vitamin D deficiency appears to disproportionately affect executive function and attention rather than memory, potentially due to cortical volume alterations. Given the widespread prevalence of vitamin D deficiency, further research is essential to elucidate its role in brain health and its potential utility in cognitive screening.

## ■ Primjeri Dobre Prakse u Organizaciji Obiteljske Medicine u Sjedinjenim Američkim Državama



Ksenija Kos

Obiteljska medicina i medicina primarne zdravstvene zaštite igraju ključnu ulogu u američkom zdravstvenom sustavu pružajući sveobuhvatnu skrb usmjerenu na pacijenta. Moja prezentacija će ukazati na inovativne pristupe organizaciji obiteljske i primarne zdravstvene zaštite, koji imaju cilj poboljšanja zdravstvene skrbi i smanjenje troškova u zdravstvu.

Jedan od najučinkovitijih modela je **Medicinski Dom Usmjeren na Pacijenta (Patient-Centered Medical Home (PCMH))**, koji naglašava koordiniranu, timsku skrb. Ovaj model značajno je poboljšao učinkovitost i smanjio učestale prijeme u bolnicu. Umjesto da bude specifično određeno, **PCMH je filozofija primarne zdravstvene zaštite** izgrađena na šest ključnih načela: **usmjerenost na pacijenta, sveobuhvatnost, timska suradnja, koordinacija, pristupačnost i fokus na kvalitetu i dobrobit.**

Model PCMH potiče pružatelje usluga i timove koji pružaju zdravstvenu skrb da pristupe pacijentima na individualizirani način rješavajući i jednostavne i složene zdravstvene probleme. Ovaj model osigurava da pacijenti dobiju skrb s **poštovanjem, dostojanstvom i suosjećanjem**, potičući razvoj odnosa između pacijenata i pružatelja zdravstvenih usluga utemeljenim na povjerenju. Davanjem prioriteta pravoj skrbi u pravo vrijeme i na najprikladniji način za svakog pacijenta, PCMH služi kao model za postizanje izvrsnosti u primarnoj zdravstvenoj zaštiti.

Osim PCMH-a, napredak u tehnologiji, kao što su **telemedicina i elektronički zdravstveni kartoni (EHR)**, proširio je pristup skrbi, posebno u ruralnim područjima. Pomak prema **modelima**

**skrbi temeljenim na vrijednostima**, uključujući **organizacije za odgovornu skrb (Accountable Care Organizations (ACO))**, potaknuo je veći fokus na preventivnu skrb i poboljšane ishode pacijenata. Osim toga, **inicijative primarne zdravstvene zaštite usmjerene na zajednicu (Community-oriented primary care (COPC) initiatives)** ojačale su vezu između pružatelja zdravstvenih usluga i lokalnog stanovništva, ba veći se društvenim odrednicama zdravlja.

Konačno, **širenje timske skrbi i programa razvoja radne snage** poboljšalo je suradnju među liječnicima, medicinskim sestrama i drugim zdravstvenim radnicima. Prikazujući primjere iz stvarnog svijeta, ova će prezentacija istaknuti kako ove strategije oblikuju obiteljsku i primarnu zdravstvenu zaštitu u Sjedinjenim Američkim Državama potičući bolju skrb za pacijente i veću učinkovitost u cijelom sustavu.

## ■ Examples of Good Practices in the Organization of Family Medicine in the United States



**Ksenija Kos**

Family and primary care medicine play a critical role in the U.S. healthcare system by providing comprehensive, patient-centered care that improves health outcomes and reduces costs. This presentation explores key best practices in family and primary care medicine, highlighting innovative approaches that enhance care delivery.

One of the most effective models is the **Patient-Centered Medical Home (PCMH)**, which emphasizes coordinated, team-based care. This model has significantly improved efficiency and reduced hospital readmissions. Rather than being a specific destination, PCMH is a philosophy of primary care built on six key principles: **patient-centeredness, comprehensiveness, team-based collaboration, coordination, accessibility, and a strong focus on quality and safety.**

The PCMH model encourages providers and care teams to meet patients where they are, addressing both simple and complex conditions. It ensures that patients receive care with **respect, dignity, and compassion**, fostering strong, trusting relationships between patients and healthcare providers. By prioritizing the right care at the right time and in the most suitable manner for each patient, PCMH serves as a model for achieving excellence in primary care.

Beyond PCMH, advancements in **technology**, such as **telemedicine and electronic health records (EHRs)**, have expanded access to care, particularly in rural areas. The shift toward **value-based care models**, including **Accountable Care Organizations (ACOs)**, has promoted a greater focus on preventive care and improved patient outcomes. Additionally,

**community-oriented primary care (COPC) initiatives** have strengthened the connection between healthcare providers and local populations, addressing social determinants of health.

Finally, the **expansion of team-based care and workforce development programs** has enhanced collaboration among physicians, nurse practitioners, and other healthcare professionals. By showcasing real-world examples, this presentation will highlight how these strategies are shaping the future of family and primary care medicine, driving better patient care and greater system-wide efficiency.

## ■ The Family Physician in a Network of Interactions: How to manage polypharmacy and multimorbidity in chronic patients?



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**Keywords:** complex patient management, polypharmacy, multimorbidity, family medicine



**Background:** The management of patients with multimorbidity and polypharmacy in primary care is an increasing concern. Family physicians must manage intricate relationships among diseases, drugs, symptoms, and psychosocial factors, which profoundly influence treatment adherence and clinical results.

**Objective:** to examine the complexity involved in managing chronic patients who are subjected to polypharmacy, highlighting the interactions among drugs, diseases, and symptoms, alongside the impact of psychosocial factors including patient adherence, familial support, financial limitations, and mental health status.

**Methods:** A review of contemporary literature and clinical guidelines regarding polypharmacy, multimorbidity, and adherence in primary care was performed. Case-based analysis demonstrates the difficulties encountered by family physicians in managing chronic patients with polypharmacy.

**Results:** Polypharmacy increases the risk of drug interactions, misinterpreting symptoms as side effects, and therapeutic burden, leading to poor adherence. Psychosocial factors can complicate treatment, requiring a thorough, tailored approach. Research shows that when psychological factors are considered, managing these patients may become four times more complex.

**Conclusion:** Family doctors struggle with polypharmacy in multimorbid patients. Beyond prescribing and managing drugs, they must decipher overlapping symptoms, reduce unnecessary adverse effects, and address the larger psychosocial determinants of health. Primary care doctors are mentally and emotionally strained by constant clinical decision-making, collaborative decision-making with patients, and interdisciplinary teamwork. This complexity demands medical competence, resilience, adaptability, and structured support. Recognizing the complexity of this profession is crucial for boosting resources, training, and systemic support for family physicians.

## **2. Glavni program**

## ■ Od hipertenzije do dijagnoze: Priča o hiperaldosteronizmu

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**Ključne riječi:** primarni hiperaldosteronizam, sekundarna hipertenzija, rezistentna hipertenzija  
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**Uvod:** Najčešći uzrok sekundarne arterijske hipertenzije je hiperaldosteronizam. Povezan je s visokim kardiovaskularnim i bubrežnim morbiditetom i mortalitetom. Može biti primarni i sekundarni. Primarni nastaje kao posljedica tumora koji luči aldosteron, bilateralne hiperplazije kore nadbubrežne žlijezde (NBŽ) ili karcinoma kore NBŽ. Sekundarni je posljedica suženja renalnih arterija uzrokovanog aterosklerozom ili fibromuskularnom hiperplazijom. Cilj rada je kroz prikaz slučaja naglasiti potrebu za većim stupnjem sumnje na sekundarnu arterijsku hipertenziju i hiperaldosteronizam kao najčešći uzrok iste.

**Prikaz slučaja:** Radilo se o bolesniku u dobi od 68 godina, s nekontroliranom arterijskom hipertenzijom i komorbiditetima (šećerna bolest, kronična bubrežna bolest). Krvni tlak nije bio kontroliran ni s pet antihipertenziva, te su se pojavljivali skokovi tlaka. U nalazima se našla hipokalemija (najniža vrijednost 2,7 mmol/l), koja nije bila ijetrogena, nakon čega se postavila sumnja na hiperaldosteronizam. Učinjeni su nalazi aldosterona i renina, rezultati kojih su upućivali na primarni hiperaldosteronizam (povišen aldosteron, suprimiran renin, povišen omjer aldosteron/renin). Bolesnik je stoga upućen endokrinologu. Realiziran je potvrđni test opterećenja fiziološkom otopinom natrijevog klorida, u kojem je izostala adekvatna supresija aldosterona te je zaključeno kako se radi o primarnom hiperaldosteronizmu. Učinjen je CT NBŽ u cilju isključenja karcinoma kore NBŽ. Kako bolesnik nije bio sklon eventualnom operacijskom liječenju, nije učinjena kateterizacija nadbubrežnih vena. U terapiji je ordiniran antagonist

mineralokortikoidnih receptora, nakon čega se prati normalizacija krvnog tlaka i korekcija hipokalemije.

**Rasprava:** U literaturi se navodi da je hiperaldosteronizam često neprepoznat. Testira se samo 2% rizične populacije. Mnoge studije potvrđuju da je primarni hiperaldosteronizam puno češći. Pristup dijagnozi primarnog hiperaldosteronizma trebao bi biti postupan, počevši od probira rizične populacije i potvrđnog testiranja. U bolesnika s nekontroliranom arterijskom hipertenzijom i hipokalemijom, potrebno je u diferencijalnoj dijagnozi razmotriti hiperaldosteronizam, kao jedan od najčešćih uzroka sekundarne hipertenzije.

**Zaključak:** Prepoznavanje, pravovremena dijagnoza i liječenje ciljanom kirurškom ili medicinskom terapijom hiperaldosteronizma, značajno će utjecati na bolji ishod liječenja ovakvih bolesnika, kao i na smanjenje kardiovaskularnog rizika.

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## ■ From Hypertension to Diagnosis: A Story of Hyperaldosteronism

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**Introduction:** The most common cause of secondary arterial hypertension is hyperaldosteronism, which is associated with high cardiovascular and renal morbidity and mortality. It can be classified as primary or secondary. Primary hyperaldosteronism results from an aldosterone-secreting tumor, bilateral adrenal cortex hyperplasia, or adrenal cortex carcinoma. Secondary hyperaldosteronism occurs due to renal artery stenosis caused by atherosclerosis or fibromuscular hyperplasia. The aim of this paper is to highlight the need for a higher degree of suspicion for secondary arterial hypertension and hyperaldosteronism as its most common cause through a case report.

**Case Report:** The case involves a 68-year-old patient with uncontrolled arterial hypertension and comorbidities, including diabetes mellitus and chronic kidney disease. Blood pressure remained uncontrolled despite treatment with five antihypertensive drugs, and the patient experienced episodic blood pressure spikes. Laboratory findings revealed hypokalemia (lowest value: 2.7 mmol/L), which was not iatrogenic, raising suspicion of hyperaldosteronism. Aldosterone and renin tests indicated primary hyperaldosteronism (elevated aldosterone, suppressed renin, and a high aldosterone-to-renin ratio). The patient was referred to an endocrinologist, and a confirmatory saline infusion test was performed, which showed inadequate suppression of aldosterone, confirming the diagnosis of primary hyperaldosteronism. A CT scan of the adrenal glands was conducted to exclude adrenal cortex carcinoma. Since the patient was not inclined to undergo surgical treatment, adrenal vein catheterization

was not performed. The patient was treated with a mineralocorticoid receptor antagonist, leading to blood pressure normalization and correction of hypokalemia.

**Discussion:** According to the literature, hyperaldosteronism is often underdiagnosed, with only 2% of at-risk individuals being tested. Numerous studies confirm that primary hyperaldosteronism is much more common than previously thought. The diagnostic approach should be systematic, starting with screening at-risk populations and confirmatory testing. In patients with uncontrolled arterial hypertension and hypokalemia, hyperaldosteronism should be considered as one of the most common causes of secondary hypertension.

**Conclusion:** Recognizing, diagnosing, and treating hyperaldosteronism in a timely manner, either through targeted surgical or medical therapy, significantly improves patient outcomes and reduces cardiovascular risk.

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**Uvod sa ciljem** Poremećaj crijevnog pražnjenja može se ispoljiti u vidu učestalog pražnjenja tekućih ili neformiranih stolica, proljev (dijareja) ili u vidu otežanog ili rijetkog pražnjenja stolice, zatvor (constipatio, opstipatio). Dijarejom se smatra količina stolice preko 200g/dan. Prema trajanju proljev se dijeli na akutni, koji traje kraće od dva tjedna, uporni u trajanju 2-4 tjedna i kronični koji traje 4 tjedna i duže. Zatvor (opstipacija, konstipacija) je po definiciji otežano i rijetko pražnjenje stolice. Cilj rada je ukazati na važnost prepoznavanja poremećaja stolice, prvenstveno kroničnih proljeva.

### Prikaz slučaja

Analizirana je povijest bolesti 35-godišnjeg pacijenta koji se vratio iz Afrike s odmora. Simptomi koje je imao su proljev, povraćanje, bolovi u truhu i temperatura do 39. Fizikalni pregled i laboratorijske pretrage s visokim CRP 140 i leukocitozom upućivale su na bakterijsku infekciju. Uzet je uzorak stolice za kulturu. Izolirana je bakterija salmonela, propisana je antibiotska terapija sulfamethoxazole, trimethoprim 400mg/80 mg u nakon koje se opće zdravstveno stanje popravilo. Nakon dva tjedna pacijent dolazi u ordinaciju sa zatvorom. Određena mu je laksativna terapija sir lactulose 667 mg/ml jedanput na dan u trajanju od pet dana, nakon koje se stolica regulirala. Sljedeći tjedan se je javila krv u stolici. Upućen je gastroenterologu. Učinjena je hitna kolonoskopija i potvrđen je ulcerozni kolitis.

### Diskusija

Procjenjuje se da je do 2020. od ulceroznog kolitisa i Chronove bolesti oboljelo 11,2 milijuna ljudi. Incidencija je 1 do 20 osoba na 100.000 stanovnika, prevalenca ulceroznog colitisa je 156 do 291 slučaj na 100 000 osoba godišnje. U usporedbi s Crohnovom bolešću, ulcerozni

kolitis ima veću prevalenciju u odraslih. Bolest je češća u Sjevernoj Americi i Europi nego u drugim regijama, najučestalije obolijevaju pacijenti u dobi 15-30 godine te oni iznad 60, dok razlike obzirom na spol nema. Protuupalni lijekovi za blagi i umjereni oblik jesu aminosalicilati, prvenstveno mesalazin često su prvi korak u liječenju ulceroznog kolitisa. Ukoliko nema odgovora na mesalazin, koriste se kortikosteroidi. Njima se u većine bolesnika postigne remisiju, ali ih se zbog njihovih brojnih i značajnih nuspojava ne smije koristiti kao trajnu terapiju i isključuju se čim se postigne remisija. Polovica zadrži remisiju bez kortikosteroida, a petina njih razvije ovisnost o kortikosteroidima. Pacijentima koji razviju ovisnost o kortikosteroidima ili su refraktorni na tu terapiju, čemu u podlozi mogu biti genetske osobine, potrebno je uvesti imunosupresore (azatioprin, metotreksat, 6-merkaptopurin) ili biološku terapiju (infliksimab, adalimumab).

Za sada nema jedinstvenog dijagnostičkog testa za potvrdu ulceroznog kolitisa, pa se dijagnoza temelji na ukupnoj analizi rezultata kliničkih, laboratorijskih, endoskopskih i patohistoloških nalaza. Vrlo je bitno odmah isključiti infekcije probavnog trakt. Endoskopija je zlatni standard za procjenu bolesnika s Crohnovom bolešću. Unatoč tomu, točna dijagnoza zahtijeva radiološke pretrage kako bi se odredio opseg i stadij bolesti, a posebno za dijagnosticiranje transmuralnih komplikacija uključujući fistule, apscese i flegmone.

**Zaključak:** Akutni proljev u velikom broju slučajeva može biti samo okidač u otkrivanju skrivenih kroničnih bolesti, a kod dugotrajnog proljeva obiteljski liječnici moraju pomišljati na druge moguće uzroke.

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## ■ Stool disorders

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**Introduction with aim :** Disorder of bowel movement can manifest itself in the form of frequent emptying of liquid or unformed stools, diarrhea (diarrhea) or in the form of difficult or rare emptying of stools, constipation (constipation, obstipatio). Diarrhea can be considered the amount of stool over 200g/day. According to the duration, diarrhea is divided into acute, which lasts less than two weeks, persistent, lasting 2-4 weeks, and chronic, lasting 4 weeks or longer. Constipation (constipation) is by definition difficult and infrequent stool emptying. The shape and consistency of the stool depends on the time that has passed since the previous emptying. The aim of the paper is to point out the importance of recognizing long-term diarrhea as well as constipation.

**Case report:** The medical history of a 35-year-old patient who returned from Africa on vacation was analyzed. The symptoms he had were diarrhea, vomiting, abdominal pain and a temperature up to 39. Physical examination and laboratory tests with high CRP 140 and leukocytosis indicated a bacterial infection. A stool sample was taken for culture. Salmonella bacteria were isolated, antibiotic therapy with sulfamethoxazole and trimethoprim 400mg/80mg was prescribed, after which the general health condition improved. After two weeks, the patient comes to the doctor's office with constipation. He was prescribed the laxative therapy lactulose cheese 667 mg/ml once a day for five days, after which the stool became regular. The next week there was blood in the stool. He was referred to a gastroenterologist. An emergency colonoscopy was performed and ulcerative colitis was confirmed.

**Discussion:** It is estimated that by 2020, 11.2 million people will be affected by ulcerative colitis and Crohn's disease. The incidence is 1 to 20 people per 100,000 inhabitants, the prevalence of

ulcerative colitis is 156 to 291 cases per 100,000 people per year. Compared to Crohn's disease, ulcerative colitis has a higher prevalence in adults. The disease is more common in North America and Europe than in other regions, the most common patients are 15-30 years old and those over 60, while the differences regarding no gender. Anti-inflammatory drugs for mild and moderate forms are aminosaliculates, primarily mesalazine, which are often the first step in the treatment of ulcerative colitis. If there is no response to mesalazine, corticosteroids are used. They achieve remission in most patients, but due to their numerous and significant side effects, they should not be used as permanent therapy and are discontinued as soon as remission is achieved. Half maintain remission without corticosteroids, and a fifth of them develop dependence on corticosteroids. Immunosuppressants (azathioprine, methotrexate, 6-mercaptopurine) or biological therapy (infliximab, adalimumab) should be administered to patients who develop dependence on corticosteroids or are refractory to this therapy, which may be due to genetic characteristics.

**Conclusion:** Acute diarrhea in a large number of cases can only be a trigger in the discovery of hidden chronic diseases, and in the case of long-term diarrhea, family doctors must think of ulcerative colitis, but when there is also constipation, colon cancer.

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## ■ Zadah iz usta – pristup dijagnostici i liječenju

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**Uvod s ciljem.** Halitoza, foetor ex ore ili zadah iz usta definira se kao neugodan miris koji potječe iz usne šupljine. Osim što uzrokuje značajnu socijalnu i psihološku nelagodu te narušava kvalitetu života, može biti znak mnogih podležćih bolesti. Cilj ovog rada je prikazati moguće uzroke halitoze te pristup dijagnostici i liječenju iz aspekta liječnika obiteljske medicine.

**Metode.** Pregledane su baze podataka UpToDate i PubMed korištenjem ključnih riječi halitoza (engl. halitosis), dijagnostika (engl. diagnostics) i liječenje (engl. treatment). Uključni kriteriji bili su dostupnost cjelovitih preglednih članaka na engleskom jeziku objavljenih u razdoblju od 2020. do 2025. godine. Navedene kriterije zadovoljilo je 15 članaka.

**Rasprava.** Halitoza se može podijeliti na pravu halitozu, pseudohalitozu i halitofobiju. Prava halitoza dodatno se klasificira prema uzrocima na oralne i ekstraoralne. Oralni uzroci čine otprilike 85% slučajeva, a uključuju parodontne bolesti, naslage na jeziku i zubni karijes. Ekstraoralni uzroci najčešće uključuju infekcije gornjih dišnih puteva, infekciju bakterijom *Helicobacter pylori* ili gastroezofagealnu refluksnu bolest, kao i sistemske bolesti poput šećerne bolesti, bolesti jetre ili bubrežne insuficijencije. Dijagnostika podrazumijeva temeljitu anamnezu, koja uključuje podatke o pušenju, prehrani i uzimanju lijekova, te klinički pregled, a rjeđe se koriste dijagnostički alati poput halimetra ili plinske kromatografije. Organoleptička procjena smatra se zlatnim standardom u dijagnostici, ali radi se o subjektivnoj metodi koja zahtijeva određeno iskustvo. Dok se oralni uzroci halitoze uspješno liječe higijenom usne šupljine i stomatološkim intervencijama, ekstraoralni uzroci zahtijevaju ciljano liječenje. U slučaju psiholoških uzroka halitoze, odnosno halitofobije, potrebno je učiniti psihologijsko testiranje te sukladno stanju provoditi farmakološko liječenje i/ili psihoterapiju.

**Zaključak.** Halitoza je čest problem koji može značajno utjecati na kvalitetu života bolesnika, a liječnik obiteljske medicine ima ključnu ulogu u prepoznavanju, dijagnosticiranju i upravljanju ovim stanjem. Sustavni pristup koji uključuje temeljitu anamnezu, klinički pregled i prepoznavanje potencijalnih oralnih, sistemskih ili psiholoških uzroka omogućuje ciljano upućivanje na dijagnostičku obradu te pravovremeni početak liječenja.

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## ■ Bad breath – approach to diagnosis and treatment

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**Introduction with aim.** Halitosis, foetor ex ore or bad breath is defined as an unpleasant odor originating from the oral cavity. In addition to causing significant social and psychological discomfort and impairing the quality of life, it can be a sign of many underlying diseases. The aim of this paper is to present the possible causes of halitosis and the approach to diagnosis and treatment from the perspective of a family medicine doctor.

**Methods.** UpToDate and PubMed databases were reviewed using the keywords halitosis, diagnostics and treatment. The inclusion criteria were the availability of complete review articles in English published in the period from 2020 to 2025. 15 articles met the above criteria.

**Discussion.** Halitosis can be divided into genuine halitosis, pseudohalitosis and halitophobia. Genuine halitosis is further classified according to causes into oral and extraoral. Oral causes account for approximately 85% of cases and include periodontal disease, plaque on the tongue, and dental caries. Extraoral causes most often include upper respiratory tract infections, *Helicobacter pylori* infection, or gastroesophageal reflux disease, as well as systemic diseases such as diabetes, liver disease, or kidney failure. Diagnostics involves a thorough medical history, which includes data on smoking, diet and medication, as well as a clinical examination, and diagnostic tools such as a halimeter or gas chromatography can also be used. Organoleptic evaluation is considered the gold standard in diagnostics, but it is a subjective method that requires certain experience. While oral causes of halitosis are successfully treated with oral hygiene and dental interventions, extraoral causes require targeted treatment. In the case of psychological causes of halitosis, i.e. halitophobia, it is necessary to perform psychological testing and, according to the condition, to carry out pharmacological treatment and/or psychotherapy.

**Conclusion.** Halitosis is a common problem that can significantly affect the patient's quality of life, and the family medicine doctor has a key role in recognizing, diagnosing and managing this condition. A systematic approach that includes a thorough anamnesis, clinical examination and identification of potential oral, systemic or psychological causes enables targeted referral for diagnostic treatment and timely initiation of treatment.

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## ■ Diferencijalna dijagnoza i terapija najčešćih stanja koja se manifestiraju simptomima žarenja u ustima, štućanja i "knede u grlu"

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**Uvod s ciljem.** Simptomi poput žarenja u ustima, štućanja i osjećaja "knede u grlu" su nespecifične smetnje koje mogu ukazivati na širok raspon različitih stanja, od benignih do potencijalno ozbiljnih. Cilj ovog rada je dati pregled diferencijalne dijagnostike (DD) te terapije stanja u kojima se navedeni simptomi najčešće susreću a važni za obiteljskog liječnika (OL).

**Metode.** Pregledane su baze podataka UpToDate i GoogleScholar korištenjem ključnih riječi sindrom pečenja u ustima, štućanja i osjećaj knedle u grlu (engl. burning mouth syndrome, hiccups, lump in the throat). Ključni kriteriji bili su dostupnost cjelovitih preglednih članaka na engleskom jeziku objavljenih u razdoblju od 2010. do 2024. godine, koji su obuhvaćali diferencijalnu dijagnostiku (DD) i liječenje navedenih stanja (engl. differential diagnosis and therapy). Navedene kriterije zadovoljilo je 25 članaka.

**Rasprava.** Sindrom pečenja jezika (BMS) je definiran kao žareća bol jezika ili oralne sluznice. Pored osjećaja pečenja u ustima može postojati i promijenjeni osjećaj okusa, dizestezija i/ili suhoće usta. Razlikujemo primarni i sekundarni BMS. Iako se kod primarnog ne može pronaći uzrok smatra se da se radi o neuropatskom mehanizmu koji se može manifestirati na tri nivoa od kojih je najučestaliji onaj s promjenama na senzornim živčanim nitima. U terapiji se mogu koristiti gabapeptini. Dijagnoza sekundarnog BMS se postavlja isključivanjem mogućih uzroka. U DD valja od učestalijih isključiti lichen planus, Sjogrenov sindrom, dijabetes, kandidijazu, pernicioznu anemiju, gastroezofagealni refluks, neadekvatne zubne proteze i kamence u pljuvačnim žljezdama te je liječenje etiološko. Štućanje je obično nespecifičan i prolazan simptom koji traje par minuta i spontano prestaje. Štućanje koje traje < 48 sati ne zahtijeva obradu. Kod štućanja koje traje duže obično se etiološki radi o strukturnim ili upalnim promjenama koje imaju utjecaj na centralni nervni sistem, vagalni ili frenički živac. Uzroci su najčešće u gastrointestinalnom sustavu (GI) (karcinomi jednjaka/želuca,

GERB, gastritis s ili bez ulkusa) ili centralno - Wallenbergov sindrom (infarkcija lateralnog dijela medule oblongate), aneurizme, demijelinizacijske bolesti i siringomijelija. Primijećena je i učestala povezanost štućanja i COVID-19 infekcije. Prvu liniju liječenja, bez obzira na trajanje, predstavljaju bihevioralne tehnike (zadržavanje daha/Valsalva, pijenje vode, masaža mekog nepca). Od farmakoterapije se preporuča empirijska upotreba IPP, baklofen, gabapeptin i klorpromazin). Globus pharyngeus/hystericus ili osjećaj „knede u grlu“ treba prvenstveno razlučiti prema smetnjama gutanja. To je najčešće manifestacija poremećaja sfinktera jednjaka, anksioznih poremećaja, kroničnog sinusitisa/rinitisa. Dijagnoza se postavlja isključivanjem potencijalno opasnijih stanja počevši od evaluacije simptoma, pregleda orofarinksa/larinksa a kod rekurirajućih ili progredirajućih simptoma se radi akt gutanja s kontrastom i gastroskopija. Temelj terapije je psihološki suport a od farmakoterapije se koriste IPP, niske doze tricikličkih antidepresiva (imipramin, amitriptilin) ili gabapeptin.

**Zaključak.** Bolesnici s nespecifičnim simptomima će se prvenstveno javljati svom liječniku obiteljske medicine. Kako su to obično stanja koja značajno utječu na kvalitetu života a ponekada mogu biti i manifestacija težih oboljenja liječnik prvog kontakta treba imati znanja odgovoriti na oba zahtjeva – adekvatnim terapijskim pristupom osigurati kvalitetu života, a istovremeno napraviti racionalnu obradu koja će isključiti potencijalno opasna stanja.

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## ■ Differential diagnosis and therapy of the most common conditions manifesting symptoms of burning mouth, hiccups and "lump in the throat"

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Introduction with aim. Symptoms such as burning in the mouth, hiccups, and the sensation of a "lump in the throat" are nonspecific complaints that can indicate a wide range of different conditions, from benign to potentially serious. This paper aims to provide an overview of the differential diagnosis (DD) and therapy of conditions where the aforementioned symptoms are most commonly encountered, which are important for family physicians (GPs).

Methods. Databases UpToDate and Google Scholar were reviewed using the keywords burning mouth syndrome, hiccups, and lump in the throat. Inclusion criteria included the availability of comprehensive review articles in English published from 2010 to 2024 that addressed differential diagnosis (DD) and treatment of these conditions (differential diagnosis and therapy). A total of 25 articles met the criteria.

Discussion. Burning mouth syndrome (BMS) is defined as burning pain in the tongue or oral mucosa. In addition to the burning sensation in the mouth, there may also be altered taste sensations, dysesthesia, and/or dry mouth. We distinguish between primary and secondary BMS. While no cause can be found in primary BMS, it is believed to be of neuropathic origin, manifesting at three levels, the most common being changes in sensory nerve fibers. Gabapentin can be used in therapy. The diagnosis of secondary BMS is made by excluding possible causes. In DD, more common conditions such as lichen planus, Sjögren's syndrome, diabetes, candidiasis, pernicious anemia, gastroesophageal reflux, inadequate dentures, and stones in the salivary glands should be ruled out, with etiological treatment being emphasized. Hiccups are generally nonspecific and transient symptoms lasting a few minutes that resolve spontaneously. Hiccups lasting < 48 hours do not require further evaluation. In cases where hiccups last longer, the etiology typically involves structural or inflammatory changes affecting the central nervous system, vagal, or phrenic nerves.

Common causes are found in the gastrointestinal system (GI) (esophageal/stomach cancers, GERD, gastritis with or without ulcers) or central issues like Wallenberg syndrome (lateral medullary infarction), aneurysms, demyelinating diseases, and syringomyelia. A frequent association between hiccups and COVID-19 infection has also been noted. First-line treatment, regardless of duration, includes behavioral techniques (breath-holding/Valsalva maneuver, drinking water, soft palate massage). For pharmacotherapy, empirical use of PPIs, baclofen, gabapentin, and chlorpromazine is recommended. Globus pharyngeus/hystericus or the sensation of a "lump in the throat" should primarily be differentiated based on swallowing difficulties. It is most commonly a manifestation of esophageal sphincter disorders, anxiety disorders, chronic sinusitis/rhinitis. Diagnosis is made by excluding potentially serious conditions, starting from symptom evaluation, oropharyngeal/laryngeal examination, and swallowing tests with contrast and gastroscopy in cases of recurrent or progressive symptoms. The basis of therapy is psychological support, and pharmacotherapy may include PPIs, low doses of tricyclic antidepressants (imipramine, amitriptyline), or gabapentin.

Conclusion. Patients with nonspecific symptoms will primarily seek out their family physician. Since these conditions typically significantly affect quality of life and can sometimes manifest more serious illnesses, the primary care physician must possess the knowledge to address both demands—ensuring a quality of life for the patient through appropriate therapeutic approaches while simultaneously conducting rational assessments to exclude potentially dangerous conditions.

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## ■ Pacijent sa zdravstvenom anksioznošću u obitelji

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**Uvod s ciljem:** Obitelj je temeljni i trajni izvor utjecaja, osnova genetskog nasljeđivanja, životnog iskustva i sustava vrijednosti. Stavovi prema brizi o zdravlju, načinu ishrane, stanovanju i emocionalnoj brizi usvajaju se unutar obitelji i ugrađuju se u kulturu življenja. Obiteljski liječnik u svom radu susreće se s raznorodnim problemima pacijenata i njihovih obitelji.. U zadnje vrijeme sve češće je prisutna zdravstvenom anksioznošću mladih. Glavni simptom zdravstvene anksioznosti je stalni strah da osoba ima ili će razviti ozbiljnu bolest. Cilj rada je ukazati na najvažnije uzroke i posljedice zdravstvene anksioznosti za pojedince i njihove obitelji zbog čega je potrebna potpora obiteljskih liječnika i drugih stručnjaka u slučajevima kad intenzitet zdravstvene anksioznosti ometa ili sprječava osobu i njegovu obitelj u svakodnevnom funkcioniranju i ostvarivanju životnih ciljeva.

**Rasprava:** Mnogi se ljudi nadaju da jednom kad napuste obitelj za sobom ostavljaju i sve probleme iz djetinstva. Međutim, mnogi opet doživljavaju slične probleme, osjećaje ,karakteristične odnose i navike i nakon napuštanja obitelji. Odgoj djece roditelja s negativnom percepcijom bolesti i zdravstvenih tegoba može utjecati da dijete, učenjem po modelu, razvije zdravstvenu anksioznost tijekom odrastanja, osobito kod promjena u funkcioniranju obitelji, stresnim situacijama i načinu života. Pored vlastitog nerazumijevanja onog što im se događa, moraju se suočavati i s nerazumijevanjem okoline, koja u početku može biti suosjećajna, ali s vremenom kad se pokaže da se ne radi o tjelesnoj bolesti, to suosjećanje se može izgubiti. Osobe s ovim problemom često u potrazi za informacijama pretražuju internet što dodatno može pojačati strah. Jednako je štetna i druga krajnost, nejavljanje liječniku, kad se potpuno ignoriraju simptomi u obitelji i kod pojedinca koji bi većinu ljudi zabrinuli i ponukali da zatraže stručnu pomoć. Kod neuspješnog suočavanja s

problemom i kad je intenzitet anksioznosti velik pomoć i potpora obiteljskog liječnika izuzetno je korisna . Procjenom funkcioniranja obitelji i pojedinca obiteljski liječnik će odlučiti hoće li problem moći samostalno riješiti ili će, u slučaju teže kliničke slike zdravstvene anksioznosti, pacijenta uputiti psihijatru.

**Zaključak:** Briga za zdravlje, kroz zdrav način života, je temelj prevencije bolesti pacijenata i njihovih obitelji. Kad briga za zdravlje postane pretjerana, i prijeđe u zdravstvenu anksioznost, koja remeti svakodnevne aktivnosti i funkcioniranje pojedinaca i njihovih obitelji, obiteljski će liječnik pružiti pomoć psihološkim savjetovanjem, uz medikamentoznu terapiju.

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## ■ Patients with health anxiety in the family

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**Introduction with aim:** Family is a fundamental and permanent source of influence, the basis of genetic inheritance, life experience and values system. Attitudes towards health care, diet, housing and emotional care are adopted within the family and are incorporated into the daily culture. Family doctor encounters various problems with its patients and their families. Recently, health anxiety is more and more present within young people. The main symptom manifests is the constant fear of having or developing a serious illness. The aim is to point out the most important causes and consequences of health anxiety on individuals and their families. It emphasizes the need for family doctors and other experts' support, particularly when the intensity of health anxiety hinders or prevents a person and his family from normal daily functioning and achieving their life goals.

**Discussion:** Many people hope that once they leave the family, they leave behind all the problems from childhood. However, many experiences similar problems, feelings, characteristic relationships and habits even after leaving the family. Parents with a negative perception of illness and health problems can negatively influence the child. Due to learning from the model (their parents), children can develop health anxiety while growing up. It is particularly manifested during changes in family functioning, stressful situations and lifestyle changes. In addition to their own misunderstanding of what is happening to them, they also have to face the misunderstanding of the environment. While they may be faced with sympathy at first, over time, when it turns out that it is not a physical illness, that sympathy may be lost. People often turn towards the internet in search of information, which can further escalate their fear. On the other hand, it can be equally harmful when symptoms are being ignored and an individual in need of help is being ignored and

not prompted to seek professional help. During the period of high anxiety and unsuccessful dealing with an issue, the help and support of a family doctor is extremely useful. By assessing the functioning of the family and the individual, doctor will decide whether he will be able to solve the problem on its own or, in the case of a more severe cases, will refer the patient to a psychiatrist.

**Conclusion:** Health care driven by a healthy lifestyle is the basis of disease prevention for patients and their families. When individual's concern for health becomes excessive, turning into the health anxiety, disturbing daily activities and functioning of individuals and their families, family doctor will provide psychological counseling, alongside the drug therapy.

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## ■ Briga o zdravlju ili zdravstvena anksioznost?

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**Uvod s ciljem:** Briga o zdravlju je temeljna preventivna aktivnost, posebno u sprječavanju i ranom otkrivanju bolesti. Brigu o zdravlju možemo definirati kroz pridržavanje zdravog načina života, u prvom redu pravilne prehrane i tjelesnog vježbanja, te primjerenog načina suočavanja sa stresom, uz izbjegavanje sredstava ovisnosti. Važna uloga obiteljskih liječnika je motivirati pacijente za brigu o zdravlju. U brigu o zdravlju ubraja se i pravovremena reakcija na simptome i znakove bolesti. Obiteljskim liječnicima važno je razlikovati uobičajenu zabrinutost pri pojavi simptoma i znakova bolesti od zdravstvene anksioznosti (novi naziv za hipohondrijazu). Cilj rada je ukratko prikazati izazove dijagnosticiranja i liječenja zdravstvene anksioznosti u svakodnevnom radu obiteljskih liječnika.

**Rasprava:** Dijagnostički i statistički priručnik za duševne poremećaje Američke psihijatrijske udruge (DSM-5), za razliku od Međunarodne klasifikacije bolesti (MKB-10), umjesto dijagnoze hipohondrijskog poremećaja, predlaže dva dijagnostička entiteta: poremećaj somatskih simptoma (engl. somatic symptom disorder-SSD) i anksiozni poremećaj zbog bolesti (engl. illness anxiety disorder-IAD). Oba entiteta dijele visoku razinu zdravstvene anksioznosti, ali u anksioznom poremećaju zbog bolesti radi se o anksioznosti zbog očekivanih, ali sada nepostojećih simptoma, za razliku od poremećaja somatskih simptoma gdje se anksioznost nadovezuje na postojeće simptome. Obiteljski će liječnici posumnjati da se radi o zdravstvenoj anksioznosti uz postojeće simptome, prateći verbalnu i neverbalnu komunikaciju s pacijentom prilikom uzimanja anamneze, fizikalnog pregleda, propisivanja terapije i upućivanja na daljnje pretrage. Dramatično iznošenje simptoma, te zahtjevi da se navedeni simptomi žurno dijagnosticiraju sofisticiranim uređajima, upozorit će obiteljske liječnika da se možda radi o poremećaju zdravstvenih simptoma. Također, učestali posjeti pacijenata zbog istih

ili različitih simptoma, uz zahtjeve za opetovanu obradu govore u prilog zdravstvene anksioznosti. Ako se radi o zdravstvenoj anksioznosti npr. zbog moguće covid 19 infekcije u budućnosti, sada bez simptoma, tada je to anksiozni poremećaj zbog bolesti.

Obiteljski će liječnik zdravstveno anksioznim pacijentima pomoći psihološkim savjetovanjem, odnosno psihoterapijom. Ako je potrebno, propisat će antidepresive i anksiolitike, što se pokazalo uspješnijim u slučajevima zdravstvene anksioznosti s prisutnim simptomima. U težim slučajevima uputiti će pacijenta psihijatru.

**Zaključak:** Zadaća obiteljskog liječnika je razlikovati zabrinutost za zdravlje od zdravstvene anksioznosti, te psihološkim savjetovanjem i psihoterapijom, uz racionalnu farmakoterapiju umanjiti posljedice zdravstvene anksioznosti.

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## ■ Health care or health anxiety?

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**Introduction with aim:** Health care is a fundamental preventive activity, especially in the prevention and early detection of diseases. Health care can be defined through adherence to a healthy lifestyle, primarily proper nutrition and physical exercise, as well as an appropriate way of coping with stress, while avoiding addictive substances. An important role of family doctors is to motivate patients to take care of their health. Taking care of health also includes a timely reaction to the symptoms and signs of the disease. It is important for family physicians to distinguish between common worry at the onset of symptoms and signs of illness and health anxiety (the new name for hypochondriasis). The aim of the paper is to briefly present the challenges of diagnosing and treating health anxiety in the daily work of family doctors.

**Discussion:** The Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (DSM-5), unlike the International Classification of Diseases (ICD-10), instead of diagnosing hypochondriacal disorder, proposes two diagnostic entities: somatic symptom disorder (SSD) and illness anxiety disorder (IAD). Both entities share a high level of health anxiety, but in illness anxiety disorder it is anxiety due to expected, but now non-existent symptoms, unlike somatic symptom disorder where anxiety builds on existing symptoms<sup>2</sup>. Family doctors will suspect that it is health anxiety in addition to the existing symptoms, monitoring verbal and non-verbal communication with the patient during history taking, physical examination, prescribing therapy and referral for further tests. The dramatic presentation of symptoms, and the demands that said symptoms be urgently diagnosed with sophisticated devices, will alert family physicians that it may be a disorder of health symptoms. Also, frequent patient visits due to the same or different symptoms, along with requests for repeated treatment, speak in

favor of health anxiety. If it is about health anxiety, e.g. due to a possible covid-19 infection in the future, now without symptoms, then it is an anxiety disorder due to the disease.

The family doctor will help health-anxious patients with psychological counseling or psychotherapy. If necessary, they will prescribe antidepressants and anxiolytics, which have been shown to be more successful in cases of health anxiety with present symptoms<sup>4</sup>. In more severe cases, the patient should be referred to a psychiatrist.

**Conclusion:** The task of the family doctor is to distinguish health concerns from health anxiety, and to reduce the consequences of health anxiety through psychological counseling and psychotherapy, along with rational pharmacotherapy.

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## ■ Does social media promote health anxiety?

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**Introduction with aim:** Social media has become a key part of modern life, allowing users to connect, communicate, and share content regardless of distance. Platforms like Facebook, Instagram, and TikTok provide a space to express yourself, share information, and interact with others. However, their popularity has less positive aspects, especially in terms of their impact on mental health. The aim of this paper is to explore the impact of social media on mental health, including challenges such as anxiety, depression and cyberchondria, as well as opportunities for socialisation and support. The paper seeks to identify the factors of negative consequences and offer recommendations for preserving mental well-being through balancing online and offline activities.

**Discussion:** According to the World Health Organization, mental health includes well-being, resilience to stress, and the ability to contribute productively to society. The use of social media can impair these aspects of mental health, even for people who have not been diagnosed with mental health disorders. Research shows a correlation between time spent on networks and phenomena such as anxiety and depression, especially in adolescents. However, it is important to note that the way you use social media is more important than the total duration of use.

People with social anxiety are particularly vulnerable, who often prefer online communication, but by doing so they can deepen the feeling of loneliness and disrupt real social relationships. This can lead to problems such as depression, low self-esteem, and substance addiction. Social networks thus become a double-edged sword – on the one hand, they provide opportunities for socialization and support, while on the other hand, they can

cause stress, envy and a sense of inferiority due to constant comparisons with idealized depictions of other users. The rise in global popularity of social media, with more than 4.2 billion active users, has further complicated these challenges. Predictions of growth of 16.7% in the coming years suggest that their impact on mental health will remain a significant topic. Negative effects, such as emotional dependence and increased anxiety, are often exacerbated by the user's inability to set boundaries or distinguish between the real and virtual worlds. The phenomenon of cyberchondria, i.e. excessive search for health information on the Internet, further contributes to these problems. Cyberchondria involves a cycle of anxiety and repetitive searching, which can worsen the psychological state of the user. This phenomenon often affects people with high levels of health anxiety, but it can also affect healthy individuals. Methodological research points to the need to educate users on critical evaluation of information and focus on reliable sources. To mitigate the negative effects of social media on mental health, experts advise setting clear boundaries on usage, choosing content that motivates, and maintaining a balance between online and offline activities. Maintaining quality interpersonal relationships and presence in the real world is key to preserving mental well-being.

**Conclusion:** Overall, while social media and digital technologies bring many benefits, their impact on mental health requires a careful approach to recognize and minimize negative consequences. Developing digital literacy and responsible behaviour in the virtual space remains a priority for individuals and society as a whole.

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## ■ Orthorexia – A Disease or Not?

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**Introduction with Aim:** Orthorexia (Orthorexia nervosa) is a relatively new term that describes a pathological preoccupation with healthy eating. This acquired disorder of self-imposed dietary rules was first described by researchers Knight and Bratman in a popular article in 1997. Orthorexia leads to distress, anxiety, social isolation, and sometimes severe malnutrition. The aim of this paper is to provide a comprehensive review of the literature to highlight the existence of this growing problem, which lacks a universally accepted definition and diagnostic criteria, as it is not classified as a disease, thereby complicating the possibility of treatment.

**Discussion:** In contrast to obesity, which is the result of an unhealthy lifestyle, lack of physical activity, and consumption of fast and genetically modified food, the media, especially social networks, have begun promoting the trend of "healthism," which encompasses healthy eating habits, health promotion, and regular exercise. This trend, as a marker of success and good health, imposes a standard of beauty – a fit, toned body, healthy eating, and regular exercise. Orthorexia often begins innocently, with the desire to improve health and eating habits, but later evolves into an obsession and fanaticism, leading to eating disorders and psycho-physical developmental issues. It is more common among vegans, vegetarians, animal rights activists, and fruitarians. Individuals with orthorexia strive to be slim, are very physically active, strictly adhere to their dietary plans, spend significant time calculating the caloric value of foods, meticulously study product labels, ensure that food is free from herbicides and pesticides, avoid fats, artificial colors, flavors, preservatives, and verify if the food is organic. They eat small meals more frequently. They prepare food in ways they believe are

healthy and often bring meals they have prepared themselves to restaurants or social gatherings, leading to social isolation, distress, and anxiety. In bulimia and anorexia, patients focus on the quantity of food they consume, while in orthorexia, they focus on consuming food they perceive as good and high-quality, which results in the exclusion of large food groups and subsequent malnutrition. In addition to anxiety, they often experience guilt or panic attacks if they consume something they deem insufficiently clean or appropriate, which can lead to depression or obsessive-compulsive disorder. Women, adolescents, and younger people who frequently use the internet and social networks are at higher risk, as research shows that, besides spreading positive attitudes about nutrition, social networks can also contribute to the development of eating disorders.

**Conclusion:** Through a literature review, this paper highlights the risk factors for the development of orthorexia, as well as the need for standardized diagnostic criteria and tools, along with further research that would enable the recognition, identification, and effective treatment of this eating disorder. Since it is not identified as a disease, there are no treatment guidelines. It is evident that this is a disorder of the mental structure of the personality, which is why psychiatrists should engage more actively with this issue.

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## ■ Strah od dijagnoze: kako početni simptomi izazivaju zdravstvenu anksioznost u kontekstu neurodegenerativnih bolesti

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**Uvod s ciljem.** Zdravstvena anksioznost postaje sve češći problem među osobama koje primijete početne simptome koji bi mogli upućivati na neurodegenerativne bolesti, poput Alzheimerove ili Parkinsonove bolesti. Ovaj strah od moguće dijagnoze može imati dubok utjecaj na mentalno zdravlje, smanjujući kvalitetu života i izazivajući dodatne psihološke poteškoće. Povezanost između simptoma koji nalikuju neurodegenerativnim bolestima i osjećaja tjeskobe i nesigurnosti čini ovu temu važnim područjem za daljnje istraživanje i razumijevanje. Cilj ovog rada je prikazati kako početni simptomi neurodegenerativnih bolesti izazivaju zdravstvenu anksioznost među pacijentima i njihovim obiteljima, čak i ukoliko je uzrok simptoma u potpunosti nevezan uz neurodegeneraciju. Također, cilj je prikazati kako rano prepoznavanje simptoma i odgovarajuća edukacija mogu pomoći u smanjenju stresa i anksioznosti te poboljšati pristup dijagnostičkim i terapijskim opcijama.

**Rasprava.** Početni simptomi neurodegenerativnih bolesti, poput blage kognitivne disfunkcije, problema s pamćenjem ili motoričkim promjenama, često su nespecifični i mogu biti uzrokovani mnogim drugim stanjima. Ovo nesigurno i nejasno iskustvo može kod ljudi izazvati snažnu zdravstvenu anksioznost, u kojoj se strah od potencijalne dijagnoze često miješa s nesigurnošću u vezi s vlastitim zdravljem. Važno je razumjeti kako ove emocije mogu negativno utjecati na njihov svakodnevni život, čineći ih podložnima depresiji, socijalnoj izolaciji i smanjenju životne aktivnosti. Edukacija, podrška i pravovremeno medicinsko savjetovanje mogu igrati ključnu ulogu u smanjenju ovog straha i izgradnji realističnijeg i zdravijeg pristupa simptomima.

**Zaključak.** Zdravstvena anksioznost izazvana strahom od neurodegenerativnih bolesti predstavlja značajan izazov za pacijente, obitelji i zdravstvene stručnjake. Razumijevanje psiholoških i emocionalnih aspekata ovog problema te razvoj strategija za podršku pacijentima ključni

su za smanjenje negativnih utjecaja na mentalno zdravlje. Integrirani pristup, koji uključuje pravovremenu edukaciju, psihološku podršku i ranu dijagnozu, može značajno poboljšati kvalitetu života onih koji se suočavaju s ovim strahovima.

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## ■ Fear of diagnosis: how initial symptoms trigger health anxiety in the context of neurodegenerative diseases

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**Introduction with aim.** Health anxiety is becoming an increasingly common issue among individuals who notice early symptoms that may indicate neurodegenerative diseases, such as Alzheimer's or Parkinson's disease. This fear of a possible diagnosis can have a profound impact on mental health, reducing quality of life and causing additional psychological difficulties. The connection between symptoms resembling neurodegenerative diseases and feelings of anxiety and uncertainty makes this topic an important area for further research and understanding. Aim of this paper is to demonstrate how the initial symptoms of neurodegenerative diseases trigger health anxiety among patients and their families, even if the cause of the symptoms is entirely unrelated to neurodegeneration. Additionally, the goal is to show how early recognition of symptoms and appropriate education can help reduce stress and anxiety, as well as improve access to diagnostic and therapeutic options.

**Discussion.** Initial symptoms of neurodegenerative diseases, such as mild cognitive dysfunction, memory problems, or motor changes, are often nonspecific and can be caused by many other conditions. This uncertain and unclear experience can lead to significant health anxiety, where the fear of a potential diagnosis is often mixed with uncertainty about one's own health. It is important to understand how these emotions can negatively impact individuals' daily lives, making them susceptible to depression, social isolation, and a reduction in life activities. Education, support, and timely medical counseling can play a crucial role in reducing this fear and fostering a more realistic and healthier approach to the symptoms.

**Conclusion.** Health anxiety triggered by the fear of neurodegenerative diseases presents a significant challenge for patients, families, and healthcare professionals. Understanding the psychological and emotional aspects of this issue, as well as developing strategies to support patients,

is crucial for reducing the negative impacts on mental health. An integrated approach, which includes timely education, psychological support, and early diagnosis, can significantly improve the quality of life for those facing these fears.

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## ■ Sinkopa zbog ortostatske hipotenzije

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**Uvod s ciljem:** Sinkopa se odnosi se na prolazni ili kratkotrajni gubitak svijesti koji je posljedica smanjenja cerebralnog protoka krvi i obično je povezan s gubitkom posturalnog tonusa, ali sa spontanom oporavkom. Cilj ovog rada je dati prikaz i opis ortostatske sinkope. Klasična ortostatska hipotenzija nastaje kada postoji trajno smanjenje krvnog tlaka od najmanje 20 mmHg sistoličkog ili 10 mmHg dijastoličkog unutar 3 minute nakon stajanja ili uspravnog položaja do 60 stupnjeva na stolu s nagnutom glavom prema gore. Ortostatska sinkopa odnosi se na sinkopu koja je posljedica posturalnog pada krvnog tlaka.

**Rasprava:** Postoji više uzroka ortostatske hipotenzije koji mogu dovesti do sinkope, uključujući neuralno posredovane (neurogene) i neneurogene posredovane uzroke. Neurogeno posredovani uzroci uključuju stanja koja uzrokuju primarno ili sekundarno zatajenje autonomnog sustava: periferna neuropatija koja se viđa kod šećerne bolesti, alkoholičara, nedostatak vitamina B12, amiloidoze, idiopatska posturalna hipotenzija, multisistemske atrofije (parkinsonizam, progresivna cerebelarna degeneracija, demencija s Lewyjevim tjelešcima), neuropatija izazvana toksinima, lijekovima ili infekcijom. Uzroci koji nisu neuralno posredovani uključuju: lijekove (antihipertenzivi, vazodilatatori), smanjeni volumen krvi (adrenalna insuficijencija, gubitak krvi, dehidracija, hipovolemija ili smanjen efektivni intravaskularni volumen). Ortostatska sinkopa može se pojaviti iznenada bez upozorenja ili joj mogu prethoditi simptomi. Povezani simptomi obično su posljedica cerebralne hipoperfuzije koja se javlja u uspravnom položaju i uključuju vrtoglavicu, osjećaj slabosti ili mučnine, dijaforezu, osjećaj topline ili zamagljen vid. Ortostatsku hipotenziju prema vremenu nastanka dijelimo na inicijalnu, klasičnu i kasnu. Incidencija raste sa dobi. Liječenje ortostatske sinkope ovisi o temeljnom uzroku i uključuje i nefarmakološke i farmakološke mjere. Mjere nefarmakološkog liječenja imaju za cilj ili povećanje venskog povratka u srce uz istovremeno smanjenje venskog skupljanja u donjim ekstremitetima ili povećanje

volumena krvi za održavanje krvnog tlaka u ležećem položaju. Edukacija pacijenata vrlo bitna je u cijelom procesu o potencijalnim precipitirajućim čimbenicima ortostatske sinkope te u dugoročnom liječenju. Za uspješno liječenje preporučuje se suradnja bolesnika s liječnikom obiteljske medicine i promjenom farmakološke i nefarmakološke terapije.

**Zaključak:** Ortostatska hipotenzija se najčešće javlja zbog promjena iz ležećega položaja u stojeći. Fizički napor ili teži obrok mogu pojačati simptome. Većina drugih pridruženih simptoma je najčešće povezana s uzrokom. Incidencija raste sa dobi, vrlo bitan je edukacija pacijenta oko prepoznavanja simptoma i metoda nefarmakološkog liječenja.

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## ■ Syncope due to orthostatic hypotension

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**Introduction with aim:** Syncope refers to a transient or short-term loss of consciousness resulting from a decrease in cerebral blood flow and is usually associated with a loss of postural tone, but with spontaneous recovery. The aim of this paper is to provide an overview and description of orthostatic syncope. Classical orthostatic hypotension occurs when there is a sustained decrease in blood pressure of at least 20 mmHg systolic or 10 mmHg diastolic within 3 minutes of standing or standing up to 60 degrees on a table with the head tilted upwards. Orthostatic syncope refers to syncope that is secondary to a postural drop in blood pressure.

**Discussion:** There are multiple causes of orthostatic hypotension that can lead to syncope, including neurally mediated (neurogenic) and nonneurogenic mediated causes. Neurogenic mediated causes include conditions that cause primary or secondary autonomic failure: peripheral neuropathy seen in diabetes mellitus, alcoholism, vitamin B12 deficiency, amyloidosis, idiopathic postural hypotension, multisystem atrophy (parkinsonism, progressive cerebellar degeneration, dementia with Lewy bodies), and neuropathy induced by toxins, drugs, or infection. Non-neurally mediated causes include: medications (antihypertensives, vasodilators), decreased blood volume (adrenal insufficiency, blood loss, dehydration, hypovolemia, or decreased effective intravascular volume). Orthostatic syncope may occur suddenly without warning or may be preceded by symptoms. Associated symptoms are usually due to cerebral hypoperfusion occurring in the upright position and include dizziness, feeling faint or nauseous, diaphoresis, feeling warm, or blurred vision. Orthostatic hypotension is divided into initial, classic, and late-onset according to the time of onset. The incidence increases with age. Treatment of orthostatic syncope depends on the underlying cause and includes both non-pharmacological and pharmacological measures. Non-pharmacological treatment measures aim to either increase venous return to the heart while reducing venous congestion in the lower

extremities or increase blood volume to maintain blood pressure in the supine position. Patient education is essential throughout the process regarding potential precipitating factors for orthostatic syncope and in long-term management. For successful treatment, it is recommended that the patient cooperate with their family doctor and change pharmacological and non-pharmacological therapy.

**Conclusion:** Orthostatic hypotension most often occurs due to changes from a lying position to a standing position. Physical exertion or a heavy meal can increase symptoms. Most other associated symptoms are most often related to the cause. The incidence increases with age, and patient education about symptom recognition and non-pharmacological treatment methods is very important.

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## ■ Neurogena sinkopa

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**Uvod s ciljem:** Neurogena sinkopa je jedan od najčešćih uzroka rekurentne sinkope u bolesnika sa strukturno normalnim srcem. Neurogena sinkopa obuhvaća širok raspon refleksogene sinkope koja uključuje vazovagalni tip, mikcionu sinkopu, preosjetljivost karotidnog sinusa i postprandijalnu sinkopu. Istraživanja sugeriraju da oslabljena prilagodba arterijskog barorefleksa na ortostatski stres, uz smanjeni vazokonstriktorski podražaj simpatičkog autonomnog sustava, pridonosi razvoju hipotenzije i bradikardije koji određuju vazovagalni odgovor<sup>1</sup>. Cilj rada je prikazati dijagnostiku i terapijski pristup pacijentima s neurogenom sinkopom u ordinaciji obiteljske medicine.

**Rasprava:** Obiteljski liječnik će isključiti ostale oblike sinkope i dijagnosticirati neurogenu sinkopu na temelju iscrpne anamneze s naglaskom na biopsihosocijalni model, fizikalnim pregledom (uključujući ortostatska mjerenja krvnog tlaka), EKG obradom, te slanjem na kardiološku i neurološku obradu. „Tilt table test“ je dijagnostički alat izbora za procjenu pacijenata s rekurentnom neurogenom sinkopom, pružajući prihvatljivu specifičnost i osjetljivost<sup>2</sup>. U bolesnika s vazovagalnom sinkopom simpatička aktivnost u mirovanju je povećana, a regulacija barorefleksa tijekom ortostatskog stresa prigušena, što dovodi do vazovagalne sinkope. Vazovagalna sinkopa se najčešće javlja prilikom dugotrajnog stajanja, vadeanja krvi, ili u sklopu akutne reakcije na stres. Farmakološka modulacija osjetljivosti baroreceptora može predstavljati obećavajući tretman neuroposredovane sinkope<sup>3</sup>. Emocionalni distres povezan je s ponavljajućom neurogenom sinkopom koja ugrožava kvalitetu života pacijenta. Pacijenti s refraktornom vazovagalnom sinkopom koji su podvrgnuti redovitoj psihoterapijskoj intervenciji imali su manje ponavljanja događaja i poboljšali kvalitetu života. U usporedbi

s kardiogenim sinkopama, neurogene sinkope imaju bolju prognozu.

**Zaključak:** Neurogena sinkopa je česti uzrok sinkope. Obiteljski liječnik, nakon eliminacije ostalih oblika sinkope, može uspješno poboljšati kvalitetu života pacijenata s neurogenom sinkopom, uz modifikaciju farmakoterapije, te psihološko savjetovanje i psihoterapiju.

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## ■ Neurogenic syncope

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**Introduction with aim:** Neurogenic syncope is one of the most common causes of recurrent syncope in patients with a structurally normal heart. Neurogenic syncope encompasses a wide range of reflexogenic syncope that includes the vasovagal type, micturition syncope, carotid sinus hypersensitivity, and postprandial syncope. Research suggests that a weakened adaptation of the arterial baroreflex to orthostatic stress, along with a reduced vasoconstrictive stimulus of the sympathetic autonomic system, contributes to the development of hypotension and bradycardia, which determine the vasovagal response<sup>1</sup>. The aim of the paper is to present the diagnosis and therapeutic approach to patients with neurogenic syncope in a family medicine practice.

**Discussion:** The family physician will eliminate other forms of syncope and diagnose neurogenic syncope based on a thorough history with an emphasis on the biopsychosocial model, physical examination (including orthostatic blood pressure measurements), ECG workup, and referral for cardiology and neurological workup. The tilt table test is the diagnostic tool of choice for the evaluation of patients with recurrent neurogenic syncope, providing acceptable specificity and sensitivity<sup>2</sup>. In patients with vasovagal syncope, sympathetic activity at rest is increased, and baroreflex regulation during orthostatic stress is dampened, which leads to vasovagal syncope. Vasovagal syncope most often occurs when standing for a long time, drawing blood, or as part of an acute reaction to stress. Pharmacological modulation of baroreceptor sensitivity may represent a promising treatment for neuromediated syncope<sup>3</sup>. Emotional distress is associated with recurrent neurogenic syncope, which threatens the patient's quality of life. Patients with refractory vasovagal syncope who underwent regular psychotherapeutic intervention had

fewer recurrences and improved quality of life<sup>4</sup>. Compared to cardiogenic syncope, neurogenic syncope has a better prognosis.

**Conclusion:** Neurogenic syncope is a common cause of syncope. The family doctor, after eliminating other forms of syncope, can successfully improve the quality of life of patients with neurogenic syncope, with the modification of pharmacotherapy, as well as psychological counseling and psychotherapy.

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## ■ Kardiogena sinkopa

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**Uvod s ciljem:** Kardiogena sinkopa je potencijalno životno ugrožavajuće stanje koje karakterizira kratkotrajni, prolazni gubitak svijesti uzrokovan srčanim poremećajima. Sinkopa je vrlo čest klinički entitet zbog kojeg bolesnici traže liječničku pomoć te je razlikovanje kardiogene od drugih uzroka sinkope ključan korak u dijagnostičkom procesu koji može reducirati recidive i brojne druge neželjene ishode. Cilj ovog predavanja je ponoviti glavne značajke kardiogene sinkope s naglaskom na dijagnozu, stratifikaciju rizika i liječenje.

**Rasprava:** Detaljno uzimanje anamnestičkih podataka, klinički pregled i odgovarajući dijagnostički postupci ključni su za dijagnozu kardijalne sinkope. Glavne karakteristike koji upućuju na srčane uzroke gubitka svijesti su podatak o ranijim srčanim bolestima, bol u prsima, sinkopa u fizičkom naporu te palpitacije. 12 kanalni EKG je prva dijagnostička metoda kojom možemo identificirati aritmije, smetnje provođenja, ali i strukturne bolesti srca. Kod suspektne kardijalne sinkope daljnje dijagnostičke pretrage podrazumijevaju ultrazvuk srca, 24-satno snimanje EKG-a i elektrofiziološko ispitivanje. Aritmije, kako bradikardni, tako i tahikardni poremećaji ritma, čest su uzrok kardijalne sinkope. Stratifikacija rizika, osobito kod pacijenata sa sumnjom na aritmije, vrlo je važan korak u određivanju vjerojatnosti ponovnog događanja i potrebe za naprednim dijagnostičkim metodama, uključujući elektrofiziološke studije ili ugradnju implantabilnog „loop recordera“. Strukturne bolesti srca, poput aortne stenoze i hipertrofijske kardiomiopatije, također mogu dovesti do sinkope i zahtijevaju slikovne i funkcionalne dijagnostičke metode. Liječenje kardiogene sinkope ovisi o etiologiji. Za aritmijske uzroke terapijske opcije uključuju antiaritmijske lijekove, ugradnju elektrostimulatora srca, implantabilnog kardioverter-defibrilatora (ICD) ili katetersku ablaciju. Strukturni uzroci ponekad zahtijevaju kirurške ili perkutane intervencije, kao što su na primjer

zamjena aortnog zaliska ili septalna miektomija kod hipertrofične kardiomiopatije.

**Zaključak:** Rana identifikacija i stratifikacija rizika bolesnika s kardiogenom sinkopom ključni su za prevenciju nepovoljnih ishoda. Multidisciplinarni pristup, koji uključuje liječnike obiteljske medicine, kardiologe, neurologe i specijaliste hitne medicine, izuzetno je važan u procesu dijagnoze i liječenja ovih bolesnika.

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## ■ Cardiogenic syncope

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**Introduction with aim.** Cardiac syncope is a potentially life-threatening condition characterized by transient loss of consciousness (TLOC) due to underlying cardiovascular causes. While syncope is a common clinical presentation, distinguishing cardiac syncope from other causes is critical, as the underlying aetiology can significantly affect patient outcome. This presentation reviews key aspects of cardiac syncope focusing on diagnosis, risk stratification, and management.

**Discussion.** A detailed clinical history, physical examination, and appropriate diagnostic work-up are essential for identifying cardiac causes of syncope. Key clinical features suggestive of cardiac syncope include a history of heart disease, syncope during exertion, and the presence of palpitations or other arrhythmic symptoms. The guidelines recommend an initial 12-lead electrocardiogram (ECG) to identify arrhythmic causes or conductance disturbances, followed by further testing such as ambulatory ECG monitoring, echocardiography, and stress testing to investigate structural heart disease and assess functional capacity. Both bradyarrhythmias and tachyarrhythmias are common causes of cardiac syncope. Risk stratification, particularly in patients with suspected arrhythmias, are another important step to determine the likelihood of recurrence and the need for advanced diagnostic modalities, including electrophysiological studies or implantable loop recorders. Structural heart conditions, such as aortic stenosis or hypertrophic cardiomyopathy, may also lead to syncope and require targeted imaging and functional assessment. Management of cardiac syncope depends on the aetiology. For arrhythmic causes, therapeutic options may include antiarrhythmic drugs, pacemaker, implantable cardioverter-defibrillator (ICD) implantation, or catheter ablation in certain cases. Structural causes sometimes necessitate

surgical or percutaneous interventions, such as valve replacement for aortic stenosis or septal myectomy for hypertrophic cardiomyopathy.

**Conclusion.** Early identification and risk stratification of cardiac syncope are crucial for preventing adverse outcomes. A multidisciplinary approach, involving general practitioners, cardiologists, neurologists, and emergency care providers, is very important to ensure optimal diagnosis and treatment for patients at risk of life-threatening events related to cardiac syncope.

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## ■ Diferencijalna dijagnostika boli perifernih zglobova

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**Uvod s ciljem.** Bol je, prema definiciji Međunarodnog udruženja za istraživanje boli (eng. *International Association for the Study of Pain* – IASP), neugodno osjetilno i emocionalno iskustvo udruženo s akutnim ili mogućim oštećenjem tkiva. Bol je uvijek subjektivna i definira se kao peti vitalni znak. Obzirom da može umanjiti i oslabiti kvalitetu života, bol je važan zdravstveni problem. Cilj ovog rada je prikazati simptome i znakove koji su značajni u prepoznavanju uzroka nastanka boli, putova prijenosa bolnog podražaja kao i patofizioloških zbivanja u organizmu koji uzrokuju bol u perifernim zglobovima.

**Metode.** Pregledane su baze podataka UpToDate i PubMed korištenjem ključnih riječi bol (engl. pain), periferni zglobovi (engl. peripheral joints), etiologija (engl. etiology). Uključni kriteriji bili su dostupnost cjelovitih preglednih članaka na engleskom jeziku objavljenih u razdoblju od 2019. do 2024. godine. Navedene kriterije zadovoljilo je 25 članaka.

**Rasprava.** Bolesti perifernih zglobova čest su razlog posjeta liječniku obiteljske medicine. One mogu značajno narušiti kvalitetu života i funkcionalnost bolesnika. Rana dijagnoza i učinkovito upravljanje ovim stanjima ključni su za sprječavanje dugoročnih komplikacija. Klinička prezentacija bolesti perifernih zglobova može uključivati slijedeće simptome: bol (akutna, kronična, lokalizirana ili difuzna), ukočenost (osobito jutarnja ukočenost kod upalnih artritisa) te gubitak funkcije i oticanje. Znakovi koji se manifestiraju u ovim stanjima su eritem, toplina, deformiteti, zvukovi pri pokretanju zgloba (krepitacije) i smanjeni opseg pokreta. Uzroci bolesti perifernih zglobova u kojima bol kao vitalni znak dominira mogu se podijeliti u bolesti kosti, periorsta i hrskavice, vanzglobni reumatizam, bolesti vezivnog tkiva, artritis povezan sa spondilozom, metaboličke i endokrine bolesti, stanja vezana

uz infekcije zgloba, stanja nakon traume zgloba, neuropatske poremećaje, maligne bolesti te farmakološki uzrokovan artritis i artralgijske. Najčešći uzrok boli perifernih zglobova u starijih osoba je osteoartritis, dok je u mlađoj populaciji bol češće posljedica tendovaginitisa ili burzitisa. Kod osteoartritisa bol je često mehanička i pogoršava se aktivnošću, dok kod upalnih stanja, poput reumatoidnog artritisa, dominiraju jutarnja ukočenost i simetrično oticanje. Giht karakterizira nagla pojava intenzivne boli i oticanja, najčešće u prvom metatarzofalangealnom zglobu.

**Zaključak.** Simptomi i znakovi boli perifernih zglobova ključni su za postavljanje rane i točne dijagnoze. Liječnik obiteljske medicine ima značajnu ulogu u prepoznavanju obrazaca boli, procjeni zdravstvenog stanja i iniciranju pravovremenog liječenja. Rano prepoznavanje upalnih znakova može spriječiti trajna oštećenja zglobova i poboljšati ishode za bolesnike.

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## ■ Differential diagnosis of peripheral joint pain

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**Introduction with aim.** According to the definition of the International Association for the Study of Pain (IASP), pain is an unpleasant sensory and emotional experience associated with acute or possible tissue damage. Pain is always subjective and is defined as the fifth vital sign. Considering that it can reduce and weaken the quality of life, pain is an important health problem. The aim of this paper is to show the symptoms and signs that are significant in identifying the causes of pain, the pathways of pain stimulus transmission as well as the pathophysiological events in the body that cause pain in peripheral joints.

**Methods.** The UpToDate and PubMed databases were reviewed using the keywords pain, peripheral joints, etiology. The inclusion criteria were the availability of complete review articles in English published in the period from 2019 to 2024. 25 articles met the above criteria.

**Discussion.** Peripheral joint diseases are a common reason for visiting a family medicine doctor. They can significantly impair the patient's quality of life and functionality. Early diagnosis and effective management of these conditions are key to preventing long-term complications. The clinical presentation of peripheral joint disease may include the following symptoms: pain (acute, chronic, localized or diffuse), stiffness (especially morning stiffness in inflammatory arthritis), and loss of function and swelling. Signs that manifest in these conditions are erythema, warmth, deformities, sounds when moving the joint (crepitations) and reduced range of motion. The causes of peripheral joint diseases in which pain as a vital sign dominates can be divided into bone, periosteum and cartilage diseases, extra-articular rheumatism, connective tissue diseases, arthritis associated with spondylosis, metabolic and endocrine diseases, conditions related to joint infections, conditions after joint trauma,

neuropathic disorders, malignant diseases and pharmacologically induced arthritis and arthralgias. The most common cause of peripheral joint pain in the elderly is osteoarthritis, while in the younger population the pain is more often a result of tendovaginitis or bursitis. In osteoarthritis, the pain is often mechanical and worsens with activity, while in inflammatory conditions, such as rheumatoid arthritis, morning stiffness and symmetrical swelling predominate. Gout is characterized by the sudden appearance of intense pain and swelling, most often in the first metatarsophalangeal joint.

**Conclusion.** Symptoms and signs of peripheral joint pain are crucial for early and accurate diagnosis. The family medicine doctor has a significant role in recognizing pain patterns, assessing health status and initiating timely treatment. Early recognition of inflammatory signs can prevent permanent joint damage and improve patient outcomes.

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## ■ Osteoartritis kroz prizmu metaboličkih i endokrinih uzroka bolesti

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**Uvod s ciljem:** Osteoartritis (OA) je kronična, progresivna, degenerativna bolest zglobova koja je ujedno i najčešća zglobna bolest i jedan od najčešćih zdravstvenih problema u svijetu. Predstavlja jedan od važnijih uzroka fizičke i radne nesposobnosti osoba srednje i starije životne dobi te se veže uz visoke troškove liječenja, visoku stopu trenutne i stalne onesposobljenosti kao i čest prijevremeni odlazak u mirovinu. Rizični faktori za nastanak bolesti su multifaktorijalni, te se uz dosadašnje statičko opterećenje i genetiku, sve više razmatraju metabolički i endokrini uzroci, što dovodi do jednog sasvim novog poimanja patofiziologije bolesti te razmatranja novih terapijskih pristupa. Cilj ovog rada je ukazati na moguće metaboličke i endokrine uzroke bolesti, kao i moguću kombinaciju istih, što dodatno otežava prepoznavanje te može maskirati kliničku sliku.

**Rasprava:** Tijekom starenja dolazi do porasta razine sistemske upale zbog povećane proizvodnje proupalnih citokina, kao što su TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-12, IL-18, te interferoni tipa 1 (IFNs I), koji je uglavnom rezultat starenja stanica i starenja imunološkog sustava. Kronična upala se smatra glavnim mehanizmom starenja i razvoja kroničnih bolesti, što je najbolje dokazano za kardiovaskularne bolesti i degenerativne bolesti. Sve više je dokaza koji govore u prilog da postoji interakcija između upale, metaboličkih i vaskularnih poremećaja, koji u zajedničkoj patofiziološkoj osnovi povezuje te bolesti. Pretilost kao akcelerator svih upalnih zbivanja osim vaskularnih i metaboličkih manifestacija, dodatno pogoršava statičku funkciju perifernih zglobova te dovodi do pogoršanja postojećeg stanja. Novije studije upravo u fokus sve više stavljaju razumijevanje uloge kronične upale niskog stupnja kao dodatnog okidača u razvoju bolesti perifernih zglobova, što dovodi do kliničkog pitanja je li razvoj OA posljednica degenerativne, metaboličke ili kumulativne uloge.

**Zaključak:** Trenutno znanje o povezanosti između starenja i razvoja bolesti povezanih sa

starenjem još uvijek je nepotpuno, a klinička procjena upale još nije standardizirana. Nedavne studije sugeriraju fenotipsku podkategorizaciju OA kako bi se bolje razumjela patogeneza i uzroci povezani s OA. Ovi podtipovi uključuju kategorije povezane sa starošću, posttraumatskim događajima i metaboličkim sindromom. Kao moguće rješenje navodi se grupiranje upalnih markera s varijablama koje ukazuju na sociodemografske i kliničke karakteristike pacijenata s OA i kardio-metaboličkim poremećajem kako bi se dobio uvid u skrivene fenotipove i temeljne patofiziološke pozadine. Navedene činjenice od ključnog su značaja za obiteljske doktore jer su prva karika u lancu u radu s pacijentima, zbog čega je potrebno uložiti dodatno vrijeme u edukaciju i implementaciju u svakodnevni klinički rad.

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## ■ The metabolic and endocrine landscape in Osteoarthritis

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**Introduction with aim:** Osteoarthritis (OA) is a chronic, progressive, degenerative joint disease that is also the most common joint disease and one of the most common health problems in the world. It represents one of the most important causes of physical and work disability in middle-aged and elderly people and is associated with high treatment costs, a high rate of current and permanent disability, and frequent early retirement. Risk factors for the development of the disease are multifactorial, and in addition to the current static load and genetics, metabolic and endocrine causes are increasingly being considered, which leads to a completely new understanding of the pathophysiology of the disease and consideration of new therapeutic approaches. The aim of this paper is to point out possible metabolic and endocrine causes of the disease, as well as a possible combination of them, which further complicates recognition and can mask the clinical picture.

**Discussion:** During aging, there is an increase in the level of systemic inflammation due to the increased production of pro-inflammatory cytokines, such as TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-12, IL-18, and type 1 interferons (IFNs I), which is mainly the result of cell aging and the aging of the immune system. Chronic inflammation is considered a major mechanism of aging and the development of chronic diseases, which is best proven for cardiovascular diseases and degenerative diseases. There is increasing evidence that there is an interaction between inflammation, metabolic and vascular disorders, which in a common pathophysiological basis connects these diseases. Obesity, as an accelerator of all inflammatory events except vascular and metabolic manifestations, further worsens the static function of peripheral joints and leads to a worsening of the existing condition. Recent studies are increasingly focusing on understanding the role of chronic low-grade inflammation as an additional trigger in the development of peripheral joint diseases,

which leads to the clinical question of whether the development of OA is a consequence of a degenerative, metabolic or cumulative role.

**Conclusion:** Current knowledge on the associations between aging and the development of age-related diseases is still incomplete and the clinical evaluation of inflammaging has not yet been standardized. Recent studies have suggested phenotypically subcategorizing OA to better understand the pathogenesis and causes related to OA. These subtypes entail age-related, post-traumatic event-related, and metabolic syndrome-related categories. Recent studies suggest a phenotypic subcategorization of OA to better understand the pathogenesis and causes associated with OA. These subtypes include categories related to age, post-traumatic events, and metabolic syndrome. A possible solution is to group inflammatory markers with variables that indicate sociodemographic and clinical characteristics of patients with OA and cardiometabolic disorders to gain insight into hidden phenotypes and underlying pathophysiological backgrounds. These facts are of key importance for family doctors because they are the first link in the chain in working with patients, so it is necessary to invest additional time in education and implementation in daily clinical work.

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## ■ Neuropathic disorders of peripheral joints

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**Introduction with aim.** Neuropathic disorders of peripheral joints represent a significant clinical challenge, especially in primary health care, because they often occur in patients with chronic diseases such as diabetes, arthritis, and post-traumatic injuries. Timely recognition of neuropathic symptoms and their connection with degenerative processes in the joints is crucial for early treatment and reduction of complications. If they are not recognized in time, these disorders can lead to serious functional impairments and decrease the quality of life of patients. This lecture aims to emphasize the key role of neurological mechanisms in the development of osteoarthritis (OA) and neuropathic disorders of peripheral joints, to emphasize the importance of early diagnosis, and to emphasize the importance of early diagnosis and timely intervention, which will be useful to both general practitioners and specialists.

**Discussion.** Periarticular nerve endings play an important role in the regulation of blood flow, proprioception, and nociception. In OA dysfunction of the neurovascular system occurs, which contributes to the loss of joint tissue integrity and the progression of the disease. A decrease in the number of proprioceptors and nociceptors interferes with the sense of joint position and pain mechanisms, which further increases the risk of structural damage. Also, studies have shown that patients with OA have altered brain activity, which can be partially normalized by total joint replacement. Damage to the nervous system of peripheral joints significantly contributes to the pathogenesis and progression of OA. Drugs used in the treatment of neurological diseases, such as antiepileptics and antidepressants, have shown

potential in alleviating the symptoms of OA. The role of family medicine doctors is crucial in early recognition of neuropathic symptoms, timely management of comorbidities, and referral of patients to specialist treatment. A multidisciplinary approach, which includes neurologists, orthopedists, and psychiatrists, is necessary to optimize the outcome and improve the quality of life of patients with neuropathic disorders of peripheral joints.

**Conclusion.** It is extremely important to consider current dilemmas for a better understanding of the etiology, diagnostic, and therapeutic procedures of neuropathic disorders of peripheral joints in the direction of a better understanding of this issue and the application of new effective therapies.

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## ■ Farmakološki artritis i artralgijske izazvane lijekovima

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**Uvod s ciljem:** Bol u zglobovima čest je razlog javljanja liječniku obiteljske medicine, a mogući uzroci su brojni i iznimno raznoliki, uključujući i primjenu lijekova i određenih vrsta cjepiva. Cilj ovog rada je prikazati lijekove koji mogu izazvati bol u zglobovima, odnosno artritis, te moguće alternativne lijekove s manje nuspojava.

**Rasprava:** Velik broj lijekova može za nuspojavu imati bol u zglobovima, a patofiziološki mehanizmi su različiti, kao i načini manifestacije koji mogu varirati od kratkotrajne i reverzibilne oligoartralgijske do dugotrajnog artritisa s trajnim posljedicama na zglobovima. Vrijeme od početka uzimanja lijeka do pojave simptoma također je promjenjivo, od nekoliko dana do nekoliko mjeseci, što dodatno otežava postavljanje dijagnoze. Od antimikrobnih lijekova artralgijske kao nuspojavu mogu manifestirati kinoloni, doksiciklin, rifampicin i antifungik vorikonazol. Bol u zglobovima i artritis poznate su nuspojave kemoterapije, a najčešće se povezuju uz inhibitore aromataze (anastrozol, letrozol i eksemestan) i paklitaksel. Artralgijske je kasna nuspojava inhibitora aromataze, javlja se nakon jednog do šest mjeseci od početka primjene, a zglobovi su obično simetrično zahvaćeni. Učinkovita može biti primjena nesteroidnog antiinflatornog lijeka (NSAIL), zamjena drugim lijekom iz iste skupine, kratki prekid uzimanja lijeka ili primjena malih doza prednizona. U težim slučajevima lijek treba ukinuti iz terapije, nakon čega se simptomi unutar četiri tjedna potpuno povlače. Farmakološki artritis kao diferencijalnu dijagnozu treba uzeti u obzir i pri uzimanju DPP-4 inhibitora, izotretinoina i nekih psihofarmaka, prvenstveno mirtazapina. Artralgijske se javlja u 3-5% slučajeva primjene DPP-4 inhibitora, obično pri uvođenju lijeka u terapiju. Ukoliko primjena NSAIL nije dovoljno učinkovita, lijek je potrebno zamijeniti drugim antihiperlipidemikom, nakon čega dolazi do poboljšanja tijekom jednog do dva mjeseca. Dokazana je povezanost primjene cjepiva protiv rubeole s pojavom artralgijske i artritisa, osobito kod odraslih. Poznato je da mnogi lijekovi mogu

dovesti do hiperuricemije s posljedičnim razvojem uričnog artritisa. Primjena diuretika jedan je od najvažnijih uzroka sekundarne hiperuricemije, prvenstveno diuretika Henleove petlje. Povećanje koncentracije mokraćne kiseline u serumu ovisno je o dozi i može se uočiti unutar nekoliko dana od početka liječenja. Hiperuricemija može biti posljedica uzimanja imunosupresiva, antituberkulotika, malih doza acetilsalicilne kiseline i omeprazole. Citotoksični kemoterapeutici mogu dovesti do naglog i značajnog porasta urične kiseline, obično 48 do 72 h nakon primjene. Bolesnike koji uzimaju lijekove koji mogu inducirati hiperuricemiju treba poticati na adekvatnu hidraciju uz periodične kontrole razine urata u krvi i praćenje simptoma koji mogu prethoditi napadu gihta.

**Zaključak:** Znanje o lijekovima koji mogu uzrokovati artritis i/ili artralgijske iznimno je bitno u svakodnevnom radu liječnika obiteljske medicine jer rano prepoznavanje povezanosti ovih simptoma s uzimanjem lijeka dovodi do bržeg ublažavanja tegoba promjenom terapije te smanjuje potrebu za nepotrebnim pretragama.

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## ■ Drug-induced arthritis and arthralgia

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**Introduction with aim:** Joint pain is a common reason for visiting the family doctor office. The possible causes are numerous and extremely diverse, including the use of medications and certain types of vaccines. The purpose of this paper is to present medications that can cause arthralgia or arthritis, as well as possible alternative medications with fewer side effects.

**Discussion:** A large number of medications can cause joint pain as a side effect, and the pathophysiologic mechanisms are diverse, as are the ways of manifestation, which can vary from short-term and reversible oligoarthralgia to long-term arthritis with permanent consequences on the joints. The time period from the start of taking the drug to the onset of symptoms is also variable, from a few days to a few months, which makes it even more difficult to make a diagnosis. Among antimicrobial drugs, quinolones, doxycycline, rifampicin, and the antifungal voriconazole can manifest arthralgia as a side effect. Joint pain and arthritis are known side effects of chemotherapy, and are most commonly associated with aromatase inhibitors (anastrozole, letrozole, and exemestane) and paclitaxel. Arthralgia is a late side effect of aromatase inhibitors, occurring one to six months after the start of use, and the joints are usually affected symmetrically. The use of a nonsteroidal anti-inflammatory drug (NSAID), replacement with another drug from the same group, a brief interruption of its use, or the use of low doses of prednisone may be effective. In more severe cases, the drug should be discontinued from therapy, after which the symptoms will completely resolve within 4 weeks. Drug-induced arthritis as a differential diagnosis should also be taken into account when taking DPP-4 inhibitors, isotretinoin and some psychotropic medications, primarily mirtazapine. Arthralgia occurs in 3-5% of cases of DPP-4 inhibitor use, usually when the drug is introduced into therapy. If the use of NSAIDs is not effective enough, the drug should be replaced with another antihyperglycemic,

after which improvement occurs over one to two months. The use of the rubella vaccine has been proven to be associated with the occurrence of arthralgia and arthritis, especially in adults. It is well known that many medications can lead to hyperuricemia with the consequent development of gouty arthritis. The use of diuretics is one of the most important causes of secondary hyperuricemia, primarily loop diuretics. The increase in serum uric acid concentration is dose-dependent and may be observed within a few days of starting treatment. Hyperuricemia can be caused by taking immunosuppressants, antituberculosis drugs, low doses of acetylsalicylic acid or omeprazole. Cytotoxic chemotherapeutic agents can lead to a sudden and significant increase in uric acid, usually 48 to 72 hours after administration. Patients taking medications that can induce hyperuricemia should be encouraged to maintain adequate hydration, with periodic monitoring of blood urate levels and monitoring for symptoms that may precede a gout attack.

**Conclusion:** Knowledge about medications that can cause arthritis and/or arthralgia is very important for family medicine physicians because early recognition of the connection with medication intake leads to faster relief of symptoms by changing therapy and reduces the need for unnecessary diagnostics.

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## ■ Fleboartroza

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**Uvod s ciljem:** Fleboartroza je istodobna prisutnost kronične venske bolesti nogu svih stadija i osteoartrisa, najčešće koljena, ali i gležnja. Cilj rada je ukazati na potrebu za dijagnostičko-terapijskim postupcima u obje bolesti, jer svaka pojedinačno pogoršava simptome one druge, znatno narušavajući kvalitetu života bolesnika.

**Rasprava:** Pojam fleboartroze poznat je unatrag pedesetak godina, kada su ga opisali njemački autori primijetivši značajnije artrotrične promjene koljena u bolesnika s varikoznim venama. Simptomi su bol u zglobu u mirovanju, uz pojačavanje boli u kretanju koje je otežano, oticanje, težina i grčevi, što su sve preklapajući nespecifični simptomi za obje bolesti. Uslijed bolova, bolesnici reduciraju kretanje što dodatno pogoršava venske simptome zbog neaktivnosti vensko-mišićne pumpe lista i/ili stopala, i doprinosi progresiji obje bolesti. Naime, osnovna patofiziološka promjena u kroničnoj venskoj bolesti je prisutnost venske hipertenzije uz pojavu manifestnog ili okultnog edema. Hrskavica, aponeuroze i ligamenti zgloba nemaju direktnu vaskularizaciju, stoga kisik i nutritivni dolaze do stanica procesom difuzije iz okolnih vaskularnih struktura. Ukoliko je prisutan edem u tkivu, prehrana tih struktura je reducirana, dolazi do propadanja i razvoja kronične upale, odnosno osteoartrisa. Ujedno, česta je anatomska pozicija varikoznih vena u području koljena, a one su posljedica aksijalnog refluksa u velikoj i maloj safenalnoj veni. Čak i prisutnost retikularnih vena i teleangiectazija u spoju s insuficijentnim perforantnim venama koljena dovodi do fleboartroze. Ukoliko posumnja na kombinaciju ovih dviju bolesti, liječnik obiteljske medicine učinit će fizikalni pregled uz opis kliničkih znakova obje bolesti te bolesnika uputi na obradu venskog i koštano-mišićnog sustava. U najvećeg broja bolesnika, flebološki pregled s ultrazvučnim pregledom obojnim dopplerom sva tri venska sustava, ukazat će

na anatomsku distribuciju i patofiziološki mehanizam nastanka bolesti. Ortopedskim pregledom uz slikovnu obradu, prvenstveno RTG, dobit će se uvid u proširenost osteoartričnih promjena te odrediti konzervativno i/ili operativno liječenje. U slučaju potvrde venske bolesti, preporuka je prvo nju liječiti. Metode su konzervativne, kombinacija kompresivne terapije čarapama, koje uvijek moraju biti iznad koljena s venoaktivnim lijekovima, i operativne endovenske i/ili kirurške metode, a sve u cilju smanjenja venske hipertenzije. To će u najvećeg dijela bolesnika s početnom i umjerenom fleboartrozom smanjiti tegobe i odgoditi potrebu za operativnim ortopedskim liječenjem. U onih s razvijenom artrozom i u potrebi za operativnim liječenjem, očekuje se manje komplikacija zahvata i brži oporavak. Ujedno, u obje skupine takav će pristup liječenju poboljšati pokretljivost, smanjiti bol i potrebu za uzimanjem protuupalnih lijekova. Kvaliteta života prije liječenja je znatno narušena zbog tegoba vezanih uz obje bolesti. Otežano je svakodnevno funkcioniranje uz povećanu potrebu za tuđom pomoći što, uz kroničnu bol, dovodi do značajnih psiholoških poteškoća, primarno anksioznosti i depresije. Stoga je za očekivati da će liječenje obje komponente fleboartroze doprinijeti poboljšanju ukupne kvalitete života.

**Zaključak:** U bolesnika s fleboartrozom potrebni su dijagnostičko-terapijski postupci obje komponente bolesti, venske i osteoartrisa. Preporučuje se započeti s liječenjem venske bolesti konzervativnim i endovenskim ili kirurškim metodama u cilju smanjenja venske hipertenzije, a potom provoditi ortopedsko liječenje. Uloga liječnika obiteljske medicine je prepoznati obje bolesti te bolesniku pružiti cjelokupnu skrb u svim fazama liječenja.

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## ■ Phleboarthrosis

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**Introduction with the aim:** Phleboarthrosis is the simultaneous presence of chronic venous disease of all stages and osteoarthritis, most often of the knee, but also of the ankle. The aim of the paper is to point out the need for diagnostic and therapeutic procedures in both diseases, because each individually worsens the symptoms of the other, significantly impairing the patient's quality of life.

**Discussion:** The term phleboarthrosis was known about fifty years ago, when it was described by German authors who noticed more significant arthritic changes in the knees in patients with varicose veins. Symptoms include pain in the joint at rest, with increasing pain on movement that is difficult, swelling, heaviness and cramps, all of which are overlapping non-specific symptoms for both diseases. Due to pain, patients reduce movement, which further worsens venous symptoms due to the inactivity of the venous-muscular pump (calf and/or foot) and contributes to the progression of both diseases. Namely, the basic pathophysiological change in chronic venous disease is the presence of venous hypertension with the appearance of manifest or occult edema. Cartilage, aponeuroses and ligaments of the joint do not have direct vascularization, therefore oxygen and nutrients reach the cells through the process of diffusion from the surrounding vascular structures. If there is edema in the tissue, the nutrition of these structures is reduced, deterioration and development of chronic inflammation, i.e. osteoarthritis, occurs. At the same time, the anatomical position of varicose veins in the knee area is common, and they are the result of axial reflux in the great and small saphenous vein. Even the presence of reticular veins and telangiectasia in conjunction with insufficient perforating veins of the knee leads to phleboarthrosis. If he suspects a combination of these two diseases, the family doctor will perform a physical examination with a description of the clinical signs of both diseases and refer the patient to treatment of the venous and musculoskeletal system. In the most of patients, a phlebological examination

with color Doppler ultrasound examination of all three venous systems will indicate the anatomical distribution and pathophysiological mechanism of the disease. Orthopedic examination with imaging, primarily X-ray, will provide insight into the extent of osteoarthritic changes and determine conservative and/or operative treatment. In case of confirmation of venous disease, it is recommended to treat it first. The methods are conservative, a combination of compression therapy with stockings, which must always be above the knee with venoactive drugs, and operative endovenous and/or surgical methods, all with the aim of reducing venous hypertension. In the most of patients with initial and moderate phleboarthrosis, this will reduce complaints and delay the need for operative orthopedic treatment. In those with developed arthrosis and in need of operative treatment, fewer procedure complications and faster recovery are expected. At the same time, in both groups, such an approach to treatment will improve mobility, reduce pain and the need to take anti-inflammatory drugs. The quality of life before treatment was significantly impaired due to the complaints related to both diseases. Daily functioning is made more difficult with an increased need for other people's help, which, along with chronic pain, leads to significant psychological difficulties, primarily anxiety and depression. Therefore, it is to be expected that the treatment of both components of phleboarthrosis will contribute to the improvement of the overall quality of life.

**Conclusion:** Patients with phleboarthrosis require diagnostic and therapeutic procedures for both components of the disease, venous and osteoarthritis. It is recommended to start with the treatment of venous disease with conservative and endovenous or surgical methods in order to reduce venous hypertension, and then carry out orthopedic treatment. The role of the family doctor is to recognize both diseases and provide the patient with overall care in all phases of treatment.

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## ■ Seksualnost i nesanica

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**Uvod.** Seksualna aktivnost ne samo da doprinosi emocionalnom zadovoljstvu, fizičkom užitku, smanjenju stresa i opuštanju, već i pozitivno utječe na kvalitetu spavanja. Nesanica, osobito kronični poremećaj spavanja, značajno ugrožava kvalitetu života, utječući na mentalno, fizičko i emocionalno zdravlje. Povezanost između nesanice i seksualne funkcije je složena i dvosmjerna – nesanica može smanjiti seksualnu želju i izvedbu, dok narušena seksualna funkcija može pogoršati kvalitetu sna. Cilj je istražiti fiziološke, hormonske i psihološke veze između spavanja i seksualne funkcije te utjecaj nesanice na seksualno zdravlje muškaraca i žena.

**Rasprava.** Spavanje je regulirano cirkadijalnim sustavom (buđenje) i sustavom pritiska na spavanje ("uspavljivanje"), koji označava potrebu za snom. Unutarnja (endogena) regulacija ritma buđenja/sna dolazi iz suprahijazmatske jezgre hipotalamusa (SCN) i utječe na periferne organe putem hipofize i drugih hipotalamičkih centara. Također, modulira odgovor na stres indirektno, kroz autonomni živčani sustav i adrenalni korteks. Postoji anatomski i funkcionalna razlika između muškaraca i žena u veličini i strukturi SCN, što vjerojatno objašnjava spolne razlike u ciklusu budnosti i spavanja, kao i u reakcijama na stres. Spolni hormoni mogu utjecati na san, no točan mehanizam još nije potpuno razjašnjen. Vanjski (egzogeni) faktori, kao što su svjetlost, tjelovježba, unos hrane, temperatura i lijekovi, također igraju važnu ulogu. Iako postoje razlike u kvaliteti sna između muškaraca i žena, one još nisu jasno definirane, osobito u kontekstu uloge hormona poput testosterona, estrogena i progesterona. Seksualna aktivnost, posebno partnerski seks uz orgazam, pokazuje pozitivnu povezanost s kvalitetom sna, jer doprinosi oslobađanju hormona poput oksitocina i prolaktina, koji potiču opuštanje i pospanost. Tome dodatno pomaže i emocionalna povezanost među partnerima.

Suprotno tome, seksualna aktivnost bez orgazma, uključujući masturbaciju, nije povezana s promjenama u spavanju, a razlike između muškaraca i žena nisu prisutne. Snižavanje razine kortizola nakon seksualnog odnosa smanjuje stres, olakšavajući uspavljivanje. S druge strane, seksualne disfunkcije mogu narušiti kvalitetu sna. Dobra kvaliteta sna ima pozitivan učinak na seksualnu aktivnost u oba spola. U žena, loša kvaliteta sna, ali ne i trajanje sna, povezana je s većim rizikom od seksualne disfunkcije. Dugotrajna nesanica iscrpljuje tijelo i um, povećavajući razinu stresa, što negativno utječe na seksualnu želju u oba spola. U muškaraca može izazvati erektilnu disfunkciju, dok kod žena smanjuje seksualno uzbuđenje. Kronični nedostatak sna također remeti hormonalnu ravnotežu, smanjujući razinu testosterona, ključnog za seksualnu želju. U žena, nesanica može utjecati na razine estrogena i progesterona, dodatno narušavajući seksualnu funkciju i povećavajući rizik od bolnih odnosa. Stres i anksioznost, česti kod osoba s nesanicom, mogu smanjiti seksualnu želju i stvarati negativnu povratnu spregu između lošeg sna i nezadovoljavajućeg seksualnog života. Depresija, koja je često povezana s nesanicom, dodatno pogoršava oba aspekta.

**Zaključak.** Seksualna funkcija i nesanica međusobno su povezane kroz složene fiziološke, hormonske i psihološke mehanizme. Holistički, multidisciplinarni pristup, koji uključuje regulaciju sna, smanjenje stresa, partnersku podršku, a po potrebi i hormonsku terapiju, može pozitivno utjecati na oba segmenta.

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## ■ Sexuality and insomnia

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**Introduction:** Sexual activity not only contributes to emotional satisfaction, physical pleasure, stress reduction, and relaxation, but also positively affects sleep quality. Insomnia, especially chronic sleep disorders, significantly disrupts quality of life, impacting mental, physical, and emotional health. The relationship between insomnia and sexual function is complex and bidirectional – insomnia can reduce sexual desire and performance, while impaired sexual function can worsen sleep quality. The aim is to explore the physiological, hormonal, and psychological connections between sleep and sexual function, as well as the impact of insomnia on sexual health in both men and women.

**Discussion.** Sleep is regulated by the circadian system (wakefulness) and the sleep pressure system ("sleepiness"), which signals the need for sleep. The internal (endogenous) regulation of the wake/sleep rhythm originates from the suprachiasmatic nucleus (SCN) of the hypothalamus and influences peripheral organs through the pituitary gland and other hypothalamic centers. It also indirectly modulates the stress response through the autonomic nervous system and adrenal cortex. There are anatomical and functional differences between men and women in the size and structure of the SCN, which likely explain some gender differences in the wakefulness and sleep cycle, as well as stress responses found in various studies. Sex hormones may affect sleep, but the exact mechanism is not fully understood. External (exogenous) factors, such as light, exercise, food intake, temperature, and medications, also play an important role. Although there are differences in sleep quality between men and women, these are not yet clearly defined, especially considering the role of hormones like testosterone, estrogen, and progesterone. Sexual activity, particularly partnered sex with orgasm, shows a positive association with sleep quality

as it promotes the release of hormones like oxytocin and prolactin, which aid relaxation and induce sleepiness. Emotional connection between partners further contributes to this effect. In contrast, sexual activity without orgasm, including masturbation, is not associated with sleep changes, and no gender differences are observed. Reducing cortisol levels after sexual intercourse decreases stress, facilitating sleep onset. On the other hand, sexual dysfunctions can impair sleep quality. Good sleep quality has a positive impact on sexual activity in both genders. In women, poor sleep quality, but not sleep duration, is linked to a higher risk of sexual dysfunction. Chronic insomnia depletes the body and mind, increasing stress levels, which negatively impacts sexual desire in both sexes. In men, it can cause erectile dysfunction, while in women, it reduces sexual arousal. Chronic sleep deprivation also disrupts hormonal balance, lowering testosterone levels, which are essential for sexual desire. In women, insomnia can affect estrogen and progesterone levels, further impairing sexual function and increasing the risk of painful intercourse. Stress and anxiety, common in individuals with insomnia, can reduce sexual desire and create a negative feedback loop between poor sleep and unsatisfying sexual life. Depression, often associated with insomnia, further exacerbates both aspects.

**Conclusion.** Sexual function and insomnia are interconnected through complex physiological, hormonal, and psychological mechanisms. A holistic, multidisciplinary approach that includes sleep regulation, stress reduction, partner support, and, if necessary, hormone therapy, can positively impact both areas.

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## ■ Nesanica – simptom ili primarna bolest?

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**Uvod s ciljem.** Nesanica, uobičajeni poremećaj spavanja, očituje se kao trajna poteškoća u uspavlivanju ili održavanju sna, unatoč adekvatnim uvjetima za spavanje. Ovi noćni poremećaji povezani su sa značajnim dnevnim oštećenjima, uključujući umor, razdražljivost i kognitivne disfunkcije. Ovaj rad ima za cilj istražiti nesanicu kao simptom i kao primarnu bolest, naglašavajući kliničke i dijagnostičke izazove u razlikovanju ove dvije klasifikacije.

**Rasprava.** Kada se nesanica javlja kao simptom, često je posljedica somatskih ili psihijatrijskih bolesti. Može biti izazvana primjenom određenih lijekova ili supstanci, ili kombinacijom navedenih čimbenika. Česti medicinski uzroci koji narušavaju normalnu fiziologiju sna uključuju bol, kongestivno zatajenje srca, benignu hiperplaziju prostate, bolesti štitnjače, sindrom nemirnih nogu i neurološka stanja (npr. moždani udar, Parkinsonovu bolest). Nesanica je također često ključni simptom psihijatrijskih poremećaja poput depresije i anksioznosti, uzrokovanih hiperbudnošću i maladaptivnim misaonim obrascima. Neki uobičajeni lijekovi također mogu pridonijeti ili izazvati nesanicu, poput inhibitora ponovne pohrane serotonina, inhibitora ponovne pohrane noradrenalina, inhibitora acetilkolinesteraze, L-dope i sistemskih steroida. Korištenje supstanci poput alkohola, kofeina i nikotina pogoršava poteškoće sa spavanjem narušavajući cirkadijalne ritmove i povećavajući razinu budnosti. Primarna nesanica, uključujući uobičajenu psihofiziološku nesanicu u rijetku idiopatsku nesanicu u djetinjstvu, javlja se neovisno o drugim stanjima. Psihofiziološka nesanica održava se povećanom pobudenošću i negativnim asocijacijama sa spavanjem, često izazvana stresom. Karakterizirana je anticipacijskom anksioznošću i maladaptivnim obrascima spavanja koji perpetuiraju stanje. Idiopatska nesanica u djetinjstvu, rjeđi podtip, smatra se genetski ili neurobiološki uvjetovanom i karakterizira je doživotni poremećaj sna. Razlikovanje nesanice kao simptoma ili primarne bolesti temelji se na detaljnoj kliničkoj anamnezi uz podršku dijagnostičkih alata.

Dnevnicima spavanja mogu pružiti informacije o obrascima i prekidima sna. Validirani upitnici poput Indeksa težine nesanice (ISI) procjenjuju ozbiljnost. Po potrebi, polisomnografija, poligrafija i aktigrafija mogu pomoći u isključivanju drugih poremećaja spavanja, poput opstruktivne apneje u snu. Kronična nesanica dijagnosticira se samo ako je neovisni klinički entitet koji nije uzrokovan komorbiditetima. Učinkovito liječenje nesanice ovisi o njezinoj klasifikaciji. Kod sekundarne nesanice, liječenje osnovnog stanja (npr. optimizacija upravljanja boli ili psihijatrijske skrbi) je od najveće važnosti. Prilagodba terapije lijekovima ili liječenje ovisnosti o supstancama također može pomoći u ublažavanju simptoma. Za primarnu nesanicu, kognitivno-bihevioralna terapija za nesanicu (CBT-I) smatra se zlatnim standardom, jer ima usporediv akutni učinak s farmakološkim tretmanima, uz dugoročne održive koristi. Farmakološke intervencije obično su rezervirane za kratkotrajnu primjenu zbog rizika od ovisnosti i tolerancije.

**Zaključak.** Razlikovanje nesanice kao simptoma i primarnog poremećaja ključno je za točnu dijagnozu i učinkovito liječenje. Dok sekundarna nesanica zahtijeva rješavanje osnovnih uzroka, primarna nesanica zahtijeva ciljanje bihevioralnih i, prema potrebi, farmakoloških intervencija. Ovaj nijansirani pristup osigurava optimalne ishode za pacijente i naglašava složenost nesanice kao kliničkog entiteta.

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## ■ Insomnia – symptom or primary disease?

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**Introduction with aim.** Insomnia, a common sleep disorder, manifests as persistent difficulty in initiating or maintaining sleep, despite adequate opportunity and a conducive sleep environment. These nocturnal disturbances are associated with significant daytime impairments, including fatigue, irritability and cognitive dysfunction. This paper aims to explore insomnia as both a symptom and a primary disease, highlighting the clinical and diagnostic challenges in distinguishing between these two classifications.

**Discussion.** When insomnia occurs as a symptom, it is often a consequence of somatic or psychiatric illnesses. It can also be triggered by the use of certain medications or drugs or by a combination of the above factors. Common medical conditions that disrupt normal sleep physiology and cause insomnia include pain, congestive heart failure, benign prostatic hypertrophy, thyroid disease, restless legs syndrome and neurological conditions (e.g. stroke, Parkinson's disease). Insomnia is also often a core symptom of psychiatric disorders such as depression and anxiety, caused by hyperarousal and maladaptive thought patterns. Some commonly prescribed medications can also contribute to or trigger insomnia. Examples include selective serotonin receptor inhibitors, norepinephrine reuptake inhibitors, acetylcholine esterase inhibitors, L-dopa and systemic steroids. Substance use, including alcohol, caffeine and nicotine, exacerbates sleep difficulties by altering circadian rhythms and increasing arousal levels. Primary insomnia, including the common psychophysiological insomnia and the rare idiopathic childhood onset insomnia, occurs independently of other conditions. Psychophysiological insomnia is perpetuated by heightened arousal and negative sleep associations, often triggered by stress. It is characterized by anticipatory anxiety and maladaptive sleep behaviors that perpetuate the condition. Idiopathic childhood insomnia, a rarer subtype, is thought to have a genetic or neurobiological basis and is characterized by lifelong sleep disturbances. The differentiation

of insomnia as a symptom or primary disease is based on a detailed clinical history supported by diagnostic tools. Sleep diaries can provide information about sleep patterns and interruptions. Validated questionnaires such as the Insomnia Severity Index (ISI) assess the severity. If necessary, polysomnography, polygraphy and actigraphy can help to rule out other sleep disorders, such as obstructive sleep apnea. Crucially, chronic insomnia is only diagnosed if it is an independent clinical focus that is not due to comorbidities. Effective treatment of insomnia depends on its classification. In secondary insomnia, treatment of the underlying condition (e.g., optimization of pain management or psychiatric care) is of utmost importance. Adjusting medication or treating substance use can also help to alleviate symptoms. For primary insomnia, cognitive behavioral therapy for insomnia (CBT-I) is considered the gold standard, as it has a comparable acute effect to pharmacological treatments while providing sustained long-term benefits. Pharmacological interventions are generally reserved for short-term use due to the risk of dependence and tolerance.

**Conclusion.** Distinguishing between insomnia as a symptom and as a primary disorder is essential for accurate diagnosis and effective treatment. While secondary insomnia requires addressing the underlying causes, primary insomnia requires targeted behavioral and when appropriate, pharmacological interventions. This nuanced approach ensures optimal outcomes for patients and highlights the complexity of insomnia as a clinical entity.

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## ■ Pristup pacijentu sa sinkopom u općoj/obiteljskoj medicini

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**Uvod s ciljem:** sinkopa je nagli gubitak svijesti izazvan smanjenom perfuzijom mozga. Karakterizira je brz početak, kratko trajanje i potpuni spontani oporavak. Etiološki razlikujemo refleksnu, kardiogenu, ortostatsku. Cilj ovog rada je dati prikaz kompleksnosti i specifičnog načina odlučivanja u obiteljskoj medicini kroz pristup pacijentu sa sinkopom. U kratkom vremenu, često i bez mogućnosti dijagnostičke obrade, važno je razmotriti sva stanja koja dolaze u obzir, od onih benignih do životno ugrožavajućih i procijeniti potrebu za hitnim transportom i bolničkim liječenjem.

**Rasprava:** Prvi korak u pristupu pacijentu sa sinkopom je kvalitetna anamneza, heteroanamneza i fizikalni pregled koji uključuje procjenu stanja svijesti, frekvencije disanja, srčane akcije, neurološkog statusa kao i podatke o tjelesnoj temperaturi. U obradi obavezno je mjerenje tlaka u ležećem položaju i pri ustajanju te EKG nalaz i nalaz pulsne oksimetrije, što je važno za diferencijalnu dijagnostiku nekih stanja. Uzrok ostaje nepoznat u trećini slučajeva. Većina pacijenata je u trenutku pregleda je asimptomatska, što predstavlja dodatni izazov u evaluaciji i stratifikaciji rizika pacijenta sa sinkopom. Stratifikacija rizika važna je kako bi pacijente niskog rizika sa sigurnošću mogli otpustiti uz odgovarajuće upute. Iznimno je važno prepoznati pacijente visokog rizika koji u podlozi imaju ozbiljnu srčanu bolest koja je u stanju dovesti do ozbiljnih komplikacija pa i nagle srčane smrti te ih je potrebno odmah primiti u bolnicu. Osim toga, nepotrebne bolničke obrade, pad kvalitete života zbog učestalih ozljeda tijekom padova, posebice kod starijih, predstavlja značajan zdravstveni problem.

**Zaključak:** Nakon bezuspješnih pokušaja da se u kliničku praksu uvedu standardizirani alati za stratifikaciju rizika sinkope, ističe se važnost obiteljskog liječnika kao osobe prvog kontakta u

ranom prepoznavanju stanja koja zahtijevaju liječenje i dijagnostičku obradu u višoj razini.

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## ■ Approach to a Patient with Syncope in General/Family Medicine

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**Introduction and Aim:** Syncope is a sudden loss of consciousness caused by reduced cerebral perfusion. It is characterized by a rapid onset, short duration, and complete spontaneous recovery. Etiologically, syncope can be classified as reflex, cardiogenic, or orthostatic. The aim of this paper is to present the complexity and specific decision-making process in family medicine when approaching a patient with syncope. In a short period of time, often without access to diagnostic tests, it is crucial to consider all possible causes, ranging from benign to life-threatening conditions, and to assess the need for urgent transport and hospital treatment.

**Discussion:** The first step in the approach to a patient with syncope is a thorough medical history, including heteroanamnesis, and a physical examination that evaluates consciousness level, respiratory rate, heart rate, neurological status, and body temperature. Essential diagnostic steps include measuring blood pressure in both supine and standing positions, performing an ECG, and assessing oxygen saturation, all of which are important for differential diagnosis. The cause of syncope remains unknown in one-third of cases. Most patients are asymptomatic at the time of examination, posing an additional challenge in risk assessment and stratification. Risk stratification is crucial for safely discharging low-risk patients with appropriate instructions while promptly recognizing high-risk patients with underlying serious cardiac conditions that may lead to severe complications, including sudden cardiac death, necessitating immediate hospitalization. Additionally, unnecessary hospital admissions and decreased quality of life due to frequent fall-related injuries, particularly in the elderly, represent significant public health concerns.

**Conclusion:** Despite unsuccessful attempts to implement standardized risk stratification tools

for syncope in clinical practice, the role of the family physician as the first point of contact remains essential in the early recognition of conditions requiring further diagnostic evaluation and specialized treatment.

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## ■ Nesanica i njezin utjecaj na metabolizam

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**Uvod s ciljem.** Nesanica predstavlja jedan od najčešćih problema na koje se žale pacijenti u ordinacijama liječnika obiteljske medicine. Učestalost nesanice raste s dobi i češća je u žena. Podaci kažu kako se 35.2% odraslih žali na neadekvatan san, a učestalost nesanice je najveća u dobnoj skupini između 45. i 54. godine (39%), dok je najniža učestalost u osoba starijih od 65 godina (26.3%). Cilj je prikazati kao nesanica utječe na metaboličke procese u organizmu.

**Rasprava.** Intervencijske studije u zdravih odraslih osoba istraživale su utjecaj nesanice na različite metaboličke domene poput unosa i potrošnje energije, poremećaja apetita - hedonističkog unosa hrane, te homeostaze glukoze. Značajan porast energetske unosa je povezan sa smanjenjem sna što dovodi do ukupne pozitivne energijske ravnoteže. Također, pozitivan energijski unos može biti i posljedica povećanog apetita. Sve navedene promjene dovode do razvoja pretilosti. Neovisno o poremećaju energetske homeostaze i promjeni tjelesne mase, manjak sna dovodi i do smanjenja inzulinske osjetljivosti. Poznato je da je nesanica povezana s komplikacijama šećerne bolesti. U osoba sa šećernom bolesti tipa 2 visoka je učestalost nesanice koja je povezana s lošijom kontrolom glikemije. Učestalost nesanice u osoba sa šećernom bolesti tipa 2 je 4 puta veća u usporedbi sa općom populacijom. Nadalje, nesanica je povezana sa 23% višom razinom glukoze i 48% višom razinom inzulina na tašte u osoba sa šećernom bolesti. Isto tako, nesanica je povezana s povišenim rizikom za više vrijednosti HbA1C, glukoze na tašte i indeksa tjelesne mase.

**Zaključak.** Nesanica je čest poremećaj spavanja i vrlo često je zanemarena kako od strane liječnika obiteljske medicine, tako i od svih ostalih bolničkih specijalista. S obzirom na visoku životnu dob populacije te visoku učestalost nesanice u populaciji kod starijih, te onih oboljelih od šećerne bolesti, preporuča se probir na nesanicu putem jednostavnih upitnika te savjetovanje.

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## ■ Insomnia and its impact on metabolism

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**Introduction with aim.** Insomnia is one of the most prevalent complaints in primary care. Prevalence of insomnia increases with age and is twice as prevalent in women. Furthermore, 35.2% of adults report insufficient sleep, with the highest prevalence among those aged 45–54 years (39%) and lowest prevalence among older adults  $\geq 65$  years (26.3%). The aim is to demonstrate how insomnia affects metabolic processes in the body.

**Discussion.** Interventional studies in healthy adults have explored the effects of total or partial sleep restriction on the following metabolic domains: energy expenditure, energy intake, dysregulated eating behaviors (hedonistic eating) and glucose homeostasis. A substantial increase in energy intake accompanies sleep restriction resulting in a net positive energy balance. This increased energy intake might be facilitated by increased hunger. These combined changes could lead to the development of obesity. Also, independent of dysregulations in energy homeostasis and weight changes, sleep restriction consistently reduces insulin sensitivity. Insomnia has also been associated with diabetes complications. Among people with type 2 diabetes, there is a high prevalence of insomnia which have been associated with worse glycemic control. The prevalence of insomnia in this population is nearly 4 times as high that reported in the general population. Furthermore, insomnia was associated with a 23% higher fasting glucose level and 48% higher fasting insulin levels in subjects with diabetes. Also, insomnia and insomnia symptoms in people with type 2 diabetes were associated with an increased risk of having a higher HbA1c, a higher fasting glucose, and a higher value of body mass index.

**Conclusion.** Insomnia is a common sleep disorder and is often overlooked both by general practitioners and by all other hospital specialists. Since there is a higher incidence of insomnia with increasing age and comorbidities such as diabetes mellitus, screening for insomnia is recommended using simple questionnaires, along with counseling.

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## ■ Vrućica u onkoloških pacijenata

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**Uvod s ciljem:** Najčešći uzrok vrućice u onkoloških pacijenata su infekcije, a neutropenijska vrućica predstavlja hitno stanje zbog visokog morbiditeta i mortaliteta. Maligne bolesti mogu biti u podlozi vrućice nepoznatog uzroka zbog citokina iz tumorskih stanica, ili zbog paraneoplastičnog sindroma. Vrućica može biti vezana i uz kemoterapiju, radioterapiju i imunoterapiju, može se javiti post-operativno te uz transfuzije krvi ili tromboemboliju. Tek uz liječenje i isključivanje infekcije možemo posumnjati na druge uzroke. Cilj rada je prikazati različite uzroke vrućice u onkoloških pacijenata te preporuke za dijagnostiku i liječenje s posebnim naglaskom na febrilnu neutropeniju kao hitno stanje.

**Rasprava:** Febrilna neutropenija se definira povišenom tjelesnom temperaturom (oralna viša od 38,3° C ili temperatura viša od 38° C tijekom ≥ 1 sata) u bolesnika koji imaju apsolutni broj neutrofila manji od 0,5 x 10<sup>9</sup>/L ili broj neutrofila za koji se očekuje smanjenje na manje od 0,5 x 10<sup>9</sup>/L u sljedećih 48 sati. Najčešće se javlja u bolesnika koji primaju citotoksičnu terapiju, uglavnom 7 dana po primjeni terapije. Vrućica ne mora uvijek biti prisutna, primjerice kod osoba na kortikosteroidnoj terapiji ili osoba starije životne dobi. Uz vrućicu se obično javlja i klinički manifestna infekcija, iako upalni odgovor može biti oslabljen radi manjka neutrofila. Zbog promptne rutinske uporabe empirijskih antibiotika, uzročnici infekcije se danas rjeđe dokumentiraju. Važni su detaljna anamneza i fizikalni pregled a najvjerojatnija mjesta za infekciju su: koža, mjesta katetera, mjesta biopsije i aspirata koštane srži, zubi, orofarinks i gingivalne površine, sinusi, pluća, abdomen, i perianalno područje. Daljnja dijagnostička obrada uključuje laboratorijske nalaze, mikrobiološke uzorke i slikovne metode ovisno o kliničkim indikacijama. Kod svih bolesnika s febrilnom neutropenijom, empirijsku antibiotsku terapiju potrebno je započeti unutar

1 sata od početka obrade te kada su (po mogućnosti) uzeti uzorci za bakterijske kulture. Odabir antibiotske terapije ovisi o svrstavanju bolesnika u skupine niskog ili visokog rizika za nastanak teške infekcije. Koriste se klinički kriteriji i bodovni sustavi poput MASCC sustava, Talcott i CISNE. Procjena rizika može pomoći pri određivanju primjene empirijske antibiotske terapije (oralno ili intravenoski), mjesta liječenja (bolničko ili izvanbolničko) i trajanja antibiotske terapije. Pacijenti koji su procijenjeni niskog rizika mogu se razmotriti za izvanbolničko liječenje nakon temeljite procjene i promatranja ≥ 4 sata. U slučaju izvanbolničkog liječenja najčešće se primjenjuje peroralna terapija ciprofloksacinom uz amoksicilin/klavulansku kiselinu. Važna je i odgovarajuća socijalna i obiteljska podrška, blizina mjesta stanovanja bolnici, te redovite kontrole obiteljskog liječnika. Empirijsko liječenje antibioticima obično se nastavlja do oporavka neutrofila. Ako se vrućica nastavi nakon 2-3 dana ili ako postoje znakovi progresivne infekcije obavezan je prijem u bolnicu. Kod ne-neutropenijske vrućice i prisutnih znakova infekcije pristupamo liječenju kao i kod ne-onkoloških pacijenata uz oprez prema mogućim atipičnim uzročnicima. Kod isključene infekcije treba razmotriti neinfektivni uzrok: vrućica izazvana tumorskim citokinima, paraneoplastični sindrom, lijekovi, tromboembolija.

**Zaključak:** Kod vrućice u onkoloških pacijenata primarno je tragati za infekcijom i postupati u skladu s kliničkim smjernicama. Najopasnije stanje predstavlja febrilna neutropenija kod koje je, zbog supresije neutrofila, visok rizik razvoja sepsa. Obiteljski liječnici imaju ključnu ulogu u prepoznavanju febrilne neutropenije, a posebno u praćenju pacijenata niskog rizika koji se liječe u izvanbolničkim uvjetima.

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## ■ Fever in cancer patients

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**Introduction with aim:** The most common cause of fever in patients with cancer is infection, and neutropenic fever is an emergency due to high morbidity and mortality. Malignant diseases can be a cause of fever of unknown origin due to cytokines from tumor cells, or due to paraneoplastic syndrome. Fever can be related to chemotherapy, radiotherapy and immunotherapy, it can occur post-operatively and with blood transfusions or thromboembolism. Only with treatment and exclusion of infection can we suspect other causes. The aim of the paper is to show the different causes of fever in oncology patients and recommendations for diagnosis and treatment with special emphasis on febrile neutropenia as medical emergency.

**Discussion:** Febrile neutropenia is defined by elevated body temperature (oral higher than 38.3°C or temperature higher than 38°C for ≥ 1 hour) in patients who have an absolute neutrophil count of less than 0.5 x 10<sup>9</sup>/L or a neutrophil count which is expected to decrease to less than 0.5 x 10<sup>9</sup>/L in the next 48 hours. It most often occurs in patients receiving cytotoxic therapy, mostly 7 days after the therapy. Fever does not always have to be present, for example in people on corticosteroid therapy or elderly people. Fever is usually accompanied by a clinically manifested infection, although inflammatory response may be weakened due to lack of neutrophils. Due to the prompt routine use of empiric antibiotics, the causative agents of infection are less often documented today. A detailed history and physical examination are important, and the most likely sites for infection are: skin, catheter sites, bone marrow biopsy and aspirate sites, teeth, oropharynx and gingival surfaces, sinuses, lungs, abdomen, and perianal area. Further diagnostic workup includes laboratory findings, microbiological samples and imaging methods depending on clinical indications. In all

patients with febrile neutropenia, empiric antibiotic therapy should be started within 1 hour of presentation and when (if possible) samples for bacterial cultures have been taken. The choice of antibiotic therapy depends on the patient's classification into low or high risk groups for severe infection. Clinical criteria and scoring systems such as the MASCC system, Talcott and CISNE are used. Risk assessment can help determine the use of empiric antibiotic therapy (oral or intravenous), the location of treatment (inpatient or outpatient) and the duration of antibiotic therapy. Patients assessed as low risk may be considered for outpatient management after thorough evaluation and observation for ≥ 4 hours. In the case of outpatient treatment, oral ciprofloxacin therapy with amoxicillin/clavulanic acid is most often used. Adequate social and family support, the proximity of the place of residence to the hospital, and regular check-ups by the family doctor are also important. Empiric antibiotic treatment is usually continued until neutrophil recovery. If the fever continues after 2-3 days or if there are signs of progressive infection, admission to the hospital is mandatory. In the case of non-neutropenic fever with signs of infection, we approach the treatment as in non-oncology patients with caution towards possible atypical pathogens. When infection is ruled out, a non-infectious cause should be considered: fever caused by tumor cytokines, paraneoplastic syndrome, drugs, thromboembolism

**Conclusion:** In case of fever in cancer patients, the priority is to look for infection and act in accordance with clinical guidelines. The most dangerous condition is febrile neutropenia, in which, due to the suppression of neutrophils, there is a high risk of developing sepsis. Family physicians have a key role in recognizing febrile neutropenia, and especially in monitoring low-risk patients treated in the outpatient setting.

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## ■ Vrućica kao simptom u ambulanti obiteljskog liječnika

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**Uvod s ciljem:** Vrućica je povišenje tjelesne temperature iznad normalnih vrijednosti, koje nastaje kao odgovor organizma na različite fiziološke, patološke ili imunološke procese. Normalna tjelesna temperatura kod odraslih osoba obično se kreće između 36,5 °C i 37,5 °C, dok se vrućica definira kao temperatura iznad 38 °C. Iako vrućica nije bolest, već simptom, ona ukazuje na prisutnost infekcija, upala, autoimunih poremećaja, tumora ili drugih patoloških stanja. Cilj rada je definirati vrućicu kao ozbiljan simptom u radu obiteljskih liječnika, koji u praksi može imati najrazličitije uzroke.

**Rasprava:** Vrućica je fiziološki odgovor organizma na različite čimbenike, poput bakterijskih, virusnih, gljivičnih infekcija ili drugih upalnih procesa, a mehanizam nastanka se pokreće kada termoregulacijski centar u hipotalamusu reagira na ove poremećaje. Najčešće se javlja kod pacijenata s akutnim infekcijama, posebno dišnih i mokraćnih puteva. Posebno je česta kod djece i kod novorođenčadi i dojenčadi i može ukazivati na ozbiljnije bolesti. Prisustvo vrućice često nije znak prisustva bolesti, već simptom različitih bolesti i stanja. Dugotrajna vrućica bez jasnih simptoma može biti izazvana različitim uvjetima i bolestima. Ovaj oblik vrućice može biti posebno izazovan za dijagnosticiranje jer ne postoji očigledan uzrok poput tipičnih simptoma infekcije ili upale. Neki od mogućih uzroka uključuju: kronične infekcije (moguće je da osoba ima dugotrajnu infekciju koja ne uzrokuje očite simptome) To mogu biti bolesti poput tuberkuloze, endokarditisa (upala srčanih zalistaka), bruceloze ili kroničnog apscesa); autoimune bolesti (poremećaji poput sistemskog lupus eritematosusa, reumatoidnog artritisa ili Stillove bolesti mogu uzrokovati vrućicu koja traje dugo bez jasnih vanjskih simptoma); maligne bolesti (neke vrste raka, poput limfoma, leukemije ili metastatskih karcinoma, mogu izazvati dugotrajnu vrućicu bez drugih očiglednih simptoma u početnim fazama bolesti) lijekovi i lijekovima; inducirane vrućice ( neki lijekovi mogu izazvati povišenu

temperaturu kao nuspojavu, što može trajati neko vrijeme i bez drugih simptoma. To uključuje lijekove poput antibiotika, antiepileptika ili lijekova za visoki krvni tlak). vrućica nepoznatog uzroka ( u nekim slučajevima, kada vrućica traje dulje vrijeme i ne može se utvrditi uzrok unatoč svim ispitivanjima, dijagnoza može biti "vrućica nepoznatog uzroka). Ovo stanje obično se dijagnosticira nakon što su isključeni svi drugi uzroci; endokrine bolesti (poremećaji poput hipertireoze ,također mogu uzrokovati povišenu temperaturu koja traje duže vrijeme, često bez drugih ozbiljnih simptoma Liječenje vrućice uz simptomatsko smanjenje temperature, uključuje i usmjeravanje na osnovne bolesti koja ju uzrokuje.

**Zaključak:** Važno je pratiti stanje pacijenta i pravovremeno dijagnosticirati uzrok vrućice kako bi se odabrala odgovarajuća terapija, bilo da je riječ o infekcijama, autoimunim bolestima ili malignim oboljenjima. Ako se javi dugotrajna vrućica bez jasnih simptoma, potrebno je konzultirati liječnika koji će provesti potrebnu obradu kako bi utvrdio točan uzrok i započeo odgovarajuće liječenje .

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## ■ Fever as a symptom in a family medicine practice

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**Introduction with aim:** Fever is an increase in body temperature above normal values, which occurs as an organism's response to various physiological, pathological or immunological processes. Normal body temperature in adults usually ranges between 36.5 °C and 37.5 °C, while fever is defined as a temperature above 38 °C. Although fever is not a disease, but a symptom, it indicates the presence of infections, inflammation, autoimmune disorders, tumours or other pathological conditions. The goal of the paper is to define fever as a serious symptom in the work of family medicine doctors, which in practice can have a wide variety of causes.

**Discussion:** Fever is the body's physiological response to various factors, such as: bacterial viral and fungal infections or other inflammatory processes. The mechanism of its occurrence is triggered when the thermoregulatory centre in the hypothalamus reacts to these disorders. It most often occurs in patients with acute infections, mostly respiratory and urinary tract infections. It is especially common in children, in newborns and infants, and may indicate more serious diseases. The presence of fever is often not a sign of disease, but a symptom of various diseases and conditions. Long-lasting fever without clear symptoms can be caused by different conditions and diseases. This form of fever can be particularly challenging to diagnose because there is no obvious cause like the typical symptoms of infection or inflammation. Some of the possible causes include chronic infections (it is possible that a person has a long-term infection that does not cause obvious symptoms). These can be diseases such as : tuberculosis, endocarditis (inflammation of the heart valves), brucellosis or chronic abscess); autoimmune diseases (disorders such as systemic lupus erythematosus, rheumatoid arthritis or Still's disease can cause fever that lasts for a long time without clear external symptoms); malignant diseases (some types of cancer, such as lymphoma, leukaemia

or metastatic cancers, can cause prolonged fever without other obvious symptoms in the initial stages of the disease) drugs and medicines; induced fever (some drugs can cause an elevated temperature as a side effect, which can last for some time without other symptoms. This includes medicines such as: antibiotics, antiepileptics or medicines for high blood pressure). Fever of unknown cause is a diagnosis in some cases, when the fever lasts for a long time and the cause cannot be determined despite all tests. This condition is usually diagnosed after all other causes have been excluded; endocrine diseases (disorders such as hyperthyroidism, can also cause an elevated temperature that lasts for a long time, often without other serious symptoms). Treatment of fever, along with symptomatic reduction of temperature, also includes targeting the underlying disease that causes it.

**Conclusion:** It is important to monitor the patient's condition and timely diagnose the cause of the fever in order to choose the appropriate therapy, whether it is infections, autoimmune diseases or malignant diseases. If a prolonged fever occurs without clear symptoms, it is necessary to consult a doctor who will carry out the necessary treatment in order to determine the exact cause and start appropriate treatment.

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## ■ Vrućica kod kroničnih bolesnika

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**Uvod:** Temperatura ljudskog tijela jedan je od ključnih vitalnih znakova. Kod odraslih kroničnih bolesnika često postoji povezanost, osim s infekcijom, ali i s komplikacijama kronične bolesti ili novonastalim stanjima. Cilj je prikazati manifestaciju temperature i povezanost s uzrocima kod kroničnih bolesnika, kao i imunološke reakcije kod onih koji manifestiraju brojne poremećaje u svom organizmu.

**Rasprava:** Vrućica je povišena tjelesna temperatura koja se javlja kada se tjelesni termostad (u hipotalamusu u mozgu) ponovno postavi na višu temperaturu, prvenstveno kao odgovor na infekciju. Povišena tjelesna temperatura koja nije uzrokovana poništavanjem zadane vrijednosti temperature naziva se hipertermija, često na kraju života. Tjelesna temperatura ovisi o dobi, zdravstvenom stanju, spolu, psihičkoj temperaturi okoline, dnevnom ciklusu, hormonalnom statusu. Međutim, umjerena vrućica može biti opasnija za odrasle koji su kronični srčani ili plućni bolesnici, jer povišena temperatura uzrokuje tahikardiju i tahipneju. Vrućica također može pogoršati psihičko stanje kod osoba s demencijom ili drugim neurodegenerativnim stanjima ili sepsom. Tvari koje uzrokuju vrućicu nazivaju se pirogeni, a kategorizirani su kao infektivni (najčešći), neoplastični (rak) i upalni (uključujući autoimune poremećaje, alergijske reakcije i neke reakcije na lijekove). Infektivni uzrok kod odraslih s kroničnim bolestima s vrućicom koja traje 4 dana ili manje (naziva se akutna vrućica) je rijedak bez superinfekcije. Neinfektivni uzrok traje dugo ili se ponavlja (leukemija, limfom i rak bubrega). Upalni poremećaji koji uzrokuju vrućicu uključuju sistemske reumatske poremećaje kao što su reumatoidni artritis, Stylusova bolest, sistemski eritematozni lupus i arteritis gigantski stanica. Vrućice nepoznatog podrijetla opisuje se kao febrilna bolest (temperatura 38,3°C ili viša)

koja traje dva tjedna ili dulje bez utvrđene etiologije ili utvrđene dijagnoze unatoč jednotjednoj bolničkoj procjeni. Smatra se da je pad tjelesne temperature s godinama pojava koja je posljedica tzv. imunosenzitivnosti ili imunosenzencija ili starenja imunološkog sustava, jer stariji pacijenti često nisu u stanju stvoriti snažan upalni odgovor na infekcije i bolesti. Njihova temperatura ne dosegne temperaturni raspon. Stariji kronični bolesnici često imaju nespecifične simptome s nekoliko lokaliziranih nalaza groznice (lažna temperatura) koja je nespecifična, kao što su oni koji se teško kreću. Virusne bolesti rijetko se nalaze u starijih osoba najčešće su iskra bolesti praćena temperaturom koja razvija burnu reakciju često zahvaćajući nekoliko organskih sustava. Tumori su čest uzrok kod starijih osoba (rak debelog crijeva), kao i temporalni arteritis. Većina bolesnika s uobičajenom hipertermijom ima tjelesnu temperaturu nižu od 38.

**Zaključak:** Liječnici bi trebali obaviti sveobuhvatnu procjenu i uzeti detaljnu anamnezu u kroničnih bolesnika, osobito kod vrućice nepoznatog porijekla. Ako je klinička slika jasna, pacijentu je potrebna minimalna dijagnostika, uključujući kompletnu krvnu sliku, sedimentacija eritrocita i testiranje razine C-reaktivnog proteina s mogućnošću radiografije prsnog koša, analize urina i urinokulture, elektrolita, jetrenih enzima, elektrofereze proteina u serumu i hormona štitnjače. Daljnje pretrage specijalista i subspecijalista uključuju hemokulture, laktat dehidrogenazu, feritin, kreatin kinazu, reumatoidni faktor i antinuklearna antitijela, serološko testiranje specifično za regiju (npr. citomegalovirus, Epstein-Barr virus, tuberkuloza, HIV) i ultrazvuk abdomena i zdjelice ili kompjutorizirana tomografija. Ako dijagnoza ostane nedostižna, PET SCEN plus kompjutorizirana tomografija može pomoći, kao i biopsija.

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## ■ Fever in chronic patients

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**Introduction:** Human body temperature is one of the key vital signs. In adult chronic patients, there is often a connection, apart from infection, but also with complications of a chronic disease or new conditions. The goal is to show the manifestation of temperature and the connection with the causes in chronic patients, as well as immune reactions in those who manifest numerous disorders in their body.

**Discussion:** A fever is an elevated body temperature that occurs when the body's thermostat (in the hypothalamus in the brain) resets to a higher temperature, primarily in response to infection. Elevated body temperature that is not caused by resetting the temperature setpoint is called hyperthermia, often at the end of life. Body temperature depends on age, state of health, gender, psychological temperature of the environment, daily cycle, hormonal status. However, moderate fever can be more dangerous for adults who have chronic heart or lung diseases, because elevated temperature causes tachycardia and tachypnea. Fever can also worsen the mental state of people with dementia or other neurodegenerative conditions or sepsis. Substances that cause fever are called pyrogens, and are categorized as infectious (most common), neoplastic (cancer), and inflammatory (including autoimmune disorders, allergic reactions, and some drug reactions). An infectious cause in adults with chronic diseases with fever lasting 4 days or less (called acute fever) is rare without superinfection. A non-infectious cause lasts a long time or recurs (leukemia, lymphoma and kidney cancer). Inflammatory disorders that cause fever include systemic rheumatic disorders such as rheumatoid arthritis, Stylus disease, systemic lupus erythematosus, and giant cell arteritis. Fever of unknown origin is described as a febrile illness (temperature 38.3°C or higher) lasting two weeks or longer

without an established etiology or established diagnosis despite a one-week hospital evaluation. It is considered that the drop in body temperature with age is a phenomenon that is a consequence of the so-called immunosenescence or aging of the immune system, because elderly patients are often unable to create a strong inflammatory response to infections and diseases. Their temperature does not reach the temperature range. Older chronic patients often have nonspecific symptoms with a few localized findings of fever (false temperature) that is nonspecific, such as those with difficulty moving. Viral diseases are rarely found in the elderly, most often the spark of the disease is accompanied by a fever that develops a violent reaction, often affecting several organ systems. Tumors are a common cause in the elderly (colon cancer), as is temporal arteritis. Most patients with usual hyperthermia have a body temperature lower than 38.

**Conclusion:** Physicians should perform a comprehensive assessment and take a detailed history in chronic patients, especially with fever of unknown origin. If the clinical picture is clear, the patient needs minimal diagnostics, including a complete blood count, erythrocyte sedimentation and C-reactive protein level testing with the possibility of a chest radiograph, analysis of urine and urine culture, electrolytes, liver enzymes, electrophoresis of serum proteins and thyroid hormones. Further tests by specialists and subspecialists include blood cultures, lactate dehydrogenase, ferritin, creatine kinase, rheumatoid factor and antinuclear antibodies, region-specific serological testing (eg cytomegalovirus, Epstein-Barr virus, tuberculosis, HIV) and abdominal and pelvic ultrasound or computed tomography. If a diagnosis remains elusive, PET SCEN plus computed tomography can help, as can biopsy.

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## ■ Vrućica u bolesnika s bubrežnim presatkom

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**Uvod s ciljem.** U bolesnika s bubrežnim presatkom vrućica je čest alarm za promptnu obradu u traganju za infekcijom. Međutim, ona nije niti osjetljiv niti specifičan znak infekcije jer se značajan udio infekcija događa bez vrućice, dok se druga značajnost odnosi na vrućice neinfektivnog uzroka. Učinjena je pretraga literature o vrućici u bolesnika s bubrežnim presatkom i sastavljena prezentacija na temelju objavljenih podataka i dugoročnog iskustva transplantacijskog nefrologa.

**Rezultati.** Većina vrućica u bolesnika s bubrežnim presatkom prouzročena je infektivnim uzročnikom, najčešće bakterijom, a epidemiologija se tijekom vremena mijenjala. Kirurške komplikacije i strana tijela poput katetera najčešći su izvor vrućice u ranom poslijetransplantacijskom razdoblju, obično infektivne prirode. Infekcije koje potječu od darovatelja bubrega su rijetke, ali se mora i na njih misliti. Može doći do reaktivacije latentne infekcije, poput tuberkuloze ili herpes zoster. Prije ere profilakse citomegalovirusne (CMV) infekcije većina febrilnih epizoda, osobito u ranom poslijetransplantacijskom razdoblju, bila je prouzročena CMV-om. Gljivične infekcije poput *Aspergillus* su češće u ovih bolesnika. Ipak, najčešći krivci za vrućicu su mokraćne infekcije i pneumonije. Treba tragati za repertoarom oportunističkih, virusnih, bakterijskih i gljivičnih infekcija, na tipičnim i manje tipičnim (poput središnjeg živčanog sustava) mjestima, žarišnim (npr. apscesi) ili diseminiranim. Boravak u bolnici je sve češće povezan s nozokomijalnim infekcijama prouzročenima rezistentnim bakterijama. Od neinfektivnih uzroka, potrebno je isključiti odbacivanje bubrežnog presatka i zloćudnu bolest (osobito tzv. PTLN, od engl. za poslijetransplantacijsku limfoproliferativnu bolest). Vrućica uzrokovana lijekovima je rijetka, no također predstavlja jednu od mogućnosti. U trećine slučajeva vrućice nepoznatog sijela (tzv. FUO, prema engl.) izvor ostaje neprepoznat

i nakon 90 dana od početka FUO. Dijagnostički postupak uključuje detaljnu anamnezu, osobito epidemiološku, fizikalni pregled, mikrobiološku i slikovnu obradu te u nekim slučajevima biopsiju bubrežnog presatka. Obrada treba pokriti širok spektar izvora vrućice, u pogledu uzročnika i sijela, prema određenom protokolu, bez odgode, a istodobno često treba uključiti empirijsku terapiju dok se čeka točna dijagnoza. Vrućica u ovih bolesnika može biti praćena brzim pogoršanjem i hitnoćom, poput sepse i septičkog šoka. Terapiju treba prilagoditi bubrežnoj funkciji i interakcijama između antimikrobnih i imunosupresivnih lijekova koje znaju biti značajne, ali i predvidive. Lijekove za snižavanje temperature treba birati među nefrotoksičnim, a nesteroidni protuupalni lijekovi pri tomu nisu dobrodošli.

**Zaključak** Vrućica u bolesnika s bubrežnim presatkom mora biti temeljito obrađena, u potrazi za infektivnim i neinfektivnim uzrocima. U imunokompromitiranog bolesnika ove obje skupine patologija nose povećan rizik za nepovoljan tijek, komplikacije i ishode, svakako rjeđe uz pravodobnu dijagnozu i liječenje. Epidemiologija se tijekom vremena promijenila zbog promjena u dijagnostici, profilaksi, imunosupresiji i liječenju. Epidemiologija se također razlikuje i u pogledu vremena protekloga nakon transplantacije. Prevencija, cijepljenje i antimikrobna profilaksa su obvezni, prema aktualnom protokolu.

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## ■ Fever in kidney transplant patient

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**Introduction with aim.** In kidney transplant recipients fever is a common alarm for a prompt work up for infection. However, neither it is a sensitive nor a specific sign of infection, significant proportion of infections pass without fever, while another significance refers to the fevers noninfectious in origin. Research of the literature about fever in kidney transplant patients was done and the presentation made based on the published data and longtime experience as nephrologist – transplantologist.

**Results** Most fevers in kidney transplant patients are caused by infectious agents, mostly bacterial, while the epidemiology has changed over time. Surgery related complications and foreign material like catheters are the most frequent origin of fever in the early post transplantation period, usually caused by infection. Donor derived infections are rare, but should be also considered. Latent infections could be reactivated, like tuberculosis or herpes zoster. Before the cytomegalovirus (CMV) prophylaxis era, the majority of the febrile episodes, especially during the first post-transplant months were due to CMV. Fungal infections like *Aspergillus* are more common in these patients. Still, urinary tract infections and pneumonias are the most frequent culprits for fever. A repertoire of opportunistic infections, viral, bacterial and fungal at typical and uncommon sites (like central nervous system), focal (e.g. abscesses) or disseminated should be looked for. Hospital sojourn is more and more related to nosocomial infections caused by resistant bacteria. Among noninfectious causes, kidney transplant rejection and malignancy (particularly so called PTLN – post transplantation lymphoproliferative disease) should be excluded. Drug fever is rare, however, it presents one of the possibilities, as well. In a third of cases with initially fever of unknown origin (FUO) it could not be turned into the known origin even after

90 days since the beginning of FUO. Diagnostics include detailed history, especially epidemiologic (and particularly in terms of seasonal epidemics), physical examination, microbiology, imaging and kidney graft biopsy in some cases. The work up should cover broad causes in terms of agents and sites through a defined procedure, without delay, along with often empiric therapy while waiting for the precise diagnosis. Fever in these patients could be followed by rapid deterioration and emergency, like sepsis and septic shock. The therapy should be adjusted to the kidney transplant function and interactions between the antimicrobials and immunosuppressive drugs that could be significant but predictable. Fever lowering drugs should be chosen among non-nephrotoxic medications, non-steroidal anti-inflammatory drugs being not welcome.

**Conclusion** Fever in kidney transplant patients must be thoroughly worked up, looking for infectious and noninfectious origin. Both groups of pathology bear higher risk for the unfavorable course, complications and outcomes, including mortality, in immunosuppressed patients, certainly less frequent if timely diagnosed and treated. Epidemiology has been changed during time, due to the changes in diagnostic possibilities, prophylaxis, immunosuppression and treatment. The epidemiology differs also regarding the time period after the transplantation. Prevention, vaccination and antimicrobial prophylaxis are mandatory, according to the current protocol.

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## ■ Umor i poremećaj rada štitnjače

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**Uvod s ciljem:** Umor je poteškoća u započinjanju i nastavljanju neke aktivnosti zbog nedostatka energije koja je praćena željom za odmorom. Štitnjača ima ključnu ulogu u regulaciji metabolizma, a hormoni koje proizvodi, tiroksin (T4) i trijodtironin (T3), izravno utječu na rad svih organa i tkiva. Poremećaji rada štitnjače, poput hipotireoze i hipertireoze, često izazivaju niz simptoma, među kojima je jedan od najučestalijih kronični umor. Zabilježeno je da do jedne trećine bolesnika, češće žena, koji se javljaju s umorom, ima bolest štitnjače. Cilj rada je prikazati povezanost umora s poremećajem funkcije štitnjače, kako bi se povećala svijest o važnosti rane dijagnoze i odgovarajućeg liječenja.

**Rasprava:** Poremećaji štitnjače mogu biti uzrokovani autoimunim bolestima, poput Hashimotovog tireoiditisa ili Gravesove bolesti, nedostatkom joda, genetskim faktorima ili utjecajem stresa i okolišnih čimbenika. Hipotireoza, stanje smanjene funkcije štitnjače, najčešće doводи do umora zbog usporavanja metaboličkih procesa. Osobe s hipotireozom često osjećaju pospanost i nedostatak energije, što značajno utječe na kvalitetu života. Početak simptoma često je postupan i prepoznaje se retrospektivno kroz promjene u životnim aktivnostima. Nasuprot tome, hipertireoza, stanje prekomjerne aktivnosti štitnjače, razvija se brže i obično je praćen drugim simptomima prekomjerne razine hormona štitnjače zbog povećane osjetljivosti tkiva na katekolamine. Promjene u kardiovaskularnoj funkciji, osobito tahikardija gotovo su uvijek prisutne i mogu pomoći u razlikovanju umora uzrokovanog hipertireozom od psihogenog umora. Umor je često povezan s mišićnom slabošću, posebno proksimalnih mišića, gubitkom težine, nervozom, emocionalnom nestabilnošću i hiperkinezama. Važno je naglasiti da umor povezan s poremećajem štitnjače često može biti

nespecifičan i sličan simptomima drugih stanja, poput anemije, depresije ili sindroma kroničnog umora. Zbog toga se nerijetko događa da bolesnici prođu dug put do ispravne dijagnoze. Klinička slika može se potvrditi laboratorijskim analizama hormona štitnjače (TSH, T3 i T4), kao i dodatnim testovima, poput ultrazvuka štitnjače ili određivanja protutijela. Pravilno liječenje, koje uključuje nadoknadu hormona kod hipotireoze ili kontrolu prekomjerne aktivnosti kod hipertireoze, često vodi do značajnog poboljšanja simptoma. Međutim, potrebno je uzeti u obzir i promjene u načinu života, poput pravilne prehrane, dovoljno sna i smanjenja stresa, kako bi se dodatno olakšala borba protiv umora.

**Zaključak:** Kronični umor često je prvi znak poremećaja rada štitnjače, ali zbog svoje nespecifičnosti može ostati neprepoznat. Pravovremena dijagnoza i liječenje ključni su za poboljšanje kvalitete života oboljelih. Bitno je educirati bolesnike o važnosti zdravog načina života i redovitih pregleda. Na taj način moguće je spriječiti dugoročne komplikacije i omogućiti bolju kontrolu simptoma, uključujući i umor, koji značajno smanjuje kvalitetu života.

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## ■ Fatigue and thyroid disorder

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Introduction and aim: Fatigue is a difficulty in initiating and sustaining activities due to a lack of energy, accompanied by a desire for rest. The thyroid gland plays a crucial role in regulating metabolism, and the hormones it produces, thyroxine (T4) and triiodothyronine (T3), directly affect the function of all organs and tissues. Thyroid dysfunctions, such as hypothyroidism and hyperthyroidism, often cause a range of symptoms, with chronic fatigue being one of the most common. Studies have shown that up to one-third of patients presenting with fatigue, particularly women, have thyroid disease. The aim of this paper is to explore the relationship between fatigue and thyroid dysfunction to raise awareness of the importance of early diagnosis and appropriate treatment.

Discussion: Thyroid disorders can result from autoimmune diseases, such as Hashimoto's thyroiditis or Graves' disease, iodine deficiency, genetic factors, or the influence of stress and environmental factors. Hypothyroidism, characterized by decreased thyroid function, often leads to fatigue due to the slowing of metabolic processes. Individuals with hypothyroidism frequently experience drowsiness and a lack of energy, significantly affecting their quality of life. The onset of symptoms is often gradual and may only be recognized retrospectively through changes in daily activities. In contrast, hyperthyroidism, characterized by excessive thyroid activity, develops more rapidly and is typically accompanied by other symptoms of excess thyroid hormone levels due to increased tissue sensitivity to catecholamines. Cardiovascular changes, particularly tachycardia, are almost always present and can help distinguish fatigue caused by hyperthyroidism from psychogenic fatigue. Fatigue is often associated with muscle weakness, particularly in proximal muscles, weight loss, nervousness,

emotional instability and hyperkinesias. It is important to emphasize that fatigue associated with thyroid dysfunction can often be nonspecific and resemble symptoms of other conditions, such as anemia, depression, or chronic fatigue syndrome. Consequently, patients often face a long journey before receiving a correct diagnosis. The clinical presentation can be confirmed through laboratory analyses of thyroid hormones (TSH, T3, and T4), as well as additional tests such as thyroid ultrasound or antibody testing. Proper treatment, including hormone replacement therapy for hypothyroidism or controlling excessive thyroid activity in hyperthyroidism, often leads to significant symptom improvement. However, lifestyle modifications, such as a balanced diet, adequate sleep, and stress reduction, should also be considered to further ease the struggle against fatigue.

Conclusion: Chronic fatigue is often the first sign of thyroid dysfunction but, due to its nonspecific nature, it may go unrecognized. Timely diagnosis and treatment are key to improving the quality of life for affected individuals. It is essential to educate patients on the importance of a healthy lifestyle and regular check-ups. By doing so, it is possible to prevent long-term complications and enable better symptom control, including fatigue, which significantly reduces the quality of life.

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## ■ Slabost i umor kod anemije i metaboličkih poremećaja u obiteljskoj medicini

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**Uvod s ciljem:** Pritužbe bolesnika na slabost (nedostatak fizičke ili mišićne snage) i umor (osjećaj iscrpljenosti ili nedostatka energije) su među najčešćim i najizazovnijim problemima s kojima se susreću obiteljski liječnici. Cilj rada je prikazati trenutna znanja o slabosti i umoru u bolesnika s poremećenim metabolizmom željeza i najčešćim metaboličkim poremećajima i pristup obiteljskog liječnika takvom bolesniku.

**Rasprava:** Patofiziološki mehanizmi koji uzrokuju slabost i umor su malo poznati. Medicinska i psihijatrijska teorija sugeriraju zaštitnu funkciju ovih simptoma. Poremećaji metabolizma željeza istaknuti su primjer stanja gdje je umor vodeći simptom. Unatoč značajnom napretku u dijagnostiranju i liječenju patologija željeza, pristup sindromu kroničnog umora u takvih bolesnika nije precizno određen. Anemija se često dijagnosticira rutinskim laboratorijskim pretragama kao slučajan nalaz. Patogeneza umora povezanog s anemijom ostaje nejasna, ali neki autori sugeriraju da abnormalnosti u energetske metabolizmu igraju ulogu u nastanku umora. Mogući mehanizam je smanjenje kisika u tkivima, posebno mišićima, što stvara kardiopulmonalni stres, izazivajući osjećaj umora. Drugi mogući mehanizam je da nedostatak željeza izravno utječe na rad mozga i dovodi do osjećaja umora. Metabolički poremećaji uključuju poremećaje u metabolizmu ugljikohidrata, lipida, proteina, minerala ili nukleinskih kiselina. Metabolički sindrom, pretilost i šećerna bolest najčešće su patologije povezane s prehranom. Ovi poremećaji remete normalan metabolički proces pretvaranja hrane u energiju na staničnoj razini. Početna anamneza i fizikalni pregled omogućuju obiteljskom liječniku da prepozna da li je problem medicinskog, psihijatrijskog ili fiziološkog porijekla. U pojedinim

slučajevima, slabost ili umor mogu biti uzrokovani višestrukim čimbenicima ili uzrok nije očigledan. Precizno razumijevanje bolesnikova opisa slabosti ili umora je imperativ. Potrebno je dobiti odgovore na pitanja o slabosti i umoru: početak i vremenski tijek; distribucija (lokalizirana, generalizirana); čimbenici pogoršanja i ublažavanja; povezani znaci i simptomi; okruženje u kojem je problem nastao; utjecaj na dnevne aktivnosti. Fizikalni pregled može pružiti bitne podatke koji se ne mogu dobiti putem intervjua ili laboratorijskih pretraga. Budući da anamneza i fizikalni pregled obično daju ispravnu dijagnozu, laboratorijske pretrage često igraju, prvenstveno, potvrdnu ulogu.

**Zaključak:** Slabost i umor se nikada ne smiju olako odbaciti, jer su od značaja za bolesnika i mogu predstavljati prvo upozorenje na bolest. Za liječnika obiteljske medicine slabost i umor kod bolesnika predstavlja ogroman izazov: diferencirati simptom koji je akutan i samoograničen, a često i beznačajan, od simptoma koji je kroničan i progresivan, a često i ozbiljan. Diferencijalno dijagnostički pristup, baziran na anamnezi, fizikalnom pregledu i ciljanom laboratorijskom ispitivanju, od ključnog je značaja za preciznu identifikaciju osnovnog uzroka. Promišljena i brižna primjena vještina obiteljskog liječnika dovodi do uspješnog rješenja problema.

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## ■ Weakness and Fatigue in Anemia and Metabolic Disorders in Family Medicine

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**Introduction with aim:** Patient complaints of weakness (lack of physical or muscle strength) and fatigue (feeling of exhaustion or lack of energy) are among the most common and challenging problems faced by family physicians. The aim of the paper is to present the current knowledge about weakness and fatigue in patients with impaired iron metabolism and the most common metabolic disorders and the family doctor's approach to such patients.

**Discussion:** There is little data on the pathophysiological mechanisms causing weakness and fatigue. Medical and psychiatric theories suggest a protective function of these symptoms. Disorders of iron metabolism are highlighted as an example of a condition where fatigue is the leading symptom. Despite significant progress in diagnosing and treating iron-related pathologies, the approach to chronic fatigue syndrome in such patients is not precisely defined. Anemia is often diagnosed through routine laboratory tests as an incidental finding. The pathogenesis of fatigue related to anemia remains unclear, but some authors suggest that abnormalities in energy metabolism play a role in the onset of fatigue. A possible mechanism is reduced oxygen delivery to tissues, particularly muscles, which creates cardiopulmonary stress, triggering feelings of fatigue. Another possible mechanism is that the lack of iron directly affects brain function, leading to fatigue. Metabolic disorders include disturbances in carbohydrate, lipid, protein, mineral, or nucleic acid metabolism. Metabolic syndrome, obesity, and diabetes mellitus are the most common diet-related pathologies. These disorders disrupt the normal metabolic process of converting food into energy at the cellular level. An initial history and physical examination allow the family doctor to recognize whether the

problem is medical, psychiatric or physiological in origin. In some cases, weakness or fatigue can be caused by multiple factors or the cause is not obvious. Accurate understanding of the patient's description of weakness or fatigue is imperative. It is necessary to get answers to questions about weakness and fatigue: onset and time course; distribution (localized, generalized); aggravating and mitigating factors; associated signs and symptoms; the environment in which the problem arose; impact on daily activities. A physical examination can provide important information that cannot be obtained through an interview or laboratory tests. Since history and physical examination usually provide the correct diagnosis, laboratory tests often play primarily a confirmatory role.

**Conclusion:** Weakness and fatigue should never be dismissed lightly, as they are significant for the patient and may represent the first warning signs of illness. For the family physician, weakness and fatigue in patients represent a huge challenge: differentiating between a symptom that is acute, self-limiting, and often insignificant, and a symptom that is chronic, progressive, and often serious. A differential diagnostic approach, based on history, physical examination, and targeted laboratory investigation, is crucial for the precise identification of the underlying cause. Thoughtful and caring application of the family doctor's skills leads to a successful resolution of the problem.

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## ■ Sindrom kroničnog umora

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**Uvod s ciljem.** Mijalgični encefalomijelitis (ME), poznat kao sindrom kroničnog umora (CFS), karakterizira teška iscrpljenost koja se ne ublažava odmorom. Umor se pogoršava dodatnim tjelesnim ili mentalnim naporom i ograničava svakodnevne aktivnosti. Cilj ovog kratkog prikaza je ukazati na važnost postavljanja sumnje i ranog prepoznavanja entiteta s ciljem poboljšanja kvalitete života oboljelih.

**Rasprava.** Posljednjih godina neka istraživanja pružila su preliminarne dokaze koji upućuju na višestruku etiologiju: neuro-imuno-endokrine interakcije, metaboličke promjene i genetske čimbenike. Trenutno ne postoji dijagnostički test ili validirani biomarker za ME/CFS. Osim umora, oboljeli mogu imati niz simptoma: malaksalost nakon napora, neuro-kognitivne simptome (konfuzija ili usporeno razmišljanje), bolove u mišićima i zglobovima, poremećaj spavanja, preosjetljivost na podražaje, simptome slični gripi. Simptomi su postojani ili se ponavljaju tijekom dugih vremenskih razdoblja i dovode do značajnog smanjenja prethodnih razina funkcioniranja. Dijagnoza je klinička, temelji se na detaljnoj anamnezi i fizikalnom pregledu. Prisutni simptomi se često preklapaju sa stanjima kao što su: reumatološki poremećaji (npr. fibromijalgija, sistemski eritematozni lupus), psihijatrijski poremećaji (npr. depresija, bipolarni poremećaj), lajmska bolest, multipla skleroza, apneja, što diferencijalnu dijagnozu čini složenom. Ne postoji uzročno liječenje bolesti, kontrola simptoma zahtijeva individualni plan liječenja. Nefarmakološki pristupi liječenju uključuju kognitivno bihevioralnu terapiju, strukturirano liječenje koje uključuje postupno povećanje tjelesne aktivnosti i adaptivnu terapiju stimulacije koja naglašava slušanje tijela i postavljanje realnih razina aktivnosti kako bi se izbjeglo prenaprezanje i pogoršanje umora.

Farmakoterapija uključuje niz lijekova poput analgetika, antikonvulziva, antidepresiva, narkotika, antivirusnih lijekova i imunomodulatora ovisno o kliničkoj slici.

**Zaključak.** Dijagnosticiranje i liječenje ME/CFS je složeno zbog preklapanja simptoma s drugim stanjima i nepostojanja specifičnih biomarkera. Postavljanje sumnje na postojanje entiteta zahtijeva izazov i multidisciplinarni pristup oboljelom s ciljem poboljšanja ishoda liječenja.

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## ■ Chronic Fatigue Syndrome

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**Introduction with aim.** Myalgic encephalomyelitis (ME), also known as chronic fatigue syndrome (CFS), is characterized by severe fatigue that is not relieved by rest. Fatigue is worsened by additional physical or mental exertion and limits daily activities. This brief review aims to highlight the importance of raising suspicion and early recognition of the entity to improve the quality of life of sufferers.

**Discussion.** In recent years, some studies have provided preliminary evidence suggesting a multiple etiology: neuro-immune-endocrine interactions, metabolic changes, and genetic factors. There is currently no diagnostic test or validated biomarker for ME/CFS. In addition to fatigue, sufferers may experience a range of symptoms: fatigue after exertion, neurocognitive symptoms (confusion or slowed thinking), muscle and joint pain, sleep disturbance, hypersensitivity to stimuli, and flu-like symptoms. Symptoms are persistent or recurrent over long periods and lead to a significant reduction in previous levels of functioning. Diagnosis is clinical, based on a detailed history and physical examination. The presenting symptoms often overlap with conditions such as: rheumatological disorders (e.g. fibromyalgia, systemic lupus erythematosus), psychiatric disorders (e.g. depression, bipolar disorder), Lyme disease, multiple sclerosis, apnea, which makes the differential diagnosis complex. There is no causal treatment for the disease, and symptom control requires an individual treatment plan. Non-pharmacological treatment approaches include cognitive behavioral therapy, structured treatment that includes an increase in physical activity, and adaptive stimulation therapy that emphasizes „listening“ to the body and setting realistic activity levels to avoid overexertion and worsening fatigue. Pharmacotherapy includes

a range of medications such as analgesics, anti-convulsants, antidepressants, narcotics, antiviral drugs, and immunomodulators depending on the clinical picture.

**Conclusion.** Diagnosing and treating ME/CFS is complex due to the overlap of symptoms with other conditions and the lack of specific biomarkers. Suspicion of the existence of the entity requires a challenging and multidisciplinary approach to the patient to improve treatment outcomes.

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## ■ Umor u neurološkim bolestima

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**Uvod s ciljem:** Prevalencija umora kod neuroloških bolesti veća je od one koja bi se očekivala samo na temelju dobi i stupnja invaliditeta. Javlja se kao čest simptom zbog kojeg se ovi pacijenti javljaju liječniku. Cilj rada je osvijestiti važnost umora kao onesposobljavajućeg simptoma kod neuroloških bolesnika u ambulanti obiteljskog liječnika.

**Rasprava:** Umor je povezan sa smanjenjem kvalitete života i invaliditetom kod multiple skleroze (MS), Parkinsonove bolesti, miastenije gravis, moždanog udara, postpolio sindroma, traumatske ozljede mozga te amiotrofične lateralne skleroze. Percepcija umora nastaje uslijed interakcije između različitih homeostatskih, psiholoških čimbenika te perifernog i središnjeg živčanog sustava. Navedeni čimbenici ukazuju, bilo direktno ili indirektno, da je umor posljedica aktivnosti središnjeg živčanog sustava. Kod neuroloških poremećaja govori se o dvije vrste umora: centralnom i perifernom umoru. Središnji umor se manifestira kod bolesti sa zahvaćanjem središnjeg živčanog sustava kao što su MS, Parkinsonova bolest, moždani udar, neurotrauma. S druge strane, periferni umor se javlja u bolesnika s poremećajima perifernog živčanog sustava (miastenija gravis, periferna neuropatija i postpolio sindrom). Periferni umor, uzrokovan poremećajima prijenosa na živčano-mišićnom spoju i metaboličkim bolestima, karakterizira se nemogućnošću održavanja sile mišićne kontrakcije. Glavne karakteristike centralnog umora su pojačana percepcija napora i smanjena izdržljivost tijekom trajnih tjelesnih i mentalnih aktivnosti. Nedosljednosti u definiranju umora doprinose trenutnoj situaciji u kojoj je umor jedno od najmanje istraživanih i najmanje razumljivih stanja. Iako postoji mnogo alata za procjenu umora, malo njih se može preporučiti za kliničku ili istraživačku primjenu. Oko 40% bolesnika s MS smatra umor najvećim opterećenjem, jačim od drugih simptoma, uključujući spastičnost i slabost. Jedna trećina s

Parkinsonovom bolesti navodi da je umor najteži simptom koji ograničava svakodnevne aktivnosti. Nefarmakološke metode liječenja uključuju tjelovježbu i osvještavanje umora. Dostupne opcije farmakološkog liječenja temeljenih na dokazima su rijetke. U bolesnika s MS imunomodulacijski i kolinergički lijekovi mogu smanjiti percepciju umora, u bolesnika koji uzimaju antidepresive teško je razdvojiti da li je smanjenje umora posljedica učinka lijeka ili posljedica odmora. Primjena transkranijalne stimulacije istosmjernom strujom (tDCS) za liječenje umora istraživana je u osoba s moždanim udarom, MS, Parkinsonovom bolešću, postpolio-sindromom i nakon traumatske ozljede mozga. Iako je korišten širok spektar parametara liječenja i mjernih ishoda za procjenu i ciljano djelovanje na umor, tDCS pokazuje obećavajuće rezultate u ublažavanju ovog simptoma. Umor nakon moždanog udara često nije dovoljno prepoznat; stoga bi zdravstveni djelatnici trebali biti svjesni pojave istog, educirati bolesnika i njegovu obitelj kako djelovati na smanjenje umora tijekom oporavka.

**Zaključak:** Liječnik obiteljske medicine treba razmišljati o umoru kao čestom simptomu brojnih neuroloških bolesti, razumjeti bolesnika kada se opetovano tuži na umor, dati mu podršku i savjete o dostupnim mogućnostima smanjenja ovog simptoma koji uvelike snižava kvalitetu života.

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## ■ Fatigue in neurological diseases

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**Introduction with aim:** The prevalence of fatigue in neurological diseases is higher than what would be expected based on age and degree of disability alone. The aim of this paper is to raise awareness of the importance of this disabling symptom in neurological patients in the family physician practice.

**Discussion:** Fatigue is associated with reduced quality of life and disability in multiple sclerosis, Parkinson's disease, myasthenia gravis, stroke, post-polio syndrome, traumatic brain injury, and amyotrophic lateral sclerosis. The perception of fatigue arises due to the interaction between various homeostatic, psychological factors and the peripheral and central nervous system. All these factors indicate, either directly or indirectly, that fatigue is a consequence of the activity of the central nervous system. In neurological disorders, two types of fatigue are reported: central and peripheral fatigue. Central fatigue is manifested in diseases affecting the central nervous system, such as multiple sclerosis, Parkinson's disease, stroke, neurotrauma. On the other hand, peripheral fatigue occurs in patients with disorders of the peripheral nervous system, such as myasthenia gravis, peripheral neuropathy, and post-polio syndrome. Peripheral fatigue, caused by transmission disorders at the neuromuscular junction and metabolic diseases, is characterized by the inability to maintain the force of muscle contraction. The main characteristics of central fatigue are increased perception of effort and reduced endurance during sustained physical and mental activities. Inconsistencies in the definition of fatigue contribute to the current situation where fatigue is one of the least researched and least understood conditions. Although there are many fatigue assessment tools, few can be recommended for clinical or research use. In multiple sclerosis, 40% of patients find fatigue to be the most burdensome, more than any other symptom, including spasticity and weakness, and one-third of Parkinson's patients report that fatigue is their

most severe symptom that limits daily activities. Non-pharmacological methods of treating fatigue include exercise and fatigue awareness. Available evidence-based pharmacological treatment options are few. In multiple sclerosis, immunomodulating and cholinergic drugs can reduce the perception of fatigue, and in the case of antidepressants, it is difficult to separate the effect on fatigue or the reduction of fatigue as a consequence of rest. The use of transcranial direct current stimulation (tDCS) for the treatment of fatigue has been investigated in people with stroke, multiple sclerosis, Parkinson's disease, post-polio syndrome and after traumatic brain injury. Although a wide range of treatment parameters and outcome measures have been used to assess and target fatigue, tDCS shows promising results in alleviating this symptom. Fatigue after stroke is often under-recognized; therefore, health-care professionals should be aware of fatigue after stroke and prepare patients and their families to reduce fatigue through assessment, education, and intervention during recovery from stroke.

**Conclusion:** The family physicians should think about fatigue as a frequent accompanying symptom of numerous neurological diseases, understand the patient when he repeatedly complains of fatigue and give him support and advice on the available options to reduce this symptom, which greatly reduces the quality of life of patients.

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## ■ Umor i gastrointestinalne bolesti

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**Uvod s ciljem.** Umor je jedan od čestih simptoma raznih bolesti i značajno utječe na kvalitetu života. Iako se često povezuje s fizičkim i psihičkim naporima, kod bolesnika s gastrointestinalnim bolestima predstavlja kompleksan osjećaj iscrpljenosti uslijed bolesti, ali i drugih čimbenika koji su još nedovoljno proučeni. Cilj ovog rada je ukazati na uzroke i mehanizme umora kod osoba oboljelih od gastrointestinalnih poremećaja te važnosti prepoznavanja i ublažavanja takvih simptoma.

**Rasprava.** Umor kod gastrointestinalnih bolesti složen je simptom s multifaktorskim uzrocima, uključujući upalu, nutritivne deficite, crijevnu disbiozu i psihološke faktore. Sam izraz „osovina crijeva-mozak” odnosi se na interakciju između gastrointestinalnog sustava i središnjeg živčanog sustava, što potvrđuju brojne studije. Upalni procesi u podlozi određenih bolesti, poput Crohnove bolesti i ulceroznog kolitisa, mogu uzrokovati oslobađanje citokina koji dovode do osjećaja umora. S druge strane, malapsorpcija uslijed oštećenja crijevne sluznice kod celijakije ili kroničnog pankreatitisa, zatim anemija, elektrolitski disbalans kod različitih gastroenteritisa i sindroma iritabilnog crijeva mogu također rezultirati osjećajem umora. Umor je relativno čest subjektivni simptom i kod bolesnika s MASLD-om, kao najčešćom kroničnom bolesti jetre.

**Zaključak.** Kod gastrointestinalnih bolesnika umor je često zanemaren ili mu se ne pridaje velika važnost, ali je vrlo bitan jer utječe na ionako već narušenu kvalitetu života tih bolesnika. Prepoznavanje i ispravno liječenje umora važni

su koraci u sveobuhvatnom pristupu liječenja gastrointestinalnih bolesti, ali i podizanju kvalitete života takvih bolesnika.

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## ■ Fatigue and gastrointestinal diseases

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**Introduction with aim.** Fatigue is one of the frequent symptoms of various diseases and significantly affects the quality of life. Although it is often associated with physical and mental efforts, in patients with gastrointestinal diseases it represents a complex feeling of exhaustion due to the disease, but also to other factors that are still insufficiently studied. The aim of this work is to point out the causes and mechanisms of fatigue in people suffering from gastrointestinal disorders and the importance of recognizing and alleviating such symptoms.

**Discussion.** Fatigue in gastrointestinal disease is a complex symptom with multifactorial causes, including inflammation, nutritional deficits, intestinal dysbiosis, and psychological factors. The very term "gut-brain axis" refers to the interaction between the gastrointestinal system and the central nervous system, which is confirmed by numerous studies. Inflammatory processes underlying certain diseases, such as Crohn's disease and ulcerative colitis, can cause the release of cytokines that lead to feelings of fatigue. On the other hand, malabsorption due to damage to the intestinal mucosa in celiac disease or chronic pancreatitis, then anemia, and electrolyte imbalance in various gastroenteritis and irritable bowel syndrome can also result in a feeling of fatigue. Fatigue is a relatively common subjective symptom in patients with MASLD, as the most common chronic liver disease.

**Conclusion.** In gastrointestinal patients, fatigue is often neglected or not given much importance, but it is very important because it affects

the already impaired quality of life of these patients. Recognition and correct treatment of fatigue are important steps in a comprehensive approach to the treatment of gastrointestinal diseases, but also in improving the quality of life of such patients.

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## ■ Kako pristupiti dijagnostici kod pacijenata s nerazjašnjenim simptomima?

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**Uvod s ciljem:** Pojam "medicinski neobjašnjivi simptomi" (MNS) odnosi se na razne somatske tegobe za koje se nakon brojnih pretraga ne može pronaći organski ili psihijatrijski uzrok te postaviti jasna dijagnoza. Njima pripisujemo do 50% posjeta ambulanti liječnika obiteljske medicine (LOM). Iako je većina ovih simptoma samoograničavajuća, u 2,5-10% oni perzistiraju, opterećujući bolesnika i zdravstveni sustav. Zbog nedostatka organske osnove, MNS predstavlja izazov za LOM-a i potiču donošenje kliničke odluke na temelju subjektivnih izjava pacijenata. Cilj ovog rada je prikazati dijagnostički pristup bolesniku s MNS-om i istaknuti ključne izazove u njegovom liječenju.

**Rasprava:** Početak obrade bolesnika s MNS-om čini detaljna osobna i obiteljska anamneza. Aktivno slušanje s empatijom je ključno, budući da pacijentu daje osjećaj da ga se čuje i razumije. Treba obratiti pozornost na skrivene biopsihosocijalne čimbenike koji mogu povećati sklonost, potaknuti pojavu ili održati MNS. Uz anamnezu slijedi vrlo detaljan i pažljiv klinički pregled s osnovnim mjeranjima (otkucaji srca, krvni tlak, tjelesna temperatura). Time poručujemo pacijentu da ozbiljno shvaćamo njegove probleme, a istovremeno uspostavljamo siguran i povjerljiv odnos. Daljnje dijagnostičke postupke potrebno je planirati zajedno s bolesnikom. Kako bi se izbjegao neproduktivan dijagnostički ciklus u kojem se pacijent upućuje na različite pretrage i specijalističke preglede, važno je s njim odmah postaviti granicu racionalne dijagnoze i to mu unaprijed objasniti. U slučaju MNS-a racionalna dijagnostika znači isključivanje opasnog tijeka i somatske bolesti. Takav pristup znači da će mnogi pacijenti ostati bez jasne dijagnoze. Za pacijenta to znači nedorečenost, bez načina razumijevanja alarmantnih simptoma, bez prognoze i posljedično život u neizvjesnosti. Dijagnoza "potvrđuje" pacijentovu patnju, jer utvrđuje bolest kao legitimnu i

društveno prihvatljivu, a također omogućuje pristup zdravstvenim i invalidskim uslugama i vršnjačkoj podršci. Za liječnika, međutim, nedostatak dijagnoze znači da se ne može pozivati na smjernice i metode liječenja utemeljene na dokazima u liječenju bolesnika, što može dovesti do osjećaja bespomoćnosti, ljutnje i frustracije. Jedan od alata koji pomaže LOM-u u suočavanju s takvim izazovima je potraga za djelomičnim odgovorima. Iako pacijent nema dijagnozu koja u potpunosti objašnjava prisutnost simptoma, često postoje djelomični odgovori koji doprinose njihovom razumijevanju. LOM-a ih treba integrirati u cjelinu i formulirati objašnjenje koje će biti „za sada dostatno“, uz prihvaćanje mogućnosti da će se s vremenom pronaći odgovarajuća dijagnoza. Mogu se koristiti i standardizirani alati kao što su Patient Health Questionnaire-15, Screening for Somatoform Symptoms, i Brief Symptom Inventory.

**Zaključak:** MNS predstavljaju veliki zdravstveni i financijski izazov. Uspostava i održavanje odnosa temeljenog na povjerenju, fokusiranje na simptome i stvaranje zajedničkog objašnjenja te maksimiziranje cjelokupnog zdravlja ključni su u liječenju bolesnika. Važno je znati da često nije moguće postaviti konačnu dijagnozu, što se pacijentu mora unaprijed objasniti. Dijagnostička obrada mora biti racionalna, što znači isključivanje opasnog tijeka somatskih bolesti, kao i minimiziranje štete koja može nastati zbog preduge ili nekonkluzivnih pretraga. Svi pacijenti trebaju podršku u upravljanju uznemirujućim simptomima i invaliditetom koji ih prati. Zadatak LOM-a je pružiti ustrajnu njegu i pratiti potencijalne znakove upozorenja koji bi mogli ukazivati na postavljanje jasne dijagnoze.

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## ■ How to approach diagnostics in patients with unexplained symptoms?

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**Introduction with aim:** The term "medically unexplained symptoms" (MUS) refers to various somatic complaints for which, despite extensive investigations, no organic or psychiatric cause can be identified, and a clear diagnosis cannot be made. These symptoms account for up to 50% of visits to general practitioners (GPs). While most of these symptoms are self-limiting, in 2.5–10% of cases, they persist, posing a burden on both patients and the healthcare system. MUS pose a challenge GPs due to the lack of an organic basis, forcing them to make clinical decisions based on patients' subjective reports. The aim of this article is to present a diagnostic approach to patients with MUS and highlight the key challenges in their management.

**Discussion:** The initial step in managing a patient with MUS is taking detailed personal and family history. Active listening with empathy is essential, as it helps the patient feel heard and understood. While taking history, attention should be paid to underlying biopsychosocial factors that may increase vulnerability, trigger the onset, or perpetuate MUS. This is followed by a very detailed and thorough clinical examination. Basic physical measurements are also performed (heart rate, blood pressure, body temperature). This conveys to the patient that their concerns are being taken seriously while establishing a safe and trusting relationship. Further diagnostic procedures need to be planned in collaboration with the patient. To avoid an unproductive diagnostic cycle, in which the patient is moved between various tests and specialists, it is crucial to establish the limits of rational diagnostics from the outset and explain these to the patient in advance. In the case of MUS, rational diagnostics involve ruling out dangerous conditions and somatic diseases. Such an approach means that many patients will remain without a clear diagnosis. For the patient, this translates to being left without a narrative, without a way to make sense of distressing symptoms, and without

a prognosis, resulting in a life of uncertainty. A diagnosis "validates" the patient's suffering by establishing the illness as legitimate and socially acceptable, while also enabling access to healthcare and disability services, as well as peer support. For the doctor, however, the absence of a diagnosis means being unable to rely on guidelines and evidence-based treatments when managing the patient, which can lead to feelings of helplessness, anger, and frustration. One of the tools that helps GPs in dealing with such challenges is the search for partial answers. Even though the patient does not have a diagnosis that fully explains the presence of MUS, there are often partial answers that contribute to understanding them. For the GP, it is important to integrate these partial answers into a coherent whole and to create an explanation that is "good enough for now," while remaining open to the possibility that it may eventually develop into a satisfactory diagnosis. Standardized tools, such as Patient Health Questionnaire-15, Screening for Somatoform Symptoms, and Brief Symptom Inventory can also be helpful in managing these cases.

**Conclusion:** MUS represents a significant healthcare and financial challenge. The cornerstone of managing these patients lies in establishing and maintaining a trust-based relationship, focusing on symptoms, developing a shared explanation, and maximizing overall health. It is important to recognize that a definitive diagnosis is often not possible, and this should be explained to the patient in advance. The diagnostic approach must be rational, meaning it should focus on ruling out dangerous conditions and somatic diseases while minimizing harm that may result from excessive and/or untested investigations. All patients require support in managing distressing symptoms and the accompanying disability. The GP's role is to provide consistent care and monitor for potential warning signs that could indicate the development of a clear diagnosis.

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## ■ Laboratorijske i mikrobiološke pretrage – manje je više

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**Uvod s ciljem:** Laboratorijske (LP) i mikrobiološke pretrage osnovni su dijagnostički alat u svakodnevnom radu liječnika, a one čiji rezultati neće promijeniti daljnji tijek dijagnostike i liječenja smatramo nepotrebnim. Svake godine u SAD-u se učini > 5 milijardi LP-a od kojih je 60% nepotrebno. Također, polovica mikrobioloških kultura urina (MKU) je suvišna, a u više od trećine rezultat je asimptomatska bakteriurija. Dio nalaza može biti i lažno pozitivan te dovesti do fenomena dijagnostičke kaskade, povećavajući šansu od nastanka medicinske pogreške i rasta troškova zdravstvenog sustava. Cilj ovog rada jest proučiti razloge, preciznost i najčešće zablude u upućivanju na najčešće LP-e i MKU.

**Rasprava:** Unatoč brojnim istraživanjima, smjernice za dijagnostiku se poštuju rjeđe od smjernica za liječenje, najčešće zbog straha od propusta. Najčešći primjer toga jest godišnje ili dvogodišnje obavljanje sistematskih pregleda sa širokom lepezom LP-a. Također, identične pretrage prije operativnih zahvata u općoj anesteziji preporučuju se svim pacijentima. Takav pristup nije pokazao kliničku korist, niti doveo do smanjenja smrtnosti od kroničnih nezaraznih bolesti. Zbog toga, sve LP-e i MKU treba činiti s jasnim indikacijama (procjenom rizika) i jasnim kliničkim pitanjima.

Istraživanjem u Velikoj Britaniji pacijenti su bili upućeni na LP-e zbog: postavljanja dijagnoze na temelju postojećih simptoma (43%), praćenja bolesti (31%), provjere djelovanja lijekova (10%), kontrole prethodno utvrđenih abnormalnosti (7%); a 1,5% LP-a učinjeno je na vlastiti zahtjev pacijenta. Samo 6,2% učinjenih LP-a dovelo je do postavljanja konačne dijagnoze, 41% LP-a bilo je nepotrebno. Liječnici su smatrali da je 75% učinjenih pretraga zaista bilo potrebno.

Učestalo tražena LP-a jest određivanje koncentracije vitamina D koje sa osjetljivošću 72% i specifičnošću od samo 65% gotovo u svih ispitanika pokazuje deficijenciju. Zbog niske razine dokaza o stvarnoj kliničkoj koristi suplementacije, nestandardizirane analize i neutvrđenih referentnih intervala, njegovo rutinsko određivanje se ne preporučuje. Pomoću urednog nalaza protutijela na tkivnu peroksidazu (anti TPO) može se isključiti postojanje autoimune bolesti štitnjače, međutim imaju nisku specifičnost (50%) zbog čega se pronalaze pozitivna i u zdravih osoba. Posljedično, učestalo izvođenje ove pretrage može dovesti do nepotrebnih daljnjih dijagnostičkih pretraga. Određivanje trijodtironina (T3) u svih bolesnika s hipotireozom i većine s hipertireozom (osim u kod T3 tireotoksikoze) je suvišno budući da snažno korelira s koncentracijom tiroksina (T4). Nadalje, trenutno ne postoji niti jedan tumorski biljag (od kojih se najčešće određuju PSA, CA19-9, CEA, CA15-3 i CA125) koji ima dovoljno visoku osjetljivost i specifičnost za korištenje u cilju rano otkrivanja malignih bolesti. Potreban je oprez prilikom izvođenja i interpretacije koncentracije D-dimera s naglaskom na jasne indikacije (znaci tromboze) budući da im je specifičnost gotovo 0%. Nisku kliničku korist ima i rutinsko određivanje koagulacijskih čimbenika, bilirubina, alkalne fosfataze, troponina, iona klorida, kalcija, magnezija i fosfata te ga treba izbjegavati. MKU nije indicirano u asimptomatskih bolesnika nakon provedene antibiotske terapije ili patološkim nalazom urina te bolesnika s postavljenim trajnim urinarnim kateterom.

**Zaključak:** Istraživanja pokazuju da se u većeg broja bolesnika mnoge LP-e izvode nepotrebno. Individualan pristup, uzimanje detaljne anamneze i statusa, postavljanje jasnog kliničkog pitanja i edukacija zdravstvenog osoblja mogu dovesti do racionalizacije upućivanja pacijenata na LP-e te MKU.

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## ■ Laboratory and microbiology testing – less is more

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**Introduction with aim:** Laboratory (LT) and microbiological tests are the basic diagnostic tool in the daily work of doctors, and any whose results will not change the further course of diagnostics and treatment is considered unnecessary. Every year in the USA > 5 billion LTs are performed, of which 60% are unnecessary. Also, half of microbiological urine cultures (MUC) are redundant, with asymptomatic bacteriuria as a result in more than a third cases. Some of the findings can be false positive and lead to the phenomenon of diagnostic cascade, increasing the chance of medical error and increasing costs to the healthcare system. The aim of this paper is to study the reasons, accuracy and most common misconceptions in referring to the most common LTs and MUCs.

**Discussion:** Despite numerous studies, diagnostic guidelines are followed less often than treatment guidelines, most often due to fear of omission. The most common example of this is the annual or biennial performance of systematic examinations with a wide range of LTs. Also, identical tests before surgical procedures under general anesthesia are recommended for all patients. Such an approach did not show clinical benefit, nor did it lead to a reduction in mortality from chronic non-communicable diseases. Therefore, all LTs and MUC should be done with clear indications (risk assessment) and clear clinical questions.

According to research in Great Britain, patients were referred to LTs for: establishing a diagnosis based on existing symptoms (43%), monitoring the disease (31%), checking the effect of drugs (10%), controlling previously established abnormalities (7%); and 1.5% of LTs was done at the patient's own request. Only 6.2% of performed LPs led to a final diagnosis and 41% of LTs were unnecessary. Doctors believed that 75% of the tests needed to be performed.

A frequently requested LT is the determination of vitamin D concentration, which with a sensitivity of 72% and a specificity of only 65% shows a deficiency in almost everybody. Due to the low level of evidence on the actual clinical benefit of supplementation, non-standardized analysis and undefined reference intervals, its routine determination is not recommended. Antibodies to tissue peroxidase (anti TPO) determination can help in exclusion of the autoimmune thyroid disease existence. However, it has low specificity (50%), which is why they are found positive even in healthy individuals. Consequently, frequent performance of this test may lead to unnecessary further diagnostic tests. Determination of triiodothyronine (T3) in all patients with hypothyroidism and most with hyperthyroidism (except in T3 thyrotoxicosis) is redundant since it strongly correlates with the concentration of thyroxine (T4). Furthermore, there is currently no tumor marker (of which PSA, CA19-9, CEA, CA15-3 and CA125 are most determined) that has a sufficiently high sensitivity and specificity for use in the early detection of malignant diseases. Caution is needed when performing and interpreting D-dimer concentrations, with an emphasis on clear indications (signs of thrombosis) since their specificity is almost 0%. Routine determination of coagulation factors, bilirubin, alkaline phosphatase, troponin, chloride, calcium, magnesium and phosphate ions also have low clinical benefits and should be avoided. MUC is not indicated in asymptomatic patients after antibiotic therapy or with pathological urine dipstick findings and those with permanent urinary catheter.

**Conclusion:** Research shows that many LTs are performed unnecessarily. An individual approach, taking a detailed history and status, stating a clear clinical question and educating healthcare professionals can lead to rationalization of patient referrals to LTs and MUC.

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## ■ Kardiovaskularne bolesti - kome, što i kada?

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**Uvod s ciljem:** Kardiovaskularne bolesti (KVB) vodeći su uzrok smrtnosti u Hrvatskoj, odgovorne za 45% svih smrtnih slučajeva. Uloga liječnika obiteljske medicine ključna je u ranoj dijagnostici i praćenju KVB-a. Međutim, izazov leži u balansiranju između prekomjerne i nedovoljne dijagnostike. Cilj ovog rada jest prikazati preporuke za izvođenje najčešćih pretraga u bolesnika bez i s KVB.

**Rasprava:** Prije svega bolesnike treba stratificirati prema kardiovaskularnom riziku koristeći SCORE-2 tablice. Niskorizične bolesnike treba klinički kontrolirati ako postoje opterećena obiteljska anamneza na KVB ili specifični simptomi, što podrazumijeva i lipidni profil. Srednjerizične bolesnike u koje ubrajamo starije od 50 godina, pušače, oboljele od šećerne bolesti i hipertenzije potrebno je podvrgnuti mjerenju gležnansko-brahijalnog indeksa (ABI), povremeno provjeriti elektrokardiogram (EKG) i svakako lipidni status. Visokorizični bolesnici, kao oni koji su preboljeli infarkt miokarda, moždani udar ili imaju neku drugu KVB, trebaju redovito praćenje lipidnog profila, ehokardiografski pregled ovisno o težini bolesti od jednom godišnje do 5 godina. Elektrokardiogram se ne izvodi rutinski već samo kod određenih simptoma ili kliničkih znakova. Holter EKG indiciran je isključivo kod sumnje na aritmije ili povećan aritmogeni potencijal npr. za fibrilaciju atrijsku. Ergometrijsko testiranje se ne preporučuje za asimptomatske bolesnike, osim kod sumnje na moguću tzv. nijemu ishemiju, npr. kod dugogodišnje šećerne bolesti. Ehokardiografija je vrlo sofisticirana, ali najviše eksploatirana dijagnostička pretraga, što dokazuje i činjenica da njezin rezultat rijetko dovede do

promjene terapijskog pristupa. Preučestala dijagnostika vodi ka prekomjernom liječenju, anksioznosti i nepotrebnim invazivnim procedurama, a samim time i povećanjem troškova i lista čekanja. S druge strane, prerijetka dijagnostika može uzrokovati kasno otkrivanje bolesti i dovesti do većeg morbiditeta i mortaliteta.

**Zaključak:** Liječnici obiteljske medicine imaju ključnu ulogu u ciljanom i racionalnom pristupu dijagnostici KVB-a. Manje nije uvijek više, ali više nije uvijek bolje – ključno je procijeniti pravi rizik i ne raditi pretrage bez jasne indikacije. Sustavan pristup i edukacija mogu smanjiti nepotrebne pretrage i poboljšati ishode liječenja.

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## ■ Cardiovascular diseases – to whom, what and when?

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**Introduction with aim:** Cardiovascular diseases (CVD) are the leading cause of mortality in Croatia, accounting for 45% of all deaths. The role of general practitioners is crucial in the early diagnosis and monitoring of CVD. However, the challenge lies in balancing between excessive and insufficient diagnostics. The aim of this paper is to discuss the recommendations for the most common cardiac function tests in patients with or without CVD.

**Discussion:** First and foremost, patients should be stratified according to risk using the SCORE-2 charts. Low-risk patients should be clinically monitored if there is a family history of CVD or specific symptoms, which include lipid profile assessment. Moderate-risk patients, including those over 50 years old, smokers, and those with diabetes or hypertension, should undergo ankle-brachial index (ABI) measurement, periodic ECG checks, and regular lipid status evaluation. High-risk patients, such as those with a history of myocardial infarction, stroke, or other CVD, require regular lipid profile monitoring and echocardiographic evaluation, depending on disease severity, ranging from annually to every five years. An electrocardiogram (ECG) is not performed routinely but rather in the presence of specific symptoms or clinical signs. Holter ECG is indicated only for suspected arrhythmias or an increased arrhythmogenic potential, such as in atrial fibrillation. Exercise stress testing is not recommended for asymptomatic patients, except in cases of suspected silent ischemia, particularly in long-term diabetes mellitus. Echocardiography is a highly sophisticated but overused diagnostic tool, as evidenced by its infrequent impact

on changing therapeutic decisions. Excessive diagnostics lead to overtreatment, patient anxiety, unnecessary invasive procedures, increased healthcare costs, and longer waiting lists. On the other hand, insufficient diagnostics result in late disease detection, contributing to higher morbidity and mortality rates.

**Conclusion:** General practitioners play a key role in a targeted and rational approach to CVD diagnostics. Less is not always more, but more is not always better; the key is to assess actual risk and avoid unnecessary testing. A systematic approach and education can help reduce unnecessary procedures and improve treatment outcomes.

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## ■ Je li svaka bol u leđima ista?

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Uvod s ciljem: Bol u leđima (lat. dorsalgia) čest je zdravstveni problem koji pogađa do 80% odraslih tijekom života. Može se podijeliti na bol u vratnom, prsnom, lumbalnom i sakralnom dijelu kralježnice. Lumbalna bol je najčešća, a može biti akutna (do 6 tjedana), subakutna (6 tjedana do 3 mjeseca) ili kronična (dulja od 3 mjeseca). Osim što može biti posljedica nespecifičnih uzroka, bol u leđima ponekad ukazuje na ozbiljnu patologiju poput hernije diska, tumora ili infekcije. Cilj ovog rada je istražiti kada su dijagnostičke pretrage zaista opravdane i korisne te osvijestiti važnost izbjegavanja nepotrebnih intervencija koje mogu doprinijeti prekomjernom opterećenju zdravstvenog sustava.

Rasprava: Unatoč činjenici da se većina slučajeva boli u leđima smatra nespecifičnom i prolaznom, nerijetko se pretjerano koristi dijagnostička obrada, uključujući radiološke pretrage poput rendgenskih pretraga (RTG), kompjuterizirane tomografije (CT) i magnetske rezonance (MRI). Prema istraživanjima, samo 5-10% slučajeva boli u leđima može se pripisati specifičnim uzrocima poput hernije diska, kompresije živca, fraktura, maligniteta ili infekcija. Međutim, bilježi se stalni porast upotrebe naprednih slikovnih metoda, što je u velikoj mjeri povezano s nepotrebnom dijagnostikom, pretjeranim oslanjanjem na tehnologiju i pritiskom pacijenata. Radiološke pretrage često otkrivaju slučajne nalaze poput bolesti intervertebralnog diska ili degenerativnih promjena koje nisu nužno uzrok boli. Primjerice, istraživanja pokazuju da 30% asimptomatskih odraslih osoba između dvadeset i trideset godina i do 60% pedesetogodišnjaka ima neki oblik bolesti intervertebralnog diska, što dovodi u pitanje kliničku opravdanost tih nalaza. Osim toga, izlaganje pacijenata nepotrebnim RTG ili CT pretragama povećava rizik od štetnog djelovanja zračenja, a financijski troškovi predstavljaju dodatni teret za zdravstveni sustav. U kliničkoj praksi preporuke

ukazuju na to da bi slikovna dijagnostika trebala biti rezervirana za slučajeve kada postoje „crvene zastave“, poput: trajnih, progresivnih ili noćnih bolova koje ne reagiraju na konzervativnu terapiju, sumnje na malignitet, infekcije, prijelome ili neurološke deficite, trajnih radikularnih bolova, koji ukazuju na moguću kompresiju živca. Nadalje, elektromioneurografija (EMNG) i neurofiziološke pretrage koriste se za diferencijaciju uzroka radikularne boli i oštećenja živaca. Kod nespecifične boli bez neuroloških simptoma, EMNG rijetko mijenja terapijski pristup, stoga je njegova primjena često suvišna. Dijagnostičke pogreške također nisu rijetkost. Jedan od problema je i prekomjerna interpretacija nalaza – primjerice, pridavanje važnosti degenerativnim promjenama na slikovnim nalazima koje su često dio normalnog starenja. Uz ove izazove, rastuća svijest o biopsihosocijalnom modelu boli u leđima naglašava potrebu za holističkim pristupom. Psihološki čimbenici, poput anksioznosti, depresije i percepcije boli, mogu značajno pogoršati simptome i trebaju biti dio procjene. Prekomjerna dijagnostika ne samo da povećava troškove i opterećuje zdravstveni sustav, već i potencijalno narušava kvalitetu života pacijenata, pridonoseći njihovoj nesigurnosti i dugoročnom pogoršanju ishoda liječenja.

Zaključak: Iako bol u leđima često zahtijeva kliničku procjenu, nepotrebne dijagnostičke pretrage mogu doprinijeti povećanju troškova, izloženosti zračenju i stvaranju anksioznosti kod pacijenata. Fokus treba biti na kliničkoj procjeni, prepoznavanju znakova „crvene zastave“ i usmjerenom pristupu dijagnostici samo u slučajevima kada postoje jasni indikatori. Integrirani pristup koji uključuje racionalnu dijagnostiku i edukaciju pacijenata može smanjiti rizik od kronične boli, smanjiti teret zdravstvenog sustava i poboljšati ishod liječenja.

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## ■ Is all back pain the same?

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**Introduction with aim:** Back pain (Latin: dorsalgia) is a common health issue affecting up to 80% of adults during their lifetime. It can be categorized into pain in the cervical, thoracic, lumbar, and sacral regions of the spine. Lumbar pain is the most common and can be acute (lasting up to 6 weeks), subacute (6 weeks to 3 months), or chronic (lasting more than 3 months). In addition to being caused by nonspecific factors, back pain can sometimes indicate serious conditions such as a herniated disc, tumors, or infections. The aim of this paper is to investigate when diagnostic tests are truly justified and beneficial, as well as to raise awareness about the importance of avoiding unnecessary interventions that can contribute to overburdening the healthcare system.

**Discussion:** Even though most cases of back pain are considered nonspecific and transient, diagnostic procedures are often overused, including imaging techniques such as X-rays, computed tomography (CT), and magnetic resonance imaging (MRI). According to research, only 5-10% of back pain cases can be attributed to specific causes, such as herniated discs, nerve compression, fractures, malignancies, or infections. However, there is a consistent increase in the use of advanced imaging methods, largely driven by unnecessary diagnostics, overreliance on technology, and patient demand. Imaging studies often reveal incidental findings such as intervertebral disc disease or degenerative changes that are not necessarily the cause of pain. For example, research shows that 30% of asymptomatic adults between twenty and thirty years of age and up to 60% of individuals in their fifties exhibit some form of intervertebral disc disease, raising questions about the clinical relevance of these findings. Moreover, exposing patients to unnecessary X-rays or CT scans increases the risk of radiation-related harm, while the financial costs represent an additional burden on the healthcare

system. Clinical practice guidelines suggest that imaging diagnostics should be reserved for cases where “red flags” are present, such as persistent, progressive, or nocturnal pain unresponsive to conservative therapy; suspected malignancy, infection, fractures, or neurological deficits; or persistent radicular pain indicating potential nerve compression. Electromyoneurography (EMNG) and neurophysiological tests are used to differentiate the causes of radicular pain and nerve damage. However, in cases of nonspecific pain without neurological symptoms, EMNG rarely alters the therapeutic approach, making its use often unnecessary. Diagnostic errors are also not uncommon. One issue is the overinterpretation of findings, such as attributing undue significance to degenerative changes seen on imaging, which are often part of the normal aging process. Amid these challenges, the growing awareness of the biopsychosocial model of back pain highlights the need for a holistic approach. Psychological factors, such as anxiety, depression, and pain perception, can significantly worsen symptoms and should be part of the assessment. Overdiagnosis not only increases costs and burdens the healthcare system but also potentially reduces patients' quality of life, contributing to insecurity and long-term worsening of treatment outcomes.

**Conclusion:** Although back pain often requires clinical evaluation, unnecessary diagnostic tests can contribute to higher costs, radiation exposure, and increased patient anxiety. The focus should be on clinical assessment, recognizing “red flag” signs, and targeted diagnostic approaches only when clear indicators are present. An integrated approach that combines rational diagnostics and patient education can reduce the risk of chronic pain, alleviate the burden on the healthcare system, and improve treatment outcomes.

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## ■ Simptomi u starih i nemoćnih pacijenata

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**Uvod:** Udio starije populacije u stalnom je porastu, a u svijetu se do 2050. u odnosu na 2015. godinu očekuje utrostručenje broja starijih od 85 godina. U Hrvatskoj je 2023. godine 22,8% stanovništva bilo starije od 65, a 2,4% starije od 85 godina. Starenje prati nepovratno opadanje funkcije organa i u odsutnosti ozljeda i bolesti, vanjskih utjecaja ili loših životnih izbora, a trenutno obuvača nekoliko generacija i traje kroz tri desetljeća. Opisuju se "mladi-stari" u 60-ima i ranim 70-ima koji su aktivni i zdravi, "stari" su ljudi u 70-im i 80-im godinama koji usporavaju, imaju kronične bolesti i neke neugodne simptome i "stari-stari" ili "najstariji-stari" koji su često vrlo bolesni, multimorbidni, invalidi i blizu smrti. Prve manifestacije starenja su smanjena sposobnost svakog organa da održi homeostazu pod stresom (bolest, ozljeda), a kardiovaskularni, bubrežni i središnji živčani sustav su najosjetljiviji. Cilj rada je prikazati glavne simptome koji su od posebnog značaja kod starijih osoba, a koje je važno da zna ljeknik obiteljske medicine koji ima glavnu ulogu u skrbi ovih osoba.

**Rasprava:** Kliničke manifestacije bolesti u osnovi su slične u odraslih osoba svih životnih dobi, ali često postoje razlike u simptomima između mladih i starijih osoba. Otežanoj procjeni simptoma pridonosi nerijetko prisutna nemogućnost preciznih i jasnih anamnestičkih podataka te aktivnog sudjelovanja u fizikalnom pregledu, a čak i blage kognitivne smetnje utječu na percepciju tegoba i simptoma. Simptomi u starijih imaju tendenciju biti podmukliji, nespecifičniji i atipičniji, a tijek bolesti može promijeniti i funkciju organa koji primarno nisu zahvaćeni. Mozak je kod starijih najosjetljiviji na stres ili bolest pa i bez njegove primarne zahvaćenosti manifestacije sistemskih bolesti rezultiraju letargijom, konfuzijom, agitacijom ili delirijem. Stariji imaju viši prag boli, odgovor na bol često je prigušen ili izostaje stoga pritužbu boli, neovisno o dijelu

tijela, treba smatrati hitnijim simptomom i pažljivo procijeniti. I febrilni odgovor izostaje ili je smanjen, a značajan dio starijih na ozbiljnu bolest i infekciju reagira hipotermijom. Najčešći razlozi povišene temperature su pneumonija, urinarne infekcije i malignitet. Relativna inaktivnost može maskirati nedostatak zraka ili bol u prsima u slučaju kardiovaskularnih bolesti, a dugo sjedenje se može manifestirati pretibijalnim edemima bez prisutne systemske bolesti. Čest simptom su i anoreksija i gubitak tjelesne mase te opća slabost, dispneja, piskanje, proljev i konstipacija, fekalna inkontinencija, poliurija, nokturija i urinarna inkontinencija. Senzorni i motorni sustav posebno su osjetljivi na starenje i prate ih deterioracija vida, sluha, pojava tinitusa, vertiga, omaglice te padovi. Česte su i smetnje spavanja, tremor, mentalna oštećenja od blage zaboravljivosti do teške demencije, depresija (koja se lako zamijeni s demencijom). I kožni tegobe su česte, posebno svrbež i promjene povezane sa suhom kožom, senilne aktiničke dermatoze, kožne neoplazme i herpes zoster. U pristupu simptomima i postavljanju dijagnoze kod starijih i iznemoglih bolesnika korisno je znati podatke o učestalosti bolesti u pojedinim dobnim skupinama.

**Zaključak:** Patofiziološki odgovor u starih i nemoćnih ima svoje specifičnosti i važno ga je znati radi pravovremenog prepoznavanja bolesti i planiranja skrbi.

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## ■ Symptoms in elderly and frail patients

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**Introduction with aim:** The proportion of the elderly population is constantly increasing, and by 2050, the number of people over 85 is expected to triple worldwide compared to 2015. In Croatia, in 2023, 22.8% of the population was over 65, and 2.4% was over 85. Aging is accompanied by an irreversible decline in organ function even in the absence of injury and disease, external influences or poor lifestyle choices, and currently covers several generations and lasts for three decades. The “young-old” are described as people in their 60s and early 70s who are active and healthy, the “old” are people in their 70s and 80s who are slowing down, have chronic diseases and some unpleasant symptoms, and the “old-old” or “oldest-old” are often very sick, multimorbid, disabled and close to death. The first manifestations of aging are the reduced ability of each organ to maintain homeostasis under stress (illness, injury), and the cardiovascular, renal and central nervous systems are the most sensitive. The aim of this paper is to present the main symptoms that are of particular importance in the elderly, and which are important for the family medicine physician who plays a major role in the care of these individuals to know.

**Discussion:** The clinical manifestations of the disease are basically similar in adults of all ages, but there are often differences in symptoms between young and elderly people. The frequent inability to provide precise and clear anamnestic data and actively participate in the physical examination contributes to the difficult assessment of symptoms, and even mild cognitive impairment affects the perception of complaints and symptoms. Symptoms in the elderly tend to be more insidious, non-specific and atypical, and the course of the disease can also change the function of organs that are not primarily affected. The brain is the most sensitive to stress or disease in the elderly, and even without its primary

involvement, manifestations of systemic diseases result in lethargy, confusion, agitation or delirium. The elderly have a higher pain threshold, the response to pain is often muted or absent, so complaints of pain, regardless of the part of the body, should be considered a more urgent symptom and carefully assessed. The febrile response is also absent or reduced, and a significant proportion of the elderly react to serious illness and infection with hypothermia. The most common causes of elevated temperature are pneumonia, urinary infections and malignancy. Relative inactivity can mask shortness of breath or chest pain in the case of cardiovascular diseases, and prolonged sitting can manifest as pretibial edema without the presence of systemic disease. Common symptoms include anorexia and weight loss, as well as general weakness, dyspnea, wheezing, diarrhea and constipation, fecal incontinence, polyuria, nocturia and urinary incontinence. The sensory and motor systems are particularly sensitive to aging and are accompanied by deterioration of vision, hearing, tinnitus, vertigo, dizziness and falls. Sleep disorders, tremors, mental impairment from mild forgetfulness to severe dementia, depression (which can easily be mistaken for dementia) are also common. Skin problems are also frequent, especially itching and changes associated with dry skin, senile actinic dermatoses, skin neoplasms and herpes zoster. When approaching symptoms and making a diagnosis in elderly and debilitated patients, it is useful to know data on the frequency of diseases in certain age groups.

**Conclusion:** The pathophysiological response in the elderly and frail has its own specificities and it is important to know it in order to recognize the disease in time and plan care.

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## ■ Simptomi u djece

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**Uvod:** Najčešći simptom akutno bolesnog djeteta je temperatura, uslijed virusne ili bakterijske infekcije. Ponavljana (ili rekurentna) bol u trbuhu jedan je od najčešćih neakutnih simptoma u djece. Najveći dio čine školska djeca. U do 95% slučajeva nije posljedica organske bolesti već se radi o funkcionalnoj boli. Cilj rada je pokazati kako pristupiti akutno bolesnom djetetu s temperaturom, procijeniti težinu bolesti te daljnje postupanje. Kod djece s ponavljanom boli u trbuhu cilj je izložiti glavne parametre procjene za razlikovanje funkcionalne od organske boli.

**Rasprava:** Visina temperature ne korelira uvijek s težinom bolesti djeteta i bitno ju je interpretirati uz cijelu kliničku sliku kako bi se procijenila ozbiljnost bolesti. Inicijalna procjena bazira se na detaljnoj anamnezi i fizikalnom pregledu. Na temelju navedenog donosi se odluka: 1) radi li se o djetetu koje se upućuje na bolničko liječenje ili se nastavlja pratiti ambulantno, 2) za one koji ne zahtijevaju hitan bolnički tretman, treba li za bolju procjenu učiniti neke dijagnostičke pretrage (npr. upalne parametre, urin, rentgen pluća). Hitno upućivanje u bolnicu zahtijevaju djeca koja su uz temperaturu poremećenog stanja svijesti, značajno narušenog općeg stanja, imaju pozitivne meningealne znake, petehijali osip te visoko febrilna novorođenčad. Za ostale ključno je procijeniti koje je ishodište infekcije te razlučiti je li virusna ili bakterijska. Najteža procjena obično je kod djece koja su visoko febrilna, a bez vodećeg simptoma, kada je teško razlikovati radi li se o virusnoj infekciji ili početnoj bakterijemiji budući nema pravog kliničkog parametra za razlikovanje. U slučaju dileme preporuča se uzimanje osnovnih laboratorijskih nalaza (krvna slika i crp) i interpretacija u odnosu na trajanje bolesti i dob djeteta. Funkcionalna ponavljana abdominalna bol dijagnosticira se klinički i svrstava prema IV Rimskim kriterijima ovisno o drugim pratećim simptomima u jedan od sljedeća četiri poremećaja: funkcionalna dispepsija, funkcionalna abdominalna bol koja se ne može drugdje svrstati,

sindrom iritabilnog crijeva i abdominalna migrena. Kako bi se dijagnostičke postupke svelo na optimalnu mjeru, a da se ne propusti organska bolest preporuča se identificirati one pacijente koji imaju u anamnezi i fizikalnom pregledu znakove upozorenja (bol koja nije lokacije oko pupka, ponavljano povraćanje, proljevi, disfagija, gubitak na težini, anemija, zaostajenje u rastu, odgođeni pubertet, perianalne promjene, pridružene temperature, artralgije, pozitivna obiteljska anamneza za celijakiju, ulkusnu bolest ili kroničnu upalnu bolest crijeva) za koje je nužna daljnja obrada. Nedostaje validiranih smjernica o točnom izboru obrade pa se kreće od neinvazivne laboratorijske obrade koja se prilagođava znacima upozorenja. Kako jedini znak celijakije mogu biti samo ponavljani bolovi, većina smjernica sugerira kako je uputno učiniti serologiju za celijakiju. Od drugih pretraga kada nema znakova alarma, najčešće se pod pritiskom roditelja čine krvna slika, crp, kalprotektin i ultrazvuk abdomena.

**Zaključak:** Febrilitet je najčešći simptom akutno bolesnog djeteta, koji je izolirano nedovoljan pokazatelj težine bolesti. Anamneza i klinički status ključni su za procjenu i odluku o daljem postupanju. Za djecu s ponavljanim bolovima u trbuhu klinički IV Rimski kriteriji većinom su dovoljni za potvrdu funkcionalne boli, a kod onih koji imaju znakove upozorenja i sumnju na organsku bolest potrebna je dalja dijagnostička obrada.

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## ■ Symptoms in children

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**Introduction:** The most common symptom of an acutely ill child is a fever, due to a viral or bacterial infection. Chronic (or recurrent) abdominal pain is one of the most common non-acute symptoms in children, with highest prevalence in school-age children. In up to 95% of cases, it is not a consequence of an organic disease, but a functional pain. The aim of this paper is to show how to approach an acutely ill child with fever, assess the severity of the illness and further work up. For children with recurrent abdominal pain, the aim is to show main parameters to distinguish patients with functional abdominal pain from organic ones.

**Discussion:** The height of the temperature doesn't regularly correlate with the severity of the child's illness. It is more important to look at the temperature in correlation with other clinical signs to predict how serious the disease really is. The initial assessment should be based on a detailed medical history and physical examination, to make a decision 1) whether the child should be referred to a hospital or can be monitored in an outpatient setting, 2) for those who do not require urgent hospital treatment, whether some diagnostic tests (e.g. inflammatory parameters, urine, chest X-ray) should be performed for more precise assessment. Urgent referral to a hospital is necessary for febrile children with decreased level of consciousness, significantly impaired general condition, positive meningeal signs, petechial rash, and for febrile newborns. For others, it is crucial to assess the infection site and make a distinction between viral and bacterial origin. The most difficult evaluation is usually in children with very high fever but without a leading symptom, when viral infection cannot be clinically differentiated from initial bacteraemia, since there is no reliable clinical parameter for clear differentiation. When in such dilemma, the recommendation is to take additional laboratory tests (complete blood count, CRP), and interpret

them according to the duration of symptoms and patient's age. Diagnose of functional recurrent abdominal pain is made clinically according to the IV Rome criteria and depending on associated symptoms classify into one of the four following disorders: functional dyspepsia, functional abdominal pain-not otherwise specified, irritable bowel syndrome and abdominal migraine. For an optimal extent of diagnostic workup, without missing organic disease, it is recommended to identify those patients with alarming features in the medical history and physical examination (pain away from midline, repeated vomiting, diarrhoea, dysphagia, weight loss, anaemia, growth retardation, delayed puberty, perianal changes, associated fever, arthralgia, positive family history of celiac disease, ulcer disease or chronic inflammatory bowel disease) for whom further work-up is necessary. However, there is still a lack of validated guidelines regarding the exact choice of the workup, but usually it starts from non-invasive laboratory tests related to alarming signs. Since the only sign of celiac disease may be recurrent abdominal pain, most guidelines suggest serologic screening for celiac disease. Other tests usually performed without any alarming signs but under parental pressure, are blood count, CRP, calprotectin, and abdominal ultrasound.

**Conclusion:** Fever is the most common symptom in an acutely ill child and alone is an insufficient indicator of the severity of the illness. Medical history and physical status are key for the assessment of a febrile child and the decision for further procedures.

For children with recurrent abdominal pain, IV Rome criteria are mostly sufficient to clarify functional pain, while those with warning signs require additional diagnostics to avoid missing an underlying organic disease.

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## ■ Unintentional Weight Loss

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**Introduction with aim:** Unintentional weight loss represents a significant clinical challenge, associated with high risk of disease and mortality. It is often a symptom of serious underlying conditions. Doctors must approach the diagnostic process thoroughly, considering various possible causes. A patient experiencing a weight loss of at least 5% of their usual body weight over the last 6 to 12 months, requires further diagnostic evaluation. The aim of this study is to define unintentional weight loss, explore its potential causes, and provide guidance on assessing a patient who is losing weight.

**Discussion:** Weight loss in a healthy individual may be indicative of a systemic disease, with causes ranging from medical, psychiatric, or social factors. It is essential to examine changes in weight during medical history, considering conditions like cancer, gastrointestinal disorders, and psychiatric issues. Other conditions to consider include cachexia syndrome related to organ failure, endocrinopathies, infections, medication side effects, substance abuse, and social factors preventing adequate access to food, poor living conditions, or stressful situations. Unintentional weight loss is typically defined as a loss of at least 5% of the patient's usual body weight over the past 6 to 12 months which is not an expected result of treatment for a known disease. All patients should be assessed, whether weight loss is their primary complaint or discovered incidentally. The decision to assess should be based on patient preferences, considering the risks of testing. The evaluation includes data collection and a thorough medical examination, and a detailed history can help in the correct diagnostic process. The medical history includes age, social factors, previous medical conditions, cancer screening status, medication use, psychiatric history, eating disorders, presence of risk factors, risk for malignancies, and infection risk. Symptom checks include weight loss, general

symptoms, and symptoms from gastrointestinal, genitourinary, neurological, endocrine, and pulmonary systems. A physical examination is the next critical step, starting with the determination of weight and documentation of vital signs. Skin color, turgor, presence of surgical scars, and signs of systemic diseases should be evaluated. Oral cavity should be examined for thrush, dental issues, thyroid enlargement, and adenopathy, along with respiratory, cardiac, abdominal abnormalities or examination of the urogenital tract. Neurological assessment includes evaluating mental status and screening for depression. If a likely diagnosis is made, the underlying condition should be treated, and further tests should be selected as needed. If the etiology remains unknown, additional laboratory investigations (blood count, urine analysis, glucose levels, kidney and liver function, albumin, electrolytes, calcium, iron, FOBT, TSH, chest X-ray, tumor markers) may be required, and referral to a specialist should be considered. If no cause is found after examinations and tests, the patient should be referred for further investigations, such as ultrasound, CT scans, MRI, or endoscopy. If a diagnosis is made, treatment should focus on the underlying cause. In undiagnosed cases, continuous monitoring and follow-ups are necessary. If weight loss continues, the physician should review the treatment, diagnosis or comorbidities.

**Conclusion:** Weight loss is a concerning symptom for family doctors as it often indicates an undiagnosed health condition, presenting a diagnostic challenge. It is essential to determine the underlying cause of weight loss, with special emphasis on identifying serious conditions, such as cancer or chronic diseases, that require prompt intervention. A structured approach to evaluating unintentional weight loss provides guidance for patient management and helps identify key elements in history-taking, physical examination, and laboratory tests that lead to diagnosis.

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## ■ Simptomi u onkoloških bolesnika

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**Uvod:** Zloćudne bolesti su u porastu u razvijanim zemljama svijeta, s 37% svih novooboljelih mladih od 65 godina u 2022. godini. U Republici Hrvatskoj najčešći su karcinom debelog i završnog crijeva, pluća i dušnika, prostate te dojke. Rano prepoznavanje maligne bolesti omogućava uspješnije liječenje stoga je uočavanje simptoma i ciljana dijagnostika izrazito bitna. Cilj rada je prikazati najčešće simptome i znakove maligne bolesti kao i simptome uz već dijagnosticiranu malignu bolest.

**Rasprava:** Simptomi se mogu podjeliti na opće i specifične za organ odnosno tip maligne bolesti. U opće simptome ubrajamo nenamjerman gubitak više od 5% tjelesne mase tijekom šest do dvanaest mjeseci ili kraće, neuobičajen umor, gubitak apetita, obilno noćno znojenje, povišenu temperaturu te neobjašnjivu bol koja ne popušta na analgetike. U specifične simptome ubrajamo rane koje ne zarastaju dulje od tri tjedana na sluznici te šest tjedana na koži, neobjašnjive modrice ili promjene madeža, rastuće i najčešće bezbolne otekline bilo gdje na tijelu, progresivni gubitak vida ili sluha, promuklost ili bolno ždrijelo koje ne prolazi, odino- ili disfagiju, dispneju, kašalj duži od osam tjedana ili iskašljavanje krvi, brz povratak simptoma gastroezofagealnog refluksa nakon prekida liječenja ili uz perzistentne noćne simptome, jutarnje povraćanje bez mučnine, promjene kože dojke ili bradavice, konstantnu nadutost ili promjene u defekaciji, hematuriju (posebno bezbolna), hematokeziju, hematemu ili melenu, vaginalno krvarenje nakon menopauze, bolne spolne odnose, bol u zglobovima ili kostima koja ne popušta na analgetike. Uz, ali i bez simptoma, promjene u laboratorijskim (mikrocitna ili normocitna anemija u muškarca, leukocitoza ili pancitopenija, trombocitoza, patološki hepatogram posebno uz povišene vrijednosti alkalne fosfataze) ili radiološkim nalazima (ekspanzivne, slabo ograničene mase uz patološku prokrvljenost, osteolitička lezija, patološki

prijelom) mogu ukazivati na malignu bolest. U dijagnostičkom pristupu uključujemo dob, spol te obiteljska anamneza, a kod općih simptoma ili slučajno nađenih patoloških nalaza koji su visoko sumnjivi na malignu bolest prvo je potrebno isključiti one regionalno najučestalije. Neki simptomi i znakovi mogu ukazivati na druge nemaligne bolesti stoga je potrebno uzeti detaljnu anamnezu, obaviti detaljan klinički pregled te dijagnostički postupak. Kod vanbolničkih pacijenata s već dijagnosticiranom malignom bolesti uz opće loše stanje najčešći simptomi su umor (70-100%), inapetencija (6-53%), bol (30-80%) i dispneja (10-70%). Ozbiljnost simptoma ovisi o vrsti raka i spolu bolesnika. Dok bolovi i umor prevladavaju u bolesnika s karcinomom središnjeg živčanog sustava ili područja glave i vrata, gubitak apetita i loše opće stanje češće se javljaju u bolesnika s karcinomom probavnog trakta, pluća, dojke ili genitalne regije. Čini se da se umor, tjeskoba i depresija pojavljuju bez obzira na vrstu raka. Opisane su i razlike u spolovima te se disfagija i nesаница češće javljaju kod muškaraca, a mučnina, povraćanje i anksioznost kod žena.

**Zaključak:** Incidencija malignih bolesti raste uz sve češće obolijevanje i mladih osoba. Rano prepoznavanje simptoma i znakova malignih bolesti od ključne je važnosti za što ranije postavljanje dijagnoze i liječenja te u konačnici i preživljenje dok kod bolesnika s već dijagnosticiranom malignom bolešću prepoznavanje i ublažavanje simptoma omogućuje bolju kvalitetu života. Simptomi i znaci komorbidnih dijagnoza nemalignih bolesti ne smiju se zanemariti.

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## ■ Symptoms in Cancer Patients

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**Introduction with aim:** Malignant diseases are on the rise in developed countries of the world with 37% of all new cases under the age of 65 in 2022. In the Republic of Croatia, the most common are cancers of the colon and rectum, lungs and trachea, prostate and breast. Early recognition of malignant disease allows for more successful treatment, therefore, noticing symptoms with targeted diagnostics are extremely important. The aim of the paper is to present the most common symptoms and signs of malignant disease, as well as symptoms associated with an already diagnosed malignant disease.

**Discussion:** Cancer symptoms can be divided into general and specific to the organ or type of malignant disease. General symptoms include unintentional loss of more than 5% of body weight over six to twelve months or less, unusual fatigue, loss of appetite, profuse night sweats, fever, and unexplained pain that does not respond to analgesics. Specific symptoms include wounds that do not heal for more than three weeks on the mucous membrane and six weeks on the skin, unexplained bruises or changes in moles, growing and most often painless swellings anywhere on the body, progressive loss of vision or hearing, hoarseness or sore throat that does not go away, dysphagia or dyspnea, cough lasting longer than eight weeks or coughing up blood, rapid return of gastroesophageal reflux symptoms after discontinuation of treatment or with persistent nocturnal symptoms, morning vomiting without nausea, changes in the skin of the breast or nipple, constant bloating or changes in defecation, hematuria (especially painless), hematochezia, hematemesis or melena, vaginal bleeding after menopause, painful intercourse, joint or bone pain that does not respond to analgesics. With or without symptoms, changes in laboratory (microcytic or normocytic anemia in men, leukocytosis or pancytopenia, thrombocytosis, pathological hepatogram especially with elevated values of

alkaline phosphatase) or radiological findings (expansive, poorly circumscribed masses with pathological blood supply, osteolytic lesion, pathological fracture) may indicate a malignant disease. In the diagnostic approach age, gender and family history should be included, and in the case of general symptoms or accidentally found pathological findings that are highly suspicious of a malignant disease, it is first necessary to exclude the regionally most frequent ones. Some symptoms and signs may indicate other non-malignant diseases, so it is necessary to take a exhaustive medical history, perform a detailed clinical examination and diagnostic procedure. In outpatients with an already diagnosed malignant disease, in addition to a general malaise, the most common symptoms are fatigue (70-100%), inappetence (6-53%), pain (30-80%) and dyspnea (10-70%). The severity of symptoms depends on the type of cancer and the patient's gender. While pain and fatigue are more prevalent in patients with cancer of the central nervous system or head and neck, loss of appetite and poor general condition are more common in patients with cancer of the digestive tract, lung, breast or genital region. Fatigue, anxiety, and depression appear to occur regardless of the type of cancer. Gender differences have also been described, with dysphagia and insomnia occurring more frequently in men, and nausea, vomiting, and anxiety in women.

**Conclusion:** The incidence of malignant diseases is increasing, with younger people also becoming increasingly ill. Early recognition of symptoms and signs of malignant diseases is crucial for early diagnosis and treatment, and ultimately survival, while in patients with an already diagnosed malignant disease, recognition and relief of symptoms allows for a better quality of life. Symptoms and signs of comorbid diagnoses of non-malignant diseases should not be ignored.

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## ■ Kožne alergije

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**Uvod s ciljem:** Alergija je neprimjereni odgovor našeg imunološkog sustava na različite čimbenike okoliša. Simptomi alergijske reakcije mogu biti opći ili lokalizirani na organ ili organski sustav putem kojeg je alergen ušao u tijelo (koža i sluznice, probavni ili dišni sustav). Kožne alergije najčešće se manifestiraju kao urtikarija, atopijski i kontaktni dermatitis. Cilj ovog rada bio je prikazati najčešće kožne alergije.

**Rasprava:** Jedna od najčešćih kožnih bolesti karakterizirana svrbežom i promjenom kože je atopijski dermatitis. To je kronična bolest mladih, uglavnom djece. Karakterizira ga suha koža koja svrbi i osip na obrazima, rukama i nogama. Kod atopijskog dermatitisa važan faktor je svrbež jer češanje i trljanje pogoršavaju upalu kože karakterističnu za tu bolest. Izlaganje nadražujućim sredstvima poput deterženata, omekšivača, sapuna i slično može pogoršati simptome, kao i sušenje kože, izlaganje vodi, temperaturne promjene i stres. Bolesnici imaju često povišenu razinu eozinofila i alergijskih protutijela IgE, ali je razlog tomu nepoznat. Liječenje je kompleksno i dugotrajno, a cilj mu je smanjiti i ukloniti simptome. Liječnik obiteljske medicine često se susreće s pacijentima različite životne dobi koji se žale na kožne promjene nakon kontakta s nekom tvari iz okoliša, a koje su karakterizirane ekcemima. Dvije glavne skupine tvari u okolišu koji uzrokuju kontaktni dermatitis su iritansi i alergeni, a osobito je čest kod osoba koje puno rade u vodi. Svrbež kože je najčešći simptom i može biti izrazito intenzivan, a područja koja zahvaća su uobičajeno šake, vrat, ruke, lice i noge. Tijekom upale, kontaktni dermatitis uzrokuje promjene na koži koja postaje crvena i ljuskava, a ponekad se razviju i sitni vodeni mjehuri. Bitno je spomenuti i urtikariju koja može biti povezana i s nastankom angioedema te zahtijeva promptno liječenje. Karakterizira je stvaranje urtikarijalnih lezija na koži izgledom središnjeg otoka okruženog

crvenilom uz pridružen svrbež i osjećaj pečenja, a razlikujemo akutnu u trajanju do 6 tjedana i kroničnu.

**Zaključak:** Promjene na koži praćene svrbežom često su posljedica alergijskih reakcija koje zahtijevaju dugotrajno liječenje i predstavljaju izazov u dijagnostičkom pristupu te je bitna uska suradnja liječnika obiteljske medicine i specijaliste dermatovenerologa.

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## ■ Symptoms in Cancer Patients

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**Introduction and aim.** Allergy is a hypersensitivity reaction of our immune system to a specific substance. Symptoms can be general or localized. Skin allergies most often manifest as urticaria, atopic and contact dermatitis. The aim of this paper was to present the most common skin conditions caused by allergy and their symptoms.

**Discussion.** One of the most common skin diseases characterized by itching and lesions is atopic dermatitis. Atopic dermatitis, is a chronic disease that causes inflammation, redness, and irritation of the skin. It is a common condition that usually begins in childhood; however, anyone can get the disease at any age. Itching is an important factor because scratching and rubbing worsen the skin inflammation. Exposure to irritants, water, temperature changes and stress can worsen symptoms. Patients often have elevated levels of eosinophils and allergic IgE antibodies, but the reason for this is unknown. Treatment is complex and long-term. A family physicians often treat patients of all ages who complain of skin changes after direct contact with substance, which are characterized by eczema. Such changes are called contact dermatitis and have nothing to do with atopic dermatitis or allergic eczema, and are especially common in people who work a lot in water. There are two types of contact dermatitis: allergic and irritant. Itchy skin is the most common symptom and can be extremely intense, the areas that are usually affected are the hands, neck, arms, face and legs. Contact dermatitis causes the skin to become blistered, dry and cracked. It is also important to mention urticaria, also known as hives, which can be associated with the development of angioedema and requires prompt treatment. It is characterized by the formation of urticarial lesions on the skin with the appearance of a central swelling surrounded by redness, accompanied by itching and a burning sensation, and can be acute, lasting up to 6 weeks, or chronic.

**Conclusion.** Itchy skin with skin changes are often the result of allergic reactions that require long-term treatment and become a challenge in the diagnostic approach, so close cooperation between a family physician and a dermatovenerologist is essential.

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## ■ Najčešće sistemske bolesti praćene svrbežom

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**Uvod s ciljem.** Kronični svrbež je vodeći simptom u brojnim dermatološkim i sistemskim bolestima, a definira se kao neugodan podražaj koji izaziva potrebu za grebanjem što može imati za posljedicu upalu, oštećenje te potom i sekundarnu infekciju kože. Koža može postati lihenificirana, suha, ljuskava, uz prisutne ekzorijacije. Prevalencija svrbeža raste s dobi, a procjenjuje se kako zahvaća oko 43% populacije starije od 65 godina. Cilj ovog rada bio je prikazati najčešće sistemske bolesti u kojih se javlja svrbež kao jedan od prisutnih simptoma.

**Rasprava.** Obzirom da je svrbež nespecifični simptom mnogih bolesti, od primarnih bolesti kože pa do sistemskih bolesti, sama klinička slika ovisna je o tome koja bolest dovodi do svrbeža. U sklopu sistemskih bolesti, dio kože koji izaziva svrbež može biti urednog statusa, a mogu biti i prisutne sekundarne kožne lezije izazvane grebanjem. Od svih sistemskih bolesti povezanih sa svrbežom, najčešći je svrbež u sklopu bubrežnih bolesti kod kojih se čak do 60% oboljelih žali na svrbež. 2/3 bolesnika u terminalnom stadiju bubrežne bolesti javlja svrbež u generaliziranom obliku, dok kod preostale trećine obično zahvaća leđa ili lice, a može biti stalno prisutan ili povremen i obično je izraženiji noću. Drugi najčešći sistemski uzrok svrbeži su bolesti jetre, odnosno u bolesnika s kolestazom gdje on nastaje kao posljedica mehaničke opstrukcije, metaboličkog disbalansa ili upalne bolesti, a najčešće zahvaća dlanove i stopala, te područja na kojima odjeća stvara trenje na koži, a može se javiti i u generaliziranom obliku. Brojne metaboličke i endokrinološke bolesti poput nedostatka vitamina D, nedostatka ili prekomjerne količine željeza, bolesti štitnjače, hiperparatiroidoze, šećerne bolesti i gihta također mogu biti uzrok svrbeži. Prilikom dijagnostičke obrade uzroka svrbeži nikako ne smijemo zaboraviti maligne bolesti i to poglavito limfoproliferativne poput Hodgkinove bolesti

koj je svrbež uz povećanje limfnih čvorova jedan od vodećih simptoma. Od ostalih sistemskih bolesti kao uzroka svrbeži valja spomenuti i neurološke bolesti poput multiple skleroze te cirkulatorne i psihogene poremećaje.

**Zaključak.** Obzirom da je svrbež simptom koji smanjuje kvalitetu života bolesnika i značajno ga ometa u njegovim svakodnevnim aktivnostima, liječnik obiteljske medicine detaljnom anamnezom, fizikalnim statusom i primjerenom dijagnostičkom obradom mora utvrditi njegov uzrok.

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## ■ The most common systemic diseases causing itching

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**Introduction.** Chronic itching is a leading symptom in numerous dermatological and systemic diseases, and is defined as an intense, distracting irritation or tickling sensation that may be felt over the skin's surface, and can result in inflammation, damage, and sometimes with secondary skin infection. The skin may become lichenified, dry, scaly, and excoriated. The prevalence of pruritus increases with age, and it affects about 43% of the population older than 65 years of age. The aim of this study was to present the most common systemic diseases in which itching occurs.

**Discussion.** Since itching is a non-specific symptom of many diseases, from primary skin diseases to systemic diseases, the clinical presentation depends on which disease is causing the itching. In systemic diseases, the part of the skin that causes itching can be with or without lesions. Of all systemic diseases associated with itching, the most common cause is kidney disease, in which up to 60% of patients complain of itching. 2/3 of patients with end-stage renal disease experience generalized itching, while in the remaining third it usually affects the back or face. It can be constantly present or intermittent and is usually more pronounced at night. The second most common systemic cause of itching is liver disease, where it occurs as a result of mechanical obstruction, metabolic imbalance, or inflammatory disease. Most often affects the palms and soles, and areas where clothing contacts the skin, but can also occur in a generalized form. Numerous metabolic and endocrinological diseases such as vitamin D deficiency, iron deficiency or hemochromatosis, thyroid disease, hyperparathyroidism, diabetes, and gout can also be a cause of itching. Diagnostic approach of itching also must consider malignant diseases, especially lymphoproliferative diseases such as Hodgkin's disease, in which itching and swollen lymph nodes are one of the leading symptoms. Other systemic diseases that can cause itching include neurological diseases such

as multiple sclerosis, circulatory and psychogenic disorders.

**Conclusion.** Patients with itching have a lower quality of life. A family medicine physician must determine cause of itching through a detailed medical history, physical status, and appropriate diagnostic workup.

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## ■ Što Svrbi u Dermatologiji?

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**Uvod s ciljem.** Pruritus, odnosno svrbež, čest je i kompleksan simptom koji se javlja u različitim dermatoloških bolesti. Prevalencija i intenzitet svrbeža ovise o osnovnoj dijagnozi. Kao najčešći simptom, svrbež se javlja u dermatoloških bolesnika s atopijskim dermatitisom, psorijazom i urtikarijom, a izražen je i kod drugih dermatozata. Svrbež značajno utječe na kvalitetu života, uzrokujući smetnje spavanja, emocionalnu iscrpljenost i socijalnu izolaciju. Cilj ovog sažetka je pregled patofizioloških mehanizama pruritusa, dijagnostičkih izazova i terapijskih pristupa, s naglaskom na kliničku praksu i najnovije smjernice.

**Rasprava.** Patofiziologija pruritusa uključuje složene procese u kojima sudjeluju periferni i središnji živčani sustav. Aktivacija specifičnih pruritogenih C-vlakana pokreće oslobađanje histamina, proteaza i proinflammatoryh citokina. Ključnu ulogu ima i disregulacija JAK-STAT signalnog puta, što predstavlja temelj za razvoj novih terapijskih opcija. Klinička procjena pruritusa zahtijeva integrirani pristup. Uz temeljit dermatološki pregled, često je potrebno provesti laboratorijsku dijagnostiku radi isključivanja sistemskih uzroka, poput bolesti jetre, bubrega, endokrinoloških ili hematoloških poremećaja. Terapijski pristup temelji se na liječenju osnovne bolesti te simptomatskoj terapiji. Lokalni pripravci poput kortikosteroida i inhibitora kalcineurina učinkoviti su u blažim oblicima pruritusa, dok se kod težih oblika koriste sistemski imunomodulatori poput dupilumaba ili fototerapija. Kronični pruritus zahtijeva multidisciplinarni pristup, uključujući psihološku podršku s ciljem smanjenja posljedica kroničnog češkanja te smanjenje rizika sekundarnih infekcija.

**Zaključak.** Pruritus ostaje značajan klinički izazov u dermatologiji, posebno kod kroničnih dermatozata. Razumijevanje njegovih kompleksnih patofizioloških mehanizama omogućilo je razvoj ciljane terapije, no još uvijek postoje

brojni nerazjašnjeni aspekti koji zahtijevaju daljnja istraživanja. Edukacija pacijenata, individualizirani terapijski pristup i razvoj terapija s boljim sigurnosnim profilom ključni su za optimizaciju ishoda liječenja.

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## ■ What Itches in Dermatology?

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**Introduction with Aim:** Pruritus, or itching, is a common and complex symptom that occurs in various dermatological diseases. The prevalence and intensity of pruritus depends on the underlying diagnosis. It is the most prominent symptom in dermatological patients with atopic dermatitis, psoriasis, and urticaria and is also pronounced in other dermatoses. Pruritus significantly impacts quality of life, causing sleep disturbances, emotional exhaustion, and social isolation. The aim of this abstract is to review the pathophysiological mechanisms of pruritus, diagnostic challenges, and therapeutic approaches, highlighting clinical practice and the latest guidelines.

**Discussion:** The pathophysiology of pruritus involves complex processes in which the peripheral and central nervous systems participate. The activation of specific pruritogenic C-fibers triggers the release of histamine, proteases, and pro-inflammatory cytokines. A key role is also played by the dysregulation of the JAK-STAT signaling pathway, which serves as the basis for the development of new therapeutic options. Clinical assessment of pruritus requires integrated approach. In addition to a thorough dermatological examination, laboratory diagnostics are often necessary to rule out systemic causes such as liver, kidney, endocrine, or hematological disorders. Therapeutic approach is based on treating the underlying disease and symptomatic therapy. Topical agents such as corticosteroids and calcineurin inhibitors are effective in milder forms of pruritus, while severe cases require systemic immunomodulators like dupilumab or phototherapy. Chronic pruritus requires a multidisciplinary approach, including psychological support to manage the consequences of chronic scratching and reduction of secondary infections risk.

**Conclusion:** Pruritus remains a significant clinical challenge in dermatology, particularly in chronic dermatoses. Understanding its complex

pathophysiological mechanisms has enabled the development of targeted therapies, yet many aspects remain unresolved and require further research. Patient education, an individualized therapeutic approach, and the development of treatments with better safety profiles are key to optimizing treatment outcomes.

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## ■ Infekcije kao uzrok svrbeža

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**Uvod s ciljem:** Svrbež je jedan od tri najčešća kožna simptoma zbog kojih se pacijenti javljaju obiteljskom liječniku. Jedan od češćih uzroka su infekcije kože koje mogu biti gljivičnog, virusnog, bakterijskog ili parazitarnog porijekla. Cilj ovog rada je prikazati najčešće infekcije koje uzrokuju svrbež kože.

**Rasprava:** Najčešća infekcija koja uzrokuje svrbež kože je gljivična infekcija. Prezentira se dobro ograničenom kožnom promjenom s crvenim, ljuskavim, uzdignutim rubom. Često su zahvaćeni nožni prsti i tabani, a koža postane suha, ljuskava, ispucala ili mekana i macerirana. Ukoliko zahvati vlasište može se manifestirati i alopecijom. Pityriasis rosea, infektivni eritem i vodene kozice su najčešće virusne infekcije koje uzrokuju svrbež kao i moluske, dobroćudni tumori kože koji su također uzrokovani virusom. Impetigo je površinska bakterijska infekcija kože sa stvaranjem krusta ili bula, a uzrokuju ga streptokoki i/ili stafilocoki. Izaziva blagu bol, neugodu i često svrbež. Paraziti su česti uzročnici svrbeži kože, prije svega svrab i ušljivost te enterobijaza. Primarni čimbenik rizika za svrab jest napučenost pa su kolektivi često žarište infekta. Bolest se prenosi s čovjeka na čovjeka bliskim kontaktom kože na kožu, spavanjem u istom krevetu, rijetko preko rublja. Glavni su simptomi intenzivan svrbež (posebice noću) te pojava crvenog osipa na mjestima koja se grebu. Ušljivost je prilično uobičajena pojava u dječjim kolektivima i nije vezana za higijenu. Svrbež je jedan od prvih simptoma, a češanjem nastaje iritacija kože i ekzorijacije na glavi. Valja spomenuti i stidne uši koje se najčešće javljaju u adolescenata i odraslih, a prenose se spolnim putem. Uz svrbež i ogrebotine, neki bolesnici imaju i regionalnu limfadenopatiju. Enterobijaza je crijevna infestacija česta u djece. Njezin je glavni simptom perianalni svrbež koji

je najizraženiji noću. Česta je među ljudima koji žive u bliskom kontaktu.

**Zaključak:** Pojedini paraziti, gljivice i bakterije čest su uzrok svrbeži kože. One imaju fizičke, psihičke i emocionalne učinke na život bolesnika te predstavljaju dijagnostički i terapijski izazov za obiteljske liječnike kao liječnike prvog kontakta.

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## ■ Infections as a cause of pruritus

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**Introduction with Aim:** Pruritus is one of the three most common skin symptoms for which patients consult their family physician. One of the common causes are skin infections: fungal, viral, bacterial, parasitic. The aim of this paper is to review the most common infections that cause pruritus.

**Discussion:** The most common infections that cause pruritus are fungal infections. A well-circumscribed skin lesion with a red, scaly, raised border is typical. Toes and soles are often affected, and the skin becomes dry, scaly, cracked or soft and macerated. Fungal infection of the scalp can manifest as alopecia. Pityriasis rosea, erythema infectiosum and chickenpox are the most common viral infections that cause pruritus, and so are molluscum contagiosum a common viral skin infection of childhood that causes small round papules with a waxy centre. Impetigo is a superficial bacterial streptococci and/or staphylococci infection of the skin and usually affects the skin around the mouth and nose, but can also appear on other parts of the body. It is characterized by redish sores and can cause slight pain, discomfort and often pruritus. The most common parasitic causes of pruritus are scabies, lice and enterobiasis. The primary risk factor for scabies is crowding and collectives are often a focus of infection. The disease is transmitted from person to person through close skin-to-skin contact and sleeping in the same bed. The main symptoms are intense pruritus (especially at night) and the appearance of a red rash in places that are scratched. Lice are quite common in children's groups and are not related to hygiene. Pruritus is one of the first symptoms, and scratching causes skin irritation and excoriations on the head. Pubic lice are often sexually transmitted in adolescents and adults. Along with pruritus and scratching, some

patients also have regional lymphadenopathy. Enterobiasis is an intestinal infestation common in children. The main symptom is perianal pruritus, which is most expressed at night. It is common among people living in close contact.

**Conclusion:** Certain parasites, fungi and bacteria are a common cause of pruritus. They have physical, psychological and emotional effects on the patient's life and represent a diagnostic and therapeutic challenge for family doctors as first-contact doctors.

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## ■ Što se krije iza kašlja?

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**Uvod s ciljem:** Pristup bolesniku s kašljem predstavlja profesionalni izazov za liječnika obiteljske medicine jer se kašalj pojavljuje u više dijagnostičkih kategorija u rasponu od relativno jednostavnih do ozbiljnih potencijalno opasnih stanja koja ugrožavaju život. Cilj ovog rada je prikazati spektar i značajke različitih oblika kašlja te specifičnost kliničke procjene i intervencije.

**Rasprava:** Kašalj je vitalni zaštitni refleks koji sprječava aspiraciju i poboljšava pročišćavanje dišnih puteva od iritansa, sekreta ili stranih tijela. Kašalj može biti posljedica različitih uzroka, a najčešći su: infekcije dišnih puteva, alergije i astma, gastroezofagealna refluksna bolest (GERB), pušenje i izloženost iritansima, kronične bolesti pluća, lijekovi, tumori dišnih puteva, srčano zatajivanje te psihogeni kašalj. Vrste kašlja mogu se razlikovati po trajanju, zvuku, prisutnosti iskašljaja i popratnim simptomima. Prema trajanju kašalj može biti akutni (do 3 tjedna u odraslih, 2 tjedna u djece), subakutni (3-8 tjedana u odraslih, 2-4 tjedna u djece) i kronični (duže od 8 tjedana u odraslih i duže od 4 tjedna u djece). Kašalj može biti suh bez iskašljaja ili s iskašljajem, može zvučati „oštro“, „mokro“ piskavo. Može biti hripav, praćen promuklošću i zaduhom i može se javljati u napadima ili pretežito noću. S obzirom na vrstu iskašljaja, kašalj može biti praćen sukrvicom ili gnojenjem. Dugotrajni kašalj je česta i onesposobljavajuća tegoba koja pogađa oko 5-10% odrasle populacije. Glavni uzroci subakutnog kašlja kod odraslih su kašalj gornjih dišnih puteva (postnazalni drip sindrom), a glavni uzroci kroničnog kašlja su astma, KOPB, sindrom hiperosjetljivosti, eozinofilni bronhitis i gastroezofagealna refluksna bolest. Posebno treba istaknuti i ne-kiselinski GERB. Kod djece su najčešći uzroci

kroničnog kašlja, perzistentni bakterijski bronhitis, astma i udisanje stranog tijela. Smjernice Europskog respiratornog društva za liječenje kroničnog kašlja naglašavaju pojam preosjetljivosti na kašalj kao pojačanu osjetljivost pacijenata na vanjske podražaje (hladan zrak, parfemi, dim i izbjeljivači) temeljeno na vagusnoj aferentnoj preosjetljivosti. Smjernice naglašavaju i potrebu za preciznom dijagnostikom i personaliziranim liječenjem s posebnim naglaskom na razlike između odraslih i djece. Anamneza i klinički pregled početak su svake kliničke procjene, a dijagnostičke pretrage koje slijede uključuju, laboratorijske analize krvi, testove plućne funkcije, radiološke pretrage te endoskopiju. Liječenje je uzročno, a kod specifičnih oblika kašlja poput rezistentnog kašlja kod sindroma hiperosjetljivosti danas se preporučuju i neuromodulatori poput gabapentina te različite nefarmakološke metode. U svrhu što boljeg zbrinjavanja bolesnika sa kašljem neophodno je slijediti utvrđene algoritme i smjernice primjerene za obiteljsku medicinu.

**Zaključak:** Pravilna dijagnostička procjena i trijaža od izuzetnog su značaja u ranom pristupu bolesnicima sa kašljem. Važno je pravovremeno prepoznati različite uzroke i mehanizme nastanka kašlja te primijeniti specifične dijagnostičke i terapijske postupke.

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## ■ What's behind the cough?

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**Introduction with aim:** Approaching a patient with cough is a professional challenge for the family physician because cough occurs in multiple diagnostic categories ranging from relatively simple to serious, potentially life-threatening conditions. The aim of this paper is to present the spectrum and characteristics of different forms of cough and the specificity of clinical assessment and intervention.

**Discussion:** Cough is a vital protective reflex that prevents aspiration and improves airway clearance of irritants, secretions, or foreign bodies. A cough can be the result of various causes the most common of which are: respiratory tract infections, allergies and asthma, gastroesophageal reflux disease (GERD), smoking and exposure to irritants, chronic lung disease, medications, airway tumors, heart failure, and psychogenic cough. Types of cough can differ in duration, sound, presence of sputum, and accompanying symptoms. Depending on the duration, cough can be acute (up to 3 weeks in adults, 2 weeks in children), subacute (3-8 weeks in adults, 2-4 weeks in children) and chronic (longer than 8 weeks in adults and longer than 4 weeks in children). Cough can be dry without sputum or with sputum, it can sound "sharp", "wet" and wheezy. It can be wheezing, accompanied by hoarseness and shortness of breath and can occur in attacks or predominantly at night. Depending on the type of sputum, cough can be accompanied by blood or pus. Long-term cough is a common and disabling condition, affecting about 5-10% of the adult population. The main causes of subacute cough in adults are upper respiratory tract cough (postnasal drip syndrome), and the main causes of chronic cough are asthma, COPD,

hypersensitivity syndrome, eosinophilic bronchitis and gastroesophageal reflux disease. Non-acid GERD should also be highlighted. In children, the most common causes of chronic cough are persistent bacterial bronchitis, asthma and foreign body inhalation. The European Respiratory Society guidelines for the management of chronic cough emphasize the concept of cough hypersensitivity as an increased sensitivity of patients to external stimuli. (cold air, perfumes, smoke and bleach) based on vagal afferent hypersensitivity. The guidelines also emphasize the need for precise diagnostics and personalized treatment, with special emphasis on the differences between adults and children. History and clinical examination are the beginning of every clinical assessment. Diagnostic tests that follow include laboratory tests, pulmonary function tests, radiological examinations and endoscopy. Treatment is causal, and for specific forms of cough like resistant cough in hypersensitivity syndrome neuromodulators such as gabapentin and various non-pharmacological methods are now recommended. In order to best care for patients with cough, it is necessary to follow established algorithms and guidelines recommended for family medicine.

**Conclusion:** Proper diagnostic assessment and triage are of utmost importance in the early approach to patients with cough. It is important to recognize the different causes and mechanisms of cough in a timely manner and to apply specific diagnostic and therapeutic procedures.

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## ■ Karakteristike kašlja kod srčanih bolesti

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**Uvod s ciljem:** Kašalj je obrambeni mehanizam dišnih putova izazvan stimulacijom živčanih završetaka lokaliziranih u grkljanu, dušniku i glavnim bronhima, no može se izazvati i inputima iz izvanplućnih organa djelovanjem preko vagalnog živca. Iako se kašalj najčešće povezuje sa simptomatologijom plućnih bolesti, brojna su stanja koja se prezentiraju kašljem, a među njima i srčane bolesti. Unatoč visokoj prevalenciji kardiovaskularnih bolesti, nedovoljno smo upoznati s mehanizmima nastanka i karakteristikama kašlja kod srčanih bolesti.

Cilj ovog rada je prikazati mehanizme nastanka i karakteristike kašlja izazvanog poremećajima rada srca kako bi pravilnim dijagnostičkim i terapijskim pristupom pravodobno reagirali i poboljšali kvalitetu života bolesnika.

**Rasprava:** Prema dosadašnjim spoznajama dva su mehanizma nastanka kašlja u bolesnika sa srčanim bolestima. Prvi mehanizam temelji se na refleksnoj interakciji između srčanih aferentnih živaca i neuralnih putova kašlja, a drugi na hemodinamskim promjenama u plućnoj cirkulaciji. Ova dva mehanizma međusobno su isprepletana tako da se često ne može jasno odvojiti o kojem se mehanizmu radi. Srčane bolesti, poput aritmija i zatajivanja srca, mogu dovesti do hemodinamskih promjena u srčanim komorama i plućnoj cirkulaciji. Ektopični otkucaji povezani su s povećanim protokom krvi u plućnom deblu zbog većeg volumena izbacivanja krvi nakon kompenzacijske stanke što posljedično dovodi do rastezanja stijenki krvnih žila i stimulacije završetaka vagalnih živaca smještenih u plućnim arterijama ili unutar plexusa koji okružuje plućno deblo. Također, srčana disfunkcija izazvana aritmijama i zatajivanjem srca dovodi do porasta tlaka u lijevom atriju i posljedično do plućne venske kongestije. Kašalj izazvan aritmijom obično je suh, slabijeg intenziteta, a prisutan je tijekom dana i noći što značajno utječe na kvalitetu sna. Bolesnici ga opisuju kao refleksnu, iznenadnu potrebu za

kašljanjem kojoj prethodi osjećaj škakljanja u grlu ili „lupanja“ u prsima. Većina bolesnika ne pokazuje nikakve auskultatorne abnormalnosti ili radiografske znakove koji upućuju na plućnu kongestiju. Aritmija se može prvi put otkriti tijekom fizikalnog pregleda, a svakako je potrebno učiniti elektrokardiogram te u daljnjoj obradi 24-satno snimanje elektrokardiograma. Primjena beta blokatora dovela je do značajnog smanjenja pojave kašlja kod određenih bolesnika sa supraventrikularnim ekstrasistolama. Kod bolesnika sa simptomima kašlja i ventrikularnim ekstrasistolama uspješnim se pokazalo liječenje antiaritmikima, ali i radiofrekventna ablacija. Kod zatajivanja srca prisutnost manje količine tekućine u alveolarnom ili intersticijskom prostoru ne može izazvati kašalj. Najčešće se javlja u uznapredovaloj fazi lijevostranog srčanog zatajivanja kada je uz kašalj prisutna zaduha u mirovanju, a simptomi se pogoršavaju kada bolesnik leži. Tada se kao osnovna simptomatska terapija koriste diuretici.

**Zaključak:** Bolesti srca dovode do pojave kašlja putem različitih mehanizama čiji segmenti još uvijek nisu u potpunosti razjašnjeni. Kašalj se kod bolesnika sa zatajivanjem srca javlja u uznapredovaloj fazi bolesti, a kod bolesnika sa srčanim aritmijama može biti prvi znak bolesti. Poznavanjem karakteristika kašlja te pravilnim dijagnostičkim i terapijskim pristupom može se značajno utjecati na smanjenje tegoba bolesnika i poboljšanje kvalitete života.

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## ■ Characteristics of cough in heart disease

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**Introduction with aim:** Cough is a defense mechanism of the airways caused by stimulation of nerve endings localized in the larynx, trachea and main bronchi, but it can also be caused by inputs from extrapulmonary organs acting via the vagus nerve. Although cough is most often associated with the symptomatology of lung diseases, there are numerous conditions that present with cough, including heart disease. Despite the high prevalence of cardiovascular diseases, we are insufficiently familiar with the mechanisms of occurrence and characteristics of cough in heart disease.

The aim of this paper is to present the mechanisms of occurrence and characteristics of cough caused by heart disorders in order to respond in a timely manner and improve the quality of life of patients with the correct diagnostic and therapeutic approach.

**Discussion:** According to current knowledge, there are two mechanisms of cough in patients with heart disease. The first mechanism is based on the reflex interaction between cardiac afferent nerves and the neural pathways of cough, and the second on hemodynamic changes in the pulmonary circulation. These two mechanisms are intertwined so that it is often not possible to clearly separate which mechanism is involved. Heart diseases, such as arrhythmias and heart failure, can lead to hemodynamic changes in the heart chambers and pulmonary circulation. Ectopic beats are associated with increased blood flow in the pulmonary trunk due to a larger volume of blood ejection after a compensatory pause, which consequently leads to stretching of the blood vessel walls and stimulation of vagal nerve endings located in the pulmonary arteries or within the plexus surrounding the pulmonary trunk. Also, cardiac dysfunction caused by arrhythmias and heart failure leads to an increase in pressure in the left atrium and consequently to pulmonary venous congestion. Cough caused by arrhythmia

is usually dry, of lower intensity, and is present during the day and night, which significantly affects the quality of sleep. Patients describe it as a reflex, sudden need to cough, preceded by a tickling sensation in the throat or a "pounding" in the chest. Most patients do not show any auscultatory abnormalities or radiographic signs indicating pulmonary congestion. Arrhythmia can be first detected during a physical examination, and an electrocardiogram should be performed, and in further work-up, a 24-hour electrocardiogram recording should be performed. The use of beta blockers has led to a significant reduction in the occurrence of cough in certain patients with supraventricular extrasystoles. In patients with symptoms of cough and ventricular extrasystoles, treatment with antiarrhythmic drugs, as well as radiofrequency ablation, has proven successful. In heart failure, the presence of a small amount of fluid in the alveolar or interstitial space cannot cause cough. It most often occurs in the advanced stage of left-sided heart failure when the cough is accompanied by shortness of breath at rest, and the symptoms worsen when the patient lies down. In this case, diuretics are used as the main symptomatic therapy.

**Conclusion:** Heart diseases lead to the appearance of cough through various mechanisms whose segments are still not fully understood. Cough in patients with heart failure occurs in the advanced stage of the disease, and in patients with cardiac arrhythmias it can be the first sign of the disease. Knowing the characteristics of cough and the correct diagnostic and therapeutic approach can significantly affect the reduction of patient complaints and improve the quality of life.

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## ■ Alergijski kašalj

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**Uvod s ciljem:** Liječnici obiteljske medicine svakodnevno se susreću s pacijentima čiji je glavni razlog posjete kašalj. Iako obrambeni mehanizam našeg tijela i naizgled jednostavan simptom iz perspektive pacijenta, kašalj je etiološki vrlo kompleksan te zahtjeva detaljnu anamnezu i fizikalni pregled kako bismo prepoznali fenotip kašlja i adekvatno ga liječili. Cilj je ovog rada pružiti nova saznanja obiteljskim liječnicima o kašlju alergijske etiologije, ranom prepoznavanju i optimalnom liječenju na razini primarne zdravstvene zaštite.

**Rasprava:** Kašalj alergijske prirode često je suh, ne produktivan no iritirajući i dugotrajan, u trajanju više od 8 tjedana u odraslih, a 4 tjedna u djece, ovisno osjetljivosti osobe i vrsti alergije. Nerijetko su mu pridružene i druge tegobe poput, kihanja, svrbeža i crvenila nosa i očiju, začepljenog nosa, glavobolje te kožnih promjena. Obično nije praćen povišenom tjelesnom temperaturom te bude izražen noću i remeti san. Uzrokovan je pretjeranom reakcijom imunološkog sustava na određene tvari odnosno alergene (prašina, grinje, trava, pelud, životinjska dlaka i slično) uslijed čega dolazi do stvaranja imunoglobulina E (IgE) i oslobađanja histamina u krvotok koji je odgovoran za nastanka navedenih simptoma. U pravilu dolazi do slijevanje mukoznog sekreta iz nosa u ždrijelo (postnazalni drip) koji podražuje na kašalj. Dijagnostika iako limitirajuća, podrazumijeva kožne alergijske testove te test iz krvi odnosno specifične IgE testove (RAST). Važno je odrediti je li kašalj povezan primjerice s alergijskim rinitisom ili astmom o čemu će ovisiti i liječenje. Liječenje podrazumijeva izbjegavanje alergena ako je moguće te farmakoterapiju oralnim antihistaminicima druge generacije, osim u slučaju izraženog noćnog kašlja, hipertoničnu otopinu, ekspektoranse, nazalni dekonjestiv i nazalni kortikosteroid. Ako se radi o sezonskom

kašlju i pridruženim ostalim tegobama uputno je s terapijom započeti ranije.

**Zaključak:** Alergijski kašalj ponekad je teško razlikovati od stanja poput bronhitisa, astme ili infekcije gornjeg respiratornog trakta. Osim što može biti dugotrajan, ovisno o intenzitetu može remetiti kvalitetu života pojedinca. Anamneza i fizikalni pregled ključni su u prepoznavanju fenotipa kašlja i u procjeni daljnje dijagnostike kako bi se pravovremeno isključili rjeđi uzroci kašlja poput bronhiektazija i ostalih plućnih bolesti te primijenilo optimalno liječenje.

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## ■ Allergic cough

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**Introduction with a goal:** Family medicine doctors, we meet patients every day whose main reason for visiting is precisely a cough. Although a defense mechanism of our body and a seemingly simple symptom from the patient's perspective, cough is etiologically very complex and requires a detailed history and physical examination in order to recognize the cough phenotype and adequately treat it. The aim of this work is to provide new knowledge to family doctors about cough of allergic etiology, early recognition and optimal treatment at the level of primary health care.

**Discussion:** An allergic cough is often dry, non-productive but irritating and long-lasting, lasting more than 8 weeks in adults and 4 weeks in children, depending on the sensitivity of the person and the type of allergy. It is often accompanied by other complaints such as sneezing, itching and redness of the nose and eyes, stuffy nose, headache and skin changes. It is usually not accompanied by an elevated body temperature and is expressed at night and disturbs sleep. It is caused by an excessive reaction of the immune system to certain substances or allergens (dust, dust mites, grass, pollen, animal hair, etc.), resulting in the production of immunoglobulin E (IgE) and the release of histamine into the bloodstream, which is responsible for the appearance of the above symptoms. As a rule, there is a flow of mucous secretion from the nose into the throat (postnasal drip), which stimulates coughing. Diagnostics, although limiting, includes skin allergy tests and a blood test or specific IgE tests (RAST). It is important to determine whether the cough is related to, for example, allergic rhinitis or asthma, on which the treatment will depend. Treatment includes avoiding allergens if possible and pharmacotherapy with oral antihistamines of the second generation, except in the case of pronounced night cough, hypertonic solution,

expectorants, nasal decongestants and nasal corticosteroids. (3,4) It is recommended if it is a seasonal cough and associated other complaints start therapy earlier.

**Conclusion:** An allergic cough is sometimes difficult to distinguish from conditions such as bronchitis, asthma or an upper respiratory tract infection. Apart from the fact that it can be long-lasting, depending on the intensity it can disturb the quality of life of the individual. Anamnesis and physical examination are key in recognizing the cough phenotype and in assessing further diagnostics in order to timely rule out less common causes of cough such as bronchiectasis and other lung diseases and apply optimal treatment.

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## ■ Psihogeni kašalj

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**Uvod s ciljem:** Psihogeni kašalj je oblik kroničnog kašlja koji nema organske uzroke, već nastaje kao posljedica psihičkih čimbenika. Ova vrsta kašlja je rijetka i predstavlja dijagnostički izazov jer se preklapa s drugim napadima kašlja i zahtijeva isključivanje svih somatskih uzroka. Psihogeni kašalj povezan je s emocionalnim i psihološkim čimbenicima, uključujući stres i tjeskobu (česti okidači kašlja su stresni događaji, stres u školi ili na poslu, te anksiozna stanja), psihosomatske poremećaje (kašalj može poslužiti kao nesvjestan način izražavanja emocionalnog stresa), traženje pažnje, uobičajeno ponašanje (kašalj se može razviti u refleksno ponašanje koje traje iako uzrok više nije prisutan). Cilj ovog rada je definirati pristup, dijagnostiku i liječenje u obiteljskoj medicini.

**Rasprava:** Dijagnoza psihogenog kašlja je dijagnoza isključenja. Važno je razlikovati:

1. Respiratorne bolesti: Astma, kronični bronhitis, plućna fibroza.
2. Infekcije: Virusne ili bakterijske respiratorne infekcije.
3. Refluksna bolest: Gastroezofagealni refluks može uzrokovati kronični kašalj.
4. Alergije i nadražaji: Prašina, dim cigareta ili kemikalije.

Dijagnostički postupci uključuju anamnezu, fizikalni pregled, RTG prsnog koša, spirometriju i laboratorijske pretrage. Ključna je suradnja s psihologom ili psihijatrom kako bi se identificirali psihološki čimbenici. Prevencija psihogenog kašlja usmjerena je na upravljanje stresom i poboljšanje mentalnog zdravlja: upravljanje stresom, učenje tehnika opuštanja (meditacija, vježbe disanja), podrška okoline (dobra komunikacija u obitelji i podrška školskog osoblja),

prepoznavanje obrazaca (edukacija bolesnika i obitelj o povezanosti psihičkog stanja i kašlja). Liječenje psihogenog kašlja kombinacija je psiholoških pristupa i simptomatskog liječenja. Psihološka intervencija uključuje kognitivno-behavioralnu terapiju (usmjerenu na prepoznavanje i promjenu obrazaca ponašanja koji održavaju kašalj), psihoterapiju (obrada stresnih situacija i traumatskih iskustava), biofeedback (poučavanje pacijenta o kontroli tjelesnih odgovora). Psihogeni kašalj rijetko se liječi lijekovima, na primjer ako ima popratnih psihičkih poremećaja, kod kojih se koriste anksiolitici (za kratkotrajno liječenje akutnog stresa), antidepresivi (za liječenje osnovnih anksioznih poremećaja ili depresije). Njihova uporaba treba biti oprezna i uvijek pod nadzorom liječnika.

**Zaključak:** Psihogeni kašalj kompleksan je poremećaj koji zahtijeva holistički pristup dijagnostici i liječenju. Uspjeh terapije ovisi o ranom prepoznavanju, kontroli osnovnih psiholoških čimbenika i bliskoj suradnji bolesnika, obitelji i medicinskog osoblja. Pravilnim pristupom moguće je kontrolirati simptome i omogućiti bolesniku kvalitetan život.

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## ■ Psychogenic cough

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**Introduction with a goal:** Psychogenic cough is a form of chronic cough that does not have an organic cause, but rather occurs as a result of psychological factors. This type of cough is rare and presents a diagnostic challenge because it overlaps with other coughing attacks and requires the exclusion of all somatic causes. Psychogenic cough is associated with emotional and psychological factors, including stress and anxiety (common triggers of cough are stressful events, stress at school or work, and anxiety states), psychosomatic disorders (cough can serve as an unconscious way of expressing emotional stress), attention seeking, habitual behavior (cough can develop into a reflex behavior that persists even though the cause is no longer present). The aim of this paper is to define the approach, diagnosis, and treatment in family medicine.

**Discussion:** The diagnosis of psychogenic cough is a diagnosis of exclusion. It is important to distinguish:

1. Respiratory diseases: Asthma, chronic bronchitis, pulmonary fibrosis.
2. Infections: Viral or bacterial respiratory infections.
3. Reflux disease: Gastroesophageal reflux disease can cause chronic cough.
4. Allergies and irritants: Dust, cigarette smoke, or chemicals.

Diagnostic procedures include a medical history, physical examination, chest X-ray, spirometry, and laboratory tests. Collaboration with a psychologist or psychiatrist is essential to identify psychological factors. Prevention of psychogenic cough focuses on stress management and improving mental health: stress management, learning

relaxation techniques (meditation, breathing exercises), environmental support (good communication in the family and support from school personnel), pattern recognition (education of the patient and family about the connection between psychological state and cough). Treatment of psychogenic cough is a combination of psychological approaches and symptomatic treatment. Psychological intervention includes cognitive-behavioral therapy (aimed at identifying and changing behavioral patterns that maintain cough), psychotherapy (processing stressful situations and traumatic experiences), biofeedback (teaching the patient about controlling bodily responses). Psychogenic cough is rarely treated with medication, for example if there are concomitant psychological disorders, in some cases anxiolytics (for short-term treatment of acute stress), antidepressants (for treatment of underlying anxiety disorders or depression) are used. Their use should be cautious and always under the supervision of a physician.

**Conclusion:** Psychogenic cough is a complex disorder that requires a holistic approach to diagnosis and treatment. The success of therapy depends on early recognition, control of underlying psychological factors and close cooperation between the patient, family and medical staff. With the right approach, it is possible to control symptoms and provide the patient with a quality life.

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## ■ Pristup bolesniku s hemoptizom

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**Uvod.** Hemoptiza je iskašljavanje krvi iz donjeg dišnog sustava. Uzroci hemoptize variraju od benignih stanja do životno ugrožavajućih stanja. Inicijalna procjena bolesnika s hemoptizom i utvrđivanje potencijalnih uzroka ključna je za odluku o daljnjim dijagnostičkim postupcima i liječenju. Cilj ovog rada je definirati najčešće diferencijalne dijagnoze i inicijalno postupanje kod bolesnika s hemoptizom.

**Metode.** Pregledane su baze podataka Google Scholar, Pubmed i UpToDate koristeći ključnu riječ „hemoptiza“ u naslovu. Kriteriji pretrage su uključivali cjelovite pregledne članke na engleskom jeziku objavljene u razdoblju od 2010. do 2024. godine, a koji su obuhvaćali riječ „hemoptiza“ u naslovu članka.

**Rasprava.** Hemoptiza može varirati od krvlju tingiranog iskašljaja do masivne hemoptize (hemoptoa) u oko 5% slučajeva. Masivna hemoptiza ima više definicija ovisno o volumenu iskašljane krvi, ali svaka koja dovodi do akutne životne ugroze se može smatrati masivnom. Etiološki se hemoptiza može podijeliti na onu koja potječe iz traheobronhalnog stabla, parenhima pluća, plućne vaskulature te jatrogene i idiopatske uzroke. Oko 30-40% posto hemoptiza ostaju kriptogene i nakon učinjene široke obrade. Najčešći uzroci hemoptiza značajno variraju geografski i demografski, a uključuju tuberkulozu, karcinom pluća, bronhiektazije, infekcije donjeg dišnog sustava i micetome. Važno je u inicijalnoj procjeni isključiti i pseudoheoptizu koja uključuje krvarenje iz gornjeg dišnog sustava ili gornjeg probavnog trakta. U prvom susretu s bolesnikom najvažnije je odrediti klinički status pacijenta, volumen iskašljane krvi (treba imati na umu da je samoprocjena bolesnika često kriva) i vrijeme iskašljavanja krvi, suziti moguće uzroke na temelju detaljne anamneze i procjene rizičnih faktora (posebno za malignitet, tuberkulozu i plućnu emboliju) te odlučiti o potrebi za hitnim upućivanjem bolesnika u bolnicu. Kod svakog bolesnika s hemoptizom potrebno je učiniti RTG prsnih organa u 2 smjera jer je lako dostupan i može nam

pomoći u lokalizaciji uzroka (iako mu osjetljivost i specifičnost nisu visoke) te osnovne laboratorijske nalaze uključujući koagulacijske parametre. Ukoliko se radi o blagoj do umjerenoj hemoptizi u stabilnog bolesnika te se na temelju inicijalne obrade postavi vjerojatna dijagnoza prvenstveno je potrebno liječiti osnovnu bolest (npr. upalu pluća ili koagulopatiju) jer je većina takvih hemoptiza samolimitirajuća. Kod ostalih uzroka u većini slučajeva potrebna je dodatna obrada, prvenstveno CT toraksa (ili CT angiografija plućnih arterija) te dijagnostička i/ili intervencijska bronhoskopija, a masivna hemoptiza zahtijeva mjere intenzivnog liječenja. Specifičan sustavni lijek za hemoptizu ne postoji. U kliničkoj praksi primjenjuju se opioidni antitusici i inhibitori fibrinolitičke aktivnosti, ali liječenje prvenstveno treba usmjeriti na osnovni uzrok. Ostale mogućnosti liječenja uključuju embolizaciju bronhalne arterije koju provodi intervencijski radiolog, intervencijsku bronhoskopiju ili kirurški zahvat.

**Zaključak.** Hemoptiza je često i za bolesnika i za liječnika uznemirujuć simptom koji zahtijeva žurnu procjenu te bi liječnici obiteljske medicine kao prvi koji se susreću s bolesnikom trebali imati jasna saznanja o diferencijalnoj dijagnozi i kriterijima za daljnju obradu.

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## ■ Approach to the patient with hemoptysis

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**Introduction.** Hemoptysis is the expectoration of blood from the lower respiratory tract. The causes of hemoptysis vary from benign conditions to life-threatening ones. The initial assessment of patients with hemoptysis and the identification of potential causes are crucial for deciding on further diagnostic procedures and treatment. The aim of this paper is to define the most common differential diagnosis and initial management of patients with hemoptysis.

**Methods.** Databases such as Google Scholar, PubMed, and UpToDate were reviewed using the keyword „hemoptysis“ in the title. The search criteria included comprehensive review articles in English published from 2010 to 2024 that contained the word „hemoptysis“ in the article title.

**Discussion.** Hemoptysis can range from blood-streaked sputum to massive hemoptysis in about 5% of cases. Massive hemoptysis has various definitions depending on the volume of expectorated blood, but any case leading to acute life-threatening situations can be considered massive. Etiologically, hemoptysis can be divided into that originating from the tracheobronchial tree, lung parenchyma, pulmonary vasculature, and iatrogenic or idiopathic causes. Approximately 30-40% of hemoptysis remains cryptogenic even after extensive workup. The most common causes of hemoptysis vary significantly geographically and demographically and include tuberculosis, lung cancer, bronchiectasis, lower respiratory tract infections, and mycetoma. It is important to rule out pseudohemoptysis in the initial assessment, which includes bleeding from the upper respiratory tract or upper gastrointestinal tract. During the first encounter with the patient, it is essential to determine the clinical status of the patient, the duration and volume of expectorated blood (keeping in mind that self-assessment by the patient is often inaccurate), narrow down possible causes based on detailed medical history and assessment of risk factors (especially for malignancy, tuberculosis, and pulmonary embolism), and decide on emergent referral to the

hospital. For every patient with hemoptysis, a chest X-ray is necessary, as it is easily accessible and can help in localizing the cause (though its sensitivity and specificity are not high), as well as basic laboratory findings including coagulation parameters. If it is a mild to moderate hemoptysis in a stable patient, and a probable diagnosis is established based on initial evaluation, it is primarily necessary to treat the underlying disease (e.g., pneumonia or coagulopathy) since most such hemoptysis are self-limiting. For other causes, additional evaluation is usually needed, primarily a chest CT (or CT angiography of the pulmonary arteries) and diagnostic and/or interventional bronchoscopy, while massive hemoptysis requires intensive care measures. There is no specific systemic treatment for hemoptysis. In clinical practice, opioid antitussives and inhibitors of fibrinolytic activity are applied, but treatment should primarily focus on the underlying cause. Other treatment options include bronchial artery embolization performed by an interventional radiologist, interventional bronchoscopy, or surgical intervention.

**Conclusion:** Hemoptysis is a distressing symptom for both patients and physicians that demands urgent assessment, and family medicine doctors, as the first points of contact should have clear knowledge of differential diagnosis and criteria for further evaluation.

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## ■ Rani znaci i prevencija demencije

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**Uvod i cilj:** Starenje donosi sa sobom mnoge bolesti, a demencije su postale svojevrsna epidemija, od koje pati čak 25 milijuna ljudi diljem svijeta, a očekuje se da će, 2025. godine, taj iznos porasti za još četiri milijuna. Trećina ljudi starijih od 85 godina boluje od nekog tipa demencije. Cilj rada je istaknuti najvažnije elemente prevencije i ranog prepoznavanja demencije, kako bi liječnici obiteljske medicine (LOM) imali bolje alate u procesima skrbi o dementnim osobama.

**Rasprava:** Vrlo je teško procijeniti je li osoba samo smetena, dekoncentrirana ili postoji trajan problem. Pacijenti se jave liječniku sa sumnjom na dementne tegobe tek nakon upozorenja okoline, rjeđe kada sami prepoznaju simptome alarma. Stoga LOM treba kontinuirano promatrati, slušati i educirati pacijente kako bi se u što ranijoj fazi detektirala demencija. Potrebno je obratiti pažnju na rane znakove: poremećaj kratkotrajnog pamćenja, poteškoće u komunikaciji, dezorijentiranost u vremenu i prostoru, otežano procjenjivanje, probleme s računanjem, zaboravljene stvari, promjene u ponašanju i raspoloženju, promjene osobnosti, gubitak inicijative. Za LOM je važno prepoznati „ključnu osobu“ u obitelji koja će otvoreno komunicirati o dementnim članovima obitelji. Stigmatizacija dementnih osoba može voditi do socijalne isključenosti i osamljenosti. Stigma je problem i cijele obitelji koja iz straha i srama skriva što se događa voljenoj osobi i često ne vjeruju da bi itko to mogao razumjeti. Zato se nerijetko unutar obitelji sakrivaju informacije o promjenama koje za člana obitelji znače rano prepoznavanje demencije. Tako se značajno kasni u intervenciji i povećava mogućnost brže progresije i težih simptoma u kasnijoj fazi bolesti. Niz aktivnosti koje se mogu provoditi, a najčešće su to uobičajene mjere zdravstvene pažnje, utječu na mogućnosti prevencije, odgodu pojave simptoma i njihov karakter. Aktivno se može utjecati na sedam pravila prevencije: kontrola arterijskog tlaka, lipida i glikemije kvaliteta sna zdrava i raznovrsna prehrana, nepušenje, društveni život, kontinuirano učenje nečeg novog. Kognitivna rezerva stvara se cijeloga života - kroz formalno i neformalno obrazovanje, različite aktivnosti,

učenje raznih vještina, izlaganje novim situacijama, ljudima i iskustvima općenito. Uz manju kognitivnu rezervu, simptomi se pojavljuju ranije, već kod manjeg stupnja oštećenja mozga. Često primjenjivane metode su igranje igara protiv istog protivnika, najbolje umjetne inteligencije (šah, remi), rješavanje križaljki istog porijekla, matematičke igre iste razine. Osoba se može svakodnevno rovjeravati i procijeniti radi li se o umoru i stresu ili se obrazac smanjene kognitivne funkcije ponavlja. Ovaj alat preporuča se i osobama srednje životne dobi, kako bi se dnevno procjenjivala kognitivna rezerva, ali i usvojila navika za ponašanje u starijoj životnoj dobi.

**Zaključak:** Kognitivno propadanje ne mora nužno biti dominantni dio starenja. Postoje uspješni alati kao pomoć u prevenciji i ranom prepoznavanju demencije. Određeni čimbenici načina života imaju veći utjecaj od gena na to hoće li se razviti bolesti povezane s pamćenjem. Briga za starije i oboljele od demencije treba uključivati aktivno nastojanje da se promijeni negativna slika o starijim osobama i starenju koje trenutno postoji u društvu. Događa se nagli porast starijeg stanovništva i životni vijek je produžen. Važan dio prevencije je uklanjanje stigmatizacije, kako u obitelji, tako i u društvu, ali i kod zdravstvenih profesionalaca.

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## ■ Early signs and prevention of dementia

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**Introduction with aim:** Aging brings with it many diseases, including dementia, which has become a kind of epidemic and affects a large number of the world's population. Dementia is continuously increasing, as many as 25 million people worldwide suffer from it, and it is expected that, this year alone, that amount will increase by another four million. As many as a third of people over the age of 85 suffer from some type of dementia. The goal of the work is to highlight the most important elements of prevention and early recognition of dementia, so that family medicine doctors (FMOs) have better tools in the processes of caring for people with dementia.

**Discussion:** It is very difficult to assess whether a person is just distracted, distracted or there is a continuous problem. Patients come to the doctor with suspicions of demented complaints only when the environment warns them that the disturbances are more frequent and recurring, less often when they recognize the alarm symptoms themselves. Therefore, LOM should continuously observe, listen and educate patients in order to detect the problem of dementia at the earliest possible stage. It is necessary to pay attention to the early signs: disorder or short-term memory, communication difficulties, disorientation in time and space, difficult assessment, calculation problems, lost things, changes in behavior and mood, personality changes, loss of initiative. Even in cases of dementia in the family, LOM has the role of identifying a "key person" who will communicate openly about demented family members. Stigmatization of demented persons can lead to social exclusion and loneliness of persons who already have cognitive difficulties. Stigma is a problem for the whole family, because the family hides what is happening to their loved one out of fear and shame, and they often do not believe that anyone could understand it. That is why information about changes that mean early recognition of dementia for a family member is often hidden within the family. This significantly delays intervention and increases the possibility of faster progression and more severe symptoms in

the later stages of the disease. A series of activities that can be carried out, and most often these are common measures of health care, which affect the possibilities of prevention, the delay in the appearance of symptoms and their character. Seven rules of prevention can be actively influenced: blood pressure and cholesterol control, blood sugar level, quality sleep, healthy and colorful diet, not smoking, social life, continuously learning something new. Cognitive reserve is created throughout life - through formal and informal education, various activities, learning various skills, exposure to new situations, people and experiences in general. In people with a lower cognitive reserve, symptoms will appear earlier, that is, with a lower degree of brain damage. Often applied methods are playing games against the same opponent, the best artificial intelligence (chess, rummy), solving crossword puzzles of the same origin, mathematical games of the same level. So you can check yourself daily and assess whether it is fatigue and stress or whether the pattern of reduced cognitive function is repeating itself. This tool is also recommended for middle-aged people, in order to assess the cognitive reserve on a daily basis, but also to adopt habits for behavior in old age.

**Conclusion:** Cognitive decline is not necessarily a part of aging. There are successful tools to help in the prevention and early recognition of dementia. Certain lifestyle factors have a greater influence than our genes on whether we develop memory-related diseases. Caring for the elderly and people with dementia should include an active effort to change the negative image of the elderly and aging that currently exists in society. There is a sudden increase in the elderly population and life expectancy has increased. An important part of prevention is the removal of stigmatization, both in the family and in society, but also among health professionals.

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## ■ Terapijske mogućnosti u liječenju demencije u ordinaciji liječnika opće/obiteljske medicine

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**Uvod.** Demencija manifestira se progresivnim i nepovratnim padom kognitivnih sposobnosti, uključujući pamćenje, jezik, mišljenje i vještine, dovoljno ozbiljno da ometa svakodnevne funkcije pojedinca. Ciljevi suvremene cjelovite skrbi su omogućiti pacijentima što dulji samostalan život u vlastitom domu te smanjiti opterećenje njegovatelja bolesnika. Cilj rada je prikazati terapijske mogućnosti u liječenju bolesnika s demencijom u ordinaciji liječnika opće/obiteljske medicine.

**Rasprava.** Zbrinjavanje bolesnika s demencijom ostaje izazov za liječnike opće/obiteljske medicine. Trenutačne preporuke za liječenje demencije preporučuju holistički pristup usmjeren na bolesnika koji uključuje kombinaciju farmakološkog i nefarmakološkog liječenja. Farmakološka terapija demencije uključuje: 2 velike skupine kognitivnih pojačivača, inhibitore acetilkolinesteraze i antagoniste N-metil-D-aspartat (NMDA) receptora, zatim antiamiloidnu terapiju Alzheimerove bolesti, antidepressive, antipsihotike, antikonvulzive uz propisanu shemu sa strane specijaliste neurolog/psihijatar. Nefarmakološko liječenje uključuje: kognitivnu stimulacijsku terapiju, psihoterapiju, kognitivnu rehabilitaciju, grupnu terapiju i trebalo bi biti sastavni dio liječenja u svim stadijima demencije ovisno o raspoloživim resursima u regiji. Liječnik opće/obiteljske medicine aktivno je uključen u zbrinjavanje bolesnika s demencijom od trenutka postavljanja dijagnoze do palijativne skrbi, pružanjem koordinirane integrirane skrbi kroz pravovremeno upućivanje odgovarajućem specijalistu, praćenjem razvoja bolesti i organizacijom socijalne podrške bolesnicima. U liječenju bi liječnici opće/obiteljske medicine također trebali obratiti pozornost na optimizaciju cjelokupne propisane terapije za upravljanje svim komorbiditetima koji mogu

utjecati na pogoršanje simptoma demencije, kako bi se smanjio kardiovaskularni rizik i postigli ciljani ciljevi za komorbiditete. Liječnik bi trebao napraviti individualizirani plan prema stadiju bolesti, komorbiditetu i raspoloživim resursima, koji će uključiti i članove uže obitelji/njegovatelje. Plan bi dodatno trebao sadržavati smjernice i edukaciju pacijenata i njegovatelja o dnevnoj strukturiranoj rutini, dobroj higijeni spavanja, prisjećanju na aktivnosti i sigurnosnim mjerama kod kuće koje mogu pomoći poboljšanju dobrobiti bolesnika s demencijom.

**Zaključak.** Liječenje bolesnika s demencijom zahtijeva multidisciplinarni pristup u kojem je liječnik opće/obiteljske medicine koordinator cjelokupne skrbi za ove bolesnike. Liječnici holističkim pristupom usmjerenim na pacijenta omogućavaju individualiziranu terapiju za pacijente sa demencijom u skladu s potrebama bolesnika i raspoloživim resursima, što omogućuje očuvanje funkcionalne neovisnosti i kvalitete života ovih bolesnika.

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## ■ Therapeutic options in the treatment of dementia in general practitioner/family doctor's office

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**Introduction.** Dementia is manifested by a progressive and irreversible decline in cognitive abilities, including memory, language, thinking and skills, severe enough to interfere with the individual's daily functions. The goals of modern comprehensive care are to enable patients to live independently in their own homes for as long as possible and to reduce the burden on the patient's caregivers. Aim of the paper is to present therapeutic options in the management of patients with dementia in general practitioner/family doctor's office

**Discussion.** The care of patients with dementia remains a challenge for general practitioners/family doctors. Current recommendations for dementia management recommend a holistic and patient-centered approach that includes a combination of pharmacological and non-pharmacological treatment. Pharmacological therapy for dementia includes: 2 large groups of cognitive enhancers, acetylcholinesterase inhibitors and N-Methyl-D-aspartate (NMDA) receptor antagonists, then anti-amyloid therapy for Alzheimer's disease, antidepressants, antipsychotics, anticonvulsants with a prescribed regimen by a specialist neurologist/psychiatrist. Non-pharmacological treatment includes: cognitive stimulation therapy, psychotherapy, cognitive rehabilitation, group therapy and should be an integral part of the treatment in all stages of dementia depending on the available resources in the region. The general practitioner/family physician is actively involved in the management of patients with dementia from the moment of diagnosis to palliative care, offering coordinated integrated care through timely referral to an appropriate specialist, monitoring the development of the disease and organizing social support for patients. In treatment,

general practitioners/family physicians should also pay attention to optimizing the patient's overall prescribed therapy to manage all comorbidities that may affect the worsening of dementia symptoms, in order to reduce cardiovascular risk and achieve targeted goals for comorbidities. The doctor's should make an individualized plan according to the stage of the disease, comorbidities and available resources, which will also include close family members/caregivers. The plan should additionally contain guidance and education for the patient and caregivers on a daily structured routine, good sleep hygiene, reminiscence of activities and safety measures at home that can help improve the well-being of patients with dementia.

**Conclusion.** The treatment of patients with dementia requires a multidisciplinary approach in which the general practitioner/family physician is a coordinator of the overall care for these patients. Physicians, through a holistic and patient-centered approach, provide individualized therapy for patients with dementia according to the patient's needs and available resources, which allows maintaining the functional independence and quality of life of these patients.

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## ■ Dementan bolesnik kao kompleksan pacijent

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**Uvod s ciljem:** Kako populacija stari, tako raste i broj ljudi koji žive s demencijom, što povećava ulogu tima primarne zdravstvene zaštite u njihovoj skrbi. Liječnici obiteljske medicine često prvi prepoznaju pojavu kognitivnog oštećenja svojih pacijenata, dok timovi primarne zdravstvene zaštite kojima oni koordiniraju imaju sve veću ulogu u dugotrajnoj skrbi za demencijne pacijente. Tim primarne zdravstvene zaštite u svemu treba imati ulogu koordinatora skrbi i edukativnu ulogu. Kako niti jedan zdravstveni sustav nema dostatne resurse, timovi primarne zdravstvene zaštite ističu poteškoće u zadovoljavanju potreba kompleksnih pacijenata kao što su demencijni pacijenti. Cilj rada je potaknuti na razmišljanje o dugotrajnoj skrbi demencijnih bolesnika i istaći teškoće na koje nailazi tim obiteljskog liječnika tijekom provođenja takve skrbi.

**Rasprava:** Globalne preporuke zdravstvenih politika zagovaraju veću uključenost timova primarne zdravstvene zaštite u skrb o demencijnim pacijentima te u osnaživanju i edukaciji neformalnih njegovatelja o takvoj specifičnoj skrbi. Anketa Udruge za Alzheimerovu bolest iz SAD-a, iz 2020. godine, pokazala je da 82% timova obiteljskih liječnika vjeruje da su na prvoj liniji skrbi za demencijne bolesnike, a 53% je dobilo pitanja u vezi s demencijom svakih nekoliko dana. Za očekivati je kako će tim obiteljskog liječnika imati sve veću ulogu u ranom otkrivanju, liječenju i koordiniranju skrbi demencijnih pacijenata. S druge strane tu je niz prepreka u skrbi za demencijne pacijente. Univerzalni problemi su nedostatak vremena, resursa i nedovoljna edukacija timova primarne zdravstvene zaštite. Timovi PZZ-a navode nedostatak samopouzdanja i osposobljenosti za dijagnosticiranje i liječenje demencije. Postoje teškoće u pristupu i komunikaciji sa stručnjacima na sekundarnoj i tercijarnoj zdravstvenoj zaštiti, koordiniranju svih dionika

sustava skrbi i upravljanju potrebama i očekivanjima pacijenata i njihovih obitelji. Stoga postoji potreba za postojanjem servisa unutar primarne zdravstvene zaštite, koji bi preuzeo dio aktivnosti i time rasteretio tim obiteljskog liječnika. **Zaključak:** Skrb o demencijnim pacijentima je kompleksna i dugotrajna. Obiteljski liječnik ima ključnu ulogu u ranoj dijagnostici bolesti, no u postdijagnostičkoj skrbi je nužno razvijati nove servise unutar primarne zdravstvene zaštite, koji će preuzeti dio kompleksne skrbi za ove pacijente.

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## ■ People with Dementia as Complex Patients

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**Introduction and Aim:** With the population growing old, the number of people living with dementia is also on the rise, which increases the role of their primary healthcare teams. General practitioners are often the ones who first recognise the advent of cognitive impairments in their patients, while the role of the primary healthcare teams they coordinate continues to grow in regard to the long-term care for dementia patients. During the treatment, the primary healthcare team must be the healthcare coordinators, as well as provide education. Since no healthcare system has adequate resources, primary healthcare teams struggle to satisfy the needs of complex patients such as those with dementia. The aim of this paper is to raise concerns about long-term healthcare of dementia patients and highlight the difficulties encountered by the general practice team in providing such care.

**Discussion:** Globally, healthcare policies recommend a greater involvement of primary healthcare teams in the care for dementia patients and in empowering informal care providers, as well as educating them about this specific type of care. A questionnaire of the USA's Alzheimer's Association from 2020 shows that 82% of primary care providers believe they are at the front lines of providing dementia care, whereas 53% were asked about dementia every few days. It is to be expected that the primary care teams will have a growing role in the early diagnosis, treating, and coordinating care for dementia patients. On the other hand, there is a slew of obstacles in dementia care. The universal issues are the lack of time and resources, and an insufficient education of primary healthcare teams. These teams point out their lack of self-confidence and qualifications needed for diagnosing and treating dementia. There are also difficulties in the approach to and communication with secondary

and tertiary healthcare professionals, in coordinating all members of the healthcare system, and in managing the needs and expectations of patients and their families. Thus, there is a need for a service within the primary healthcare that would take over some of the activities and therefore ease the burden of the primary healthcare team.

**Conclusion:** Providing care to dementia patients is complex and long-term. The general practitioner has a key role in the early diagnosis of the disease, but it is necessary to develop the post-diagnosis care so that it includes new services, incorporated within the primary healthcare, which would take over some of the complex care provided to these patients.

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## ■ Mogućnosti bolničke skrbi o dementnim bolesnicima

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**Uvod:** Alzheimerova bolest (AB) najčešća je neurodegenerativna bolest i najčešći uzrok dementnog sindroma. Bolest se manifestira kognitivnim propadanjem i psihijatrijskim simptomima (depresija, apatija, iritabilnost, impulzivnost, agitacija i psihoza). U terapiji je trenutno dostupno samo simptomatsko liječenje. Osim kod AB, dementni sindrom se još javlja i u sklopu drugih neurodegenerativnih bolesti te kao posljedica vaskularnih bolesti, traume, tumora i upalnih procesa.

**Rasprava:** AB karakterizira kontinuirana progresija kognitivnog propadanja sa skokovitim pogoršanjima u periodima stresa. Istraživanja su pokazala da hospitalizacija negativno utječe ne samo na kliničku prezentaciju već i na sam tijek bolesti. Ovi bolesnici bivaju duže hospitalizirani, imaju veću stopu ponovne hospitalizacije i veći intrahospitalni mortalitet u usporedbi sa bolesnicima bez demencije. Pojava večernjeg nemira (tzv "sundown" efekt) i smetnji sna povezana je sa manjkom fizičke aktivnosti koja im se u bolničkim uvjetima ne može osigurati. Starije osobe izložene češćoj hospitalizaciji imaju bržu stopu kognitivnog propadanja, naročito ukoliko je neurodegenerativni proces već započeo. Neuropsihijatrijski simptomi, koji se često pogoršavaju za vrijeme hospitalizacije, isto tako negativno utječu na brzinu progresije demencije. Hospitalizacija također povećava rizik za uvođenje antipsihotika u terapiju što dodatno ima negativne posljedice na morbiditet i mortalitet bolesnika.

**Zaključak:** S obzirom na negativne posljedice hospitalizacije na morbiditet i mortalitet bolesnika sa dementnim sindromom, osnova skrbi i liječenja ove grupe bolesnika primarno bi trebala biti ambulantna.

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## ■ Hospital Care Options for Dementia Patients

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**Introduction with aim:** Alzheimer's disease (AD) is the most common neurodegenerative disease and the leading cause of dementia syndrome. It manifests as cognitive decline and psychiatric symptoms, including depression, apathy, irritability, impulsivity, agitation, and psychosis. Currently, only symptomatic treatment is available. Dementia syndrome occurs not only in AD but also in other neurodegenerative diseases and as a result of vascular diseases, trauma, tumors, and inflammatory processes.

**Discussion:** AD is characterized by continuous cognitive decline with episodic deteriorations during periods of stress. Research has shown that hospitalization negatively affects both the clinical presentation and the course of the disease. Dementia patients experience longer hospital stays, higher readmission rates, and increased in-hospital mortality compared to non-dementia patients. The occurrence of evening restlessness (the so-called "sundowning" effect) and sleep disturbances is associated with a lack of physical activity, which cannot be adequately provided in a hospital setting. Older adults exposed to frequent hospitalizations experience a more rapid rate of cognitive decline, particularly if a neurodegenerative process has already begun. Neuropsychiatric symptoms, which often worsen during hospitalization, further accelerate dementia progression. Additionally, hospitalization increases the likelihood of introducing antipsychotic medications,

which negatively impact morbidity and mortality in these patients.

**Conclusion:** Given the negative impact of hospitalization on morbidity and mortality in patients with dementia syndrome, the primary approach to care and treatment for this patient group should be outpatient management.

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### **3. Asocijacija**

## ■ From Initial Symptomatology to Definitive Diagnosis: Challenges and Barriers in Primary Care Practice

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This project provides a comprehensive examination of the diagnostic journey in primary care settings, delineating the intricate process from initial symptom assessment to the conclusive identification of diseases.

Through an in-depth case study of a patient initially presenting with a non-symptomatic rash, we demonstrate how primary care practices can serve as a crucial nexus for early detection of complex, severe, and occasionally rare diseases such as Cutis Myeloid Leukaemia. This case exemplifies the pivotal role that advanced diagnostic tools, interdisciplinary collaboration and strategic patient management play in overcoming the inherent challenges with in primary care diagnostics.

Further explored are the systemic barriers—such as limited resources, time constraints and „insurance complications”—that slow the diagnostic process.

We discuss the integration of artificial intelligence and telemedicine as transformative approaches that can enhance diagnostic accuracy, streamline referrals and facilitate continuous care.

Additionally, the study highlights the importance of emotional support and patient education through out the diagnostic process, advocating for a holistic approach to patient care that incorporates both technological advancements and human-centered strategies.

This research not only sheds light on the existing challenges faced by family physicians but also propose sactionable strategies to enhance the overall efficiency and effectiveness of primary care diagnostics.

By addressing these challenges, the project contributes valuable insights into improving patient outcomes and advancing the future of family medicine.

## ■ Dostupnost suvremenih dijagnostičkih metoda liječnicima obiteljske medicine i suradnja sa sekundarnom razinom

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**Uvod s ciljem:** Suvremene dijagnostičke metode podrazumijevaju korištenje uređaja i instrumenata, vještina i znanja koji liječnicima omogućuju postavljanje točne dijagnoze. Dijagnostičke metode uključuju: rendgenske preglede i kontrastne rendgenske snimke, te nove tehnike kao što su ultrazvuk, kompjuterizirana tomografija - CT (ili skener) i nuklearna magnetska rezonancija - NMR. Primarna zdravstvena zaštita, au njoj i liječnici opće prakse, temelj su zdravstvenog sustava, jer su oni prvi u kontaktu s bolesnikom, kontinuirano brinući o zdravlju pojedinca i obitelji, bez obzira na dob i spol bolesnika. Cilj izlaganja je predstaviti dostupnost suvremenih dijagnostičkih metoda liječnicima opće medicine u rješavanju zdravstvenih problema njihovih pacijenata te kakva je suradnja sa sekundarnom razinom zdravstvene zaštite u Srbiji.

**Rasprava:** Prema Zakonu o zdravstvenoj zaštiti i Pravilniku o načinu i postupku ostvarivanja prava iz obaveznog zdravstvenog osiguranja sva prava osiguranih osoba i pacijenata ostvaruju preko liječnika opće medicine – izabranih doktora u domovima zdravlja. Starenje stanovništva, multimorbiditet sa složenim zdravstvenim problemima povećali su zahtjeve pred liječnike u pružanju zdravstvenih usluga stanovništvu. Uz anamnezu i klinički pregled, potrebne su dodatne dijagnostičke pretrage. U slučaju bolova u leđima koji se šire u preponu i lijevu nogu, u sklopu dijagnostike potrebno je bolesnika uputiti u laboratorij na standardne laboratorijske pretrage, RTG lumbosakralne regije, kao i ultrazvučni pregled urogenitalnog trakta i zdjelice. Ako su takvi pregledi već učinjeni, potrebno je učiniti CT ili NMR. U većim domovima zdravlja postoji specijalistička služba s RTG-om i ultrazvukom, a u njih pacijente upućuju liječnici opće prakse. Ukoliko to

nije slučaj, pacijenta izabrani liječnik upućuje na sekundarnu razinu zdravstvene zaštite i zakazuje te preglede. Za CT i NMR preglede potrebno je mišljenje i prijedlog odgovarajućeg specijaliste, pregledi se zakazuju, a za NMR postoje „liste čekanja“. Za dijagnostiku i praćenje bolesnika s kroničnom opstruktivnom plućnom bolešću spirometrijom liječnik opće medicine upućuje bolesnika pulmologu na sekundarnu razinu. Pacijenti s kardiovaskularnim bolestima zbog dugog čekanja kod specijalista na sekundarnoj razini holter EKG praćenje i holter mjerenje tlaka rade u privatnim zdravstvenim ustanovama. Sve to usporava konačnu dijagnozu, pa su pacijenti prisiljeni obavljati specijalističke preglede i dijagnostiku u privatnim zdravstvenim ustanovama koje sami plaćaju. Za rješavanje zdravstvenih problema pacijenata opće medicine, osim znanja, potrebno je ojačati i kadrovsku i tehničku opremljenost.

**Zaključak:** Suvremene dijagnostičke metode i suradnja sa sekundarnom razinom nedovoljno su dostupni liječnicima opće prakse. Potrebno je ojačati opću medicinu u vremenskom i tehničkom smislu.

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## ■ Availability of modern diagnostic methods to doctors in general medicine and their cooperation with secondary level

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**Introduction with aim:** Modern diagnostic methods involve the use of devices and instruments, skills and knowledge that enable doctors to make a precise diagnosis. Diagnostic methods include: x-rays and contrast x-rays, and techniques such as ultrasound, computerized tomography - CT (or scanner) and nuclear magnetic resonance - NMR. Primary health care, with general practitioners, is the basis of healthcare system, because they are the first in contact with the patient, they continuously take care of their health, regardless of the patient's age and sex. The aim of the paper is to show how available are modern diagnostic methods to doctors in general medicine in order to solve health problems of their patients and what is the cooperation with the secondary level health care in Serbia.

**Discussion:** According to the Law on Health Care and the Rulebook on the Method and Procedure of Implementation rights from compulsory health insurance, all rights of insured persons and patients are realized through doctors of general medicine - selected doctors in health centers. Aging population, multimorbidity with complex health problems have put an increasing demands in front of doctors in providing health services to the population. In addition to anamnesis and clinical examinations, the application of additional diagnostic examinations is necessary. Let us look at the example: for back pain with spreading to the groin and left leg, in order to make a diagnosis, it is necessary to refer the patient to the laboratory to make standard laboratory analyses, X-ray imaging of the lumbosacral region, as well as ultrasound examination of the urogenital tract and pelvis. If such examinations have already been carried out before, it is necessary to do CT or NMR imaging. In larger health centers there

is a specialist service with X-ray and ultrasound, and the general practitioner refers his patient to them. If this is not the case, on the instructions of the selected doctor, the patient is referred to the secondary level of health care and examinations are scheduled. For CT and NMR examinations, an opinion and proposal of the appropriate one is given by required specialists. Examinations are scheduled, and there are "waiting lists" for NMR. For diagnostics and monitoring of patients with chronic obstructive pulmonary disease by spirometry, the general practitioner sends the patient to a pulmonologist at the secondary level. Patients with cardiovascular disease for holter ECG monitoring and blood pressure holter, have examinations performed in private health institutions, due to the long wait at the secondary specialist level. All this slows down the performing of final diagnosis, so patients are forced to undergo specialist examinations and diagnostics in private health care institutions and that pay for themselves. To solve health problems of patients in general medicine, in addition to knowledge, it is necessary to strengthen medical staff, but also technical equipment.

**Conclusion:** Neither modern diagnostic methods, no cooperation of general practitioners with secondary level are sufficiently available. It is necessary to strengthen general medicine in terms of time and technique equipment.

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## ■ Simptomi i znaci zdravstvenog sustava

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Kriza kvalitete u zdravstvenom sustavu široko je poznata, a studije ističu značajnu štetu uzrokovanu postojećim problemima kvalitete zdravstvene skrbi. Zdravstveni djelatnici izražavaju zabrinutost, prijavljujući smanjenje svoje sposobnosti pružanja kvalitetne skrbi.

Zdravstveni sustav se teško može nazvati sustavom. Umjesto toga, to je niz visoko decentraliziranih sektora. Akademske institucije često nisu uspjevale odgovoriti na potrebe društva i zbog toga su postale izolirane u svom uskom razmišljanju.

Slabo se prilagođavamo potrebama pacijenata. Kako populacija stari, sve je više bolesnika s kroničnim bolestima. Studije pokazuju da učinkovito liječenje kroničnih stanja mora biti kontinuirano u svim okruženjima i vrstama pružatelja usluga. Kliničari trebaju surađivati jedni s drugima i s pacijentima kako bi razvili zajedničke planove skrbi s dogovorenim ciljevima i koracima provedbe.

S druge strane, postoji rastući konzumerizam u zdravstvu, što se očituje povećanjem pristupa zdravstvenim informacijama na internetu i drugim medijima, a naše usvajanje potrebnih informacijskih tehnologija je sporo, reakcija na različite potrebe pacijenata je neadekvatna. Dodatno postoji i nedostatak radne snage, a radni uvjeti su često loši.

Ova pitanja pridonose stalnim izazovima u pružanju visokokvalitetne skrbi usmjerene na pacijenta. Zbog svih ovih anomalija put do postavljanje dijagnoza od prvobitnih simptoma do konačne dijagnoze mnogo puta može biti dug, što je u odnosu na pacijentovo zdravlje izgubljeno vrijeme.

Rješenja ovih organizacijskih problema zahtijevaju bolje upravljanje resursima, unapređenje međusobne koordinacije, ulaganje u tehnologiju

i obrazovanje zdravstvenih radnika, te veći fokus na pacijenta i njegovu iskustvo unutar sistema.

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## ■ Symptoms and signs of healthcare system

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The quality crisis in healthcare is widely recognised and studies point to the significant damage caused by existing quality problems in healthcare. Healthcare professionals express concern and report that they are less and less able to provide high quality care.

The healthcare system can hardly be described as a system. Instead, it consists of a series of highly decentralised sectors. Academic institutions have often failed to respond to the needs of society and are therefore isolated in their narrow thinking.

We adapt poorly to the needs of patients. As the population ages, there are more and more patients with chronic diseases. Studies show that effective chronic disease management must be continuous across all settings and providers. Clinicians should work with each other and with patients to develop shared care plans with agreed goals and implementation steps.

On the other hand, there is a growing consumerisation of healthcare, manifested in increasing access to health information via the internet and other media, and our adoption of the necessary information technologies is slow, the response to the various needs of patients is inadequate. There is also a lack of staff and working conditions are often poor.

These problems contribute to making it increasingly difficult to provide high-quality, patient-centred care. Because of all these anomalies, the path from the first symptoms to the final diagnosis is often long, which means a loss of time for the patient's health.

Solutions to these organisational problems require better management of resources, improved mutual coordination, investment in technology

and healthcare workforce training, and a greater focus on the patient and their experience within the system.

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## ■ Odlučivanje i dijagnoza - Holistička uloga primarne zdravstvene zaštita

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**Uvod s ciljem:** Postavljanje dijagnoze može biti teško u primarnoj zdravstvenoj zaštiti gdje je teško dijagnosticirati ozbiljne bolesti, poput raka ili drugih. Cilj ovog rada je prezentirati osnovne informacije o pravilima kliničkog odlučivanja pri postavljanju dijagnoze u primarnoj zdravstvenoj zaštiti.

**Rasprava:** liječnici integriraju velike količine dijagnostičkih informacija, uključujući simptome, povijest bolesti i dijagnostičke testove, u svoje odlučivanje. Dijagnostički proces zahtijeva vještine koje ovise o znanju, iskustvu i intuiciji. Unatoč dostupnosti dijagnostičkih postupaka i testova, mnoge bolesti ostaju neotkrivene do kasne faze. Postavljanje dijagnoze u primarnoj zdravstvenoj zaštiti može biti zbunjujuća aktivnost ne samo da su sinonim za organsku bolest, već se mogu odnositi i na stanje (socijalni slučaj, nezaposlenost i sl.), a obiteljski liječnici nemaju zadatak postaviti dijagnozu. Simptom je način na koji pacijent komunicira s nama. Izraz "Pravilo kliničke odluke" ima mnogo definicija, ali u osnovi je to alat koji kvantificira i kombinira jednostavne dostupne kliničke pokazatelje kako bi se definirao novi parametar u primarnoj zdravstvenoj zaštiti, ovaj se parametar može lako generirati kombiniranjem znakova, simptoma i dodatnih dostupni rezultati laboratorija, funkcionalnih testova ili slikovnih rezultata. Mogu se koristiti za procjenu rezultata koji se odnosi na vjerojatnost prisutnosti ili odsutnosti određene bolesti (dijagnoza) ili ishoda (prognoza). Neki pacijenti mogu zamisliti simptome, a drugi imaju tendenciju kombinirati zasebne, slične simptome za jedno stanje .. ili događaj (koji se naziva teleskopiranjem) češće je odlučujući nego u bolnici. Pravila kliničke odluke (CDR) mogu pomoći liječnicima opće prakse u diferencijalnoj dijagnozi, nakon početne sumnje, koja rezultira određenim 'činom radnje': 'isključenjem' bez

daljnjeg testiranja, potrebom za daljnjim testiranjem ili specifičnim liječenjem. Unutar primarne zdravstvene zaštite, stanja će se često vidjeti u evolucijskoj fazi u kojoj se karakteristike simptoma mijenjaju, od trenutka kada pacijent stigne do specijalističke službe kada je opis simptoma možda postao fiksiraniji i, štoviše, pacijent će imati dodatno vremena za razmišljanje o njegovoj priči. Simptomi nisu uvijek povezani s organskim bolestima. Kompleksni pacijenti često imaju nezadovoljene potrebe za njegom, odgođenu odluku, neodgovarajuće korištenje zdravstvenih usluga (probir) mogu poboljšati intervencije povezane s potrebama donošenja odluke, tj. osobne vrijednosti pacijenta i temelje se na dokazima. Intervencije potpore odlučivanju imaju za cilj zadovoljiti potrebe donošenja odluka (a) rješavanjem sukoba odluka, (b) poboljšanjem znanja i informacija i njihovim dijeljenjem, (c) razjašnjavanjem vrijednosti, preferencija i očekivanja pacijenata i (d) identificiranjem resursa koji su im potrebni, uključujući socijalna podrška. Kliničari će prihvatiti CDR samo ako je njegova uporaba jasno klinički korisna, ako je CDR uključen u smjernice. Zapravo, poznato je da su mnogi čimbenici prepreke. U konačnici, glavna vrijednost CDR-a leži u smanjenju složenosti kombiniranja simptoma i znakova s preporukama za donošenje odluka u smislu, tipično, "prekid" bez daljnjeg testiranja, potrebe za daljnjim testiranjem ili specifičnog liječenja korištenje CDR-a.

**Zaključak:** prednost obiteljskih liječnika je izbjegavanje nepotrebnih upućivanja na sveobuhvatnu dijagnostiku i specijalističke konzultacije, a CDR su posebno pogodni za tu svrhu. Korištenje pravila odlučivanja može pomoći mladim liječnicima da razviju svoju kliničku prosudbu, ali mogu pomoći i iskusnijim liječnicima u donošenju brzih odluka o složenim dijagnozama ili potencijalno opasnim stanjima.

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## ■ Decision making and diagnosis - Holistic role of primary health care

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**Introduction with aim:** Making a diagnosis can be difficult in primary care where serious diseases, such as cancer or others, are difficult to diagnose. The aim of this paper is to present basic information about the rules of clinical decision-making when establishing a diagnosis in primary health care.

**Discussion:** Physicians integrate large amounts of diagnostic information, including symptoms, medical history, and diagnostic tests, into their decision making. The diagnostic process requires skills that depend on knowledge, experience and intuition. Despite the availability of diagnostic procedures and tests, many diseases remain undiagnosed until a late stage. Making a diagnosis in primary health care can be a confusing activity, not only are they synonymous with an organic disease, but they can also refer to a condition (social case, unemployment, etc.), and family doctors have no task. diagnose. The symptom is the way the patient communicates with us. The term "Clinical Decision Rule" has many definitions, but basically it is a tool that quantifies and combines simple available clinical indicators to define a new parameter in primary care, this parameter can be easily generated by combining signs, symptoms and additional available laboratory results, functional tests or imaging results. They can be used to evaluate the result related to the probability of the presence or absence of a certain disease (diagnosis) or outcome (prognosis). Some patients can imagine the symptoms, and others tend to combine separate, similar symptoms for a single condition or event (called telescoping) is more often decisive than in the hospital. Clinical decision rules (CDRs) can assist GPs in differential diagnosis, after initial suspicion, which results in a specific 'action': 'exclusion' without further testing, need for further testing or specific treatment. Within

primary care, conditions will often be seen in an evolutionary phase where symptom characteristics change, from the time the patient reaches the specialist service when the symptom description may have become more fixed and, moreover, the patient will have had additional time to reflect on their story. Symptoms are not always related to organic diseases. Complex patients often have unmet care needs, delayed decision, inappropriate use of health services (screening) can improve interventions related to decision-making needs. i.e. personal values of the patient and are based on evidence. Decision support interventions aim to meet decision-making needs by: (a) resolving decision conflicts, (b) improving and sharing knowledge and information, (c) clarifying patients' values, preferences and expectations, and (d) identifying the resources they need, including social support. Clinicians will only accept CDR if its use is clearly clinically beneficial, if CDR is included in guidelines. In fact, many factors are known to be obstacles. Ultimately, the main value of the CDR lies in reducing the complexity of combining symptoms and signs with recommendations for decision-making in terms of, typically, "discontinuation" without further testing, the need for further testing, or specific treatment using the CDR.

**Conclusion:** the advantage of family doctors is to avoid unnecessary referrals for comprehensive diagnostics and specialist consultations, and CDRs are particularly suitable for this purpose. Using decision rules can help junior doctors develop their clinical judgment, but they can also help more experienced doctors make quick decisions about complex diagnoses or potentially dangerous conditions.

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## **5. Mladi nastavnici**

## ■ Klinička slika celijakije u odrasloj dobi

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**Uvod s ciljem:** Celijakija je kronična autoimuna bolest koju izaziva gluten u osoba s genskom predispozicijom, karakterizirana je doživotnim nepodnošenjem glutena. Dugo se smatralo da se javlja isključivo u dječjoj dobi. Utvrđeno je da se može pojaviti u bilo kojoj životnoj dobi s prevalencijom od 1%. Prema recentnijim podacima, vršak incidencije se registrira u petom ili šestom desetljeću života. Zbog raznolikosti i nespecifičnosti simptoma bolest u velikog broja bolesnika ostaje neprepoznata. Cilj je ovog rada ukazati na netipične simptome celijakije u odrasloj dobi.

**Rasprava:** Celijakija ima šaroliku kliničku sliku, ako se ne liječi, može uzrokovati teške komplikacije. Za razliku od jasnih i tipičnih simptoma bolesti u dječjoj dobi, u odraslih osoba simptomima se često na „prvi pogled“ ne mogu povezati s probavnim sustavom. U dijelu odraslih osoba bolest se manifestira isključivo ekstraintestinalnim simptomima kao što su umor i iscrpljenost. Anemija je najčešća hematološka manifestacija, nastaje zbog nedostatka željeza, folne kiseline i vitamina B12. Promjene na koži tipa dermatitis herpetiformis ima 10% bolesnika. U trenutku dijagnoze 40 % oboljelih ima povišene jetrene enzime. Bolest može utjecati na plodnost žena uzrokujući ponavljajuće spontane pobačaje, a neprepoznata se može klinički očitovati tek tijekom trudnoće i puerperija. S obzirom na šaroliku prezentaciju bolesti definirani su podtipovi celijakije: klasična, atipična, tiha i latentna. Klasična celijakija ima tipične simptome poremećaja probavnog sustava. Za atipičnu celijakiju karakteristični su ekstraintestinalni simptomi. Bolest može biti i potpuno asimptomatska. U tom slučaju, ako su u bolesnika pozitivni serološki testovi uz atrofiju sluznice, bolest nazivamo "tihom", u slučaju pozitivnih seroloških testova, bez promjena na sluznici crijeva bolest se naziva "latentnom". Visokorizična stanja koja predstavljaju mogući komorbiditet celijakiji su: anemija, osteopenija,

dijabetes tipa I, autoimunosni hepatitis, primarna bilijarna ciroza, genski sindromi poput Turnerova i Downova sindroma, autoimunosne endokrinopatije poput bolesti štitnjače i Addisonove bolesti, neurološke bolesti poput ataksije, miastenije, epilepsije i IgA-nefropatija. U nekim regijama period do postavljanja konačne dijagnoze celijakije je i više od 10 godina. Ako bolest dugo ostane nedijagnosticirana, postaju vidljivi znakovi malapsorpcijskog sindroma. Malapsorpcija kalcija i D vitamina može uzrokovati osteopeniju i osteoporozu. Povećana je incidencija malignoma. Mogu se pojaviti i psihološke smetnje.

**Zaključak:** Liječnici obiteljske medicine kao osobe prvog kontakta moraju pri postojanju atipičnih ekstraintestinalnih simptoma u bolesnika diferencijalno dijagnostički razmisliti o celijakiji, bolesti sa „tisuću lica“. Stoga je bitno postići bolju svijest o epidemiologiji i kliničkoj slici ove bolesti kako bi pravovremenim postavljanjem dijagnoze utjecali na kvalitetu života bolesnika .

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## ■ Clinical presentation of celiac disease in adults

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**Introduction:** Celiac disease is a chronic autoimmune disease caused by gluten in people with a genetic predisposition, and is characterized by lifelong intolerance to gluten. The disease occurs in 1% of the population at any age. Although it was long thought to occur almost exclusively in childhood, it has been established that it can occur at any age. According to more recent data, the peak incidence is registered in the fifth or sixth decade of life. It is poorly diagnosed, it is believed that many patients are unrecognized due to the variety and non-specificity of symptoms. This lecture aims to point out the atypical symptoms of celiac disease in adulthood.

**Discussion:** Celiac disease has a very diverse clinical presentation, and if it is not treated, it can lead to the development of severe complications. In contrast to the onset of the disease in children, when the majority have clear and typical symptoms of chronic bowel disease, in adults the symptoms can be very "silent" and often cannot be connected to the digestive system at first glance. A large proportion of adult patients do not have problems with the digestive system at all and the disease is manifested exclusively by extraintestinal symptoms. Among the most common symptoms in adulthood are fatigue and exhaustion. Anemia is the most common hematological manifestation. Dermatitis herpetiformis is present in 10% of patients. At the time of diagnosis, 40% of patients have elevated liver enzymes. The disease can affect women's fertility and can cause recurrent spontaneous abortions, and an unrecognized disease can manifest itself clinically only during pregnancy and the puerperium. Given the presentation of the disease, subtypes of celiac disease are defined as classic, atypical, silent, and latent. Classic celiac disease has typical digestive system symptoms. Extraintestinal symptoms characterize atypical celiac disease, and the disease can be completely asymptomatic.

In this case, when the patient has positive serological tests with obvious mucosal atrophy, the disease is called "silent", and in the case of positive serological tests, but without changes in the intestinal mucosa, the disease is called "latent". High-risk conditions for the parallel occurrence of celiac disease are: anemia, osteopenia, type I diabetes, autoimmune hepatitis, primary biliary cirrhosis, genetic syndromes such as Turner's and Down's syndrome, autoimmune endocrinopathies such as thyroid disease and Addison's disease, neurological diseases such as ataxia, myasthenia, epilepsy and IgA -nephropathy. In some regions, the period until the final diagnosis of celiac disease is more than 10 years. If the disease remains undiagnosed for a long time, signs of malabsorption syndrome become visible. Anemia develops due to a lack of iron, folic acid, and vitamin B12. Malabsorption of calcium and vitamin D leads to osteopenia and osteoporosis. The incidence of malignant tumors increases. Psychological disturbances may also appear.

**Conclusion:** Atypical extraintestinal symptoms of celiac disease are often not recognized and not associated with the actual diagnosis, and the possibility of "silent", asymptomatic celiac disease is not often taken into account. Family medicine doctors are the patient's first contact with the health care system, so it is essential to achieve a better awareness of the epidemiology and clinical presentation of this disease.

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## ■ Bakterijski gastroenterokolitisi: antibiotska terapija i kliconoštvo

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**Uvod s ciljem:** Jedan od najčešćih simptoma zbog kojih se bolesnici javljaju u ordinacije obiteljske medicine jest proljev nastao uslijed gastroenterokolitisa. Te su bolesti dominantno virusne etiologije, no u svakodnevnoj praksi važno je razmišljati i o njihovim bakterijskim uzročnicima. Bakterijski gastroenterokolitisi (BG) najčešće su kratkotrajna i samoograničavajuća oboljenja, no mogu se prezentirati i dramatičnijom kliničkom slikom te znatnim odstupanjima laboratorijskih nalaza od referentnog intervala. Nakon preboljenog BG-a, posebice onih uzrokovanih bakterijama roda *Salmonella*, bakterije mogu biti prisutne u probavilu i iz njega se lučiti tjednima, što nazivamo kliconoštvom. Zbog navedenog, često se javlja pitanje potrebe antibiotskog liječenja akutnog BG-a odnosno prolongiranog kliconoštva. Cilj ovog rada je dati praktične informacije o kliničkoj procjeni oboljelih od gastroenteritisa u ordinacijama obiteljske medicine, kada koju vrstu antimikrobnog lijeka propisati te kako postupiti u slučaju kliconoštva.

**Rasprava:** Prema internacionalnim i hrvatskim smjernicama, prilikom procjene svakog gastroenterokolitisa ključno je pomnim kliničkim pregledom procijeniti opće stanje oboljelih, tip i izraženost simptoma te hidriranost. Detaljna anamneza može pomoći u određivanju najvjerojatnijeg uzročnika oboljenja. Ne savjetuje se rutinski provoditi laboratorijske ni specifične mikrobiološke pretrage, budući da liječenje neće ovisiti o tim rezultatima. Najčešće je terapija akutnog bakterijskog gastroenteritisa simptomatska, s naglaskom na adekvatnu rehidraciju i upotrebu probiotika; bolest se spontano povuče unutar nekoliko dana. Antibiotska se terapija u slučajevima blagog do umjerenog gastroenteritisa izbjegava zbog izostanka učinka na skraćivanje trajanja bolesti i ublažavanje simptoma. Osim toga, primjena antibiotika nosi rizik od razvoja antibiotske rezistencije, moguće komplikacije stanja (klostridijski proljev, hemolitičko-uremijski sindrom) te

produljenja kliconoštva. U slučaju razvoja teže bolesti, koja se procjenjuje na temelju razvijenih simptoma, epidemioloških podataka i rizičnih faktora za širenje infekcije na druge organske sustave, potrebno je provesti dodatnu dijagnostičku obradu radi procjene bubrežne funkcije. Utvrđivanjem uzročnika gastroenterokolitisa, početno propisana empirijska antibiotska terapija zamijenit će se ciljanom po prispjeću rezultata mikrobioloških pretraga. Kliconoštvo bakterijskog roda *Salmonella* nakon preboljenog akutnog infekta traje prosječno 5 tjedana, najčešće nema epidemiološkog značaja i nije opasno za okolinu. Kronično kliconoštvo može trajati i više od godine dana. U slučaju da kliconoša nema simptome bolesti, ne rukuje direktno s hranom (koja naknadno neće biti termički obrađena), nije u kontaktu s imunokompromitiranim osobama te se u izolatu ne radi o tifoidnim sojevima, antimikrobno liječenje nije potrebno. Praćenje kliconoštva i duljina izolacije ovisi o vrsti posla koji osoba obavlja te o lokalnim javnozdravstvenim propisima.

**Zaključak:** BG zbog kojih se bolesnici javljaju u ordinacije obiteljske medicine najčešće su bolesti blagog i kratkog kliničkog tijeka; izuzev kliničkog pregleda dodatna dijagnostika i antibiotska terapija nije potrebna. Obiteljski liječnik mora procijeniti bolesnikovo stanje i faktore rizika temeljem kojih će se odlučiti za propisivanje antimikrobnog lijeka, uzimajući u obzir da neopravdano propisivanje antibiotske terapije može imati negativne posljedice na bolesnikovo zdravlje i okolinu.

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## ■ Bacterial gastroenterocolitis: antibiotic therapy and asymptomatic carriage

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**Introduction with aim:** One of the most common symptoms reported by patients to family medicine physicians is diarrhea caused by gastroenterocolitis. These diseases are predominantly of viral etiology, but in everyday practice it is important to take into account their bacterial causative agents as well. Bacterial gastroenterocolitis is usually a short-term and self-limiting disease, however its clinical presentation and the results of laboratory findings can also be quite dramatic. After recovery from bacterial gastroenteritis, especially caused by bacteria of the *Salmonella* genus, bacteria can be present in the digestive tract and be secreted from it for weeks, referred to as asymptomatic carriage. Given all of the above, the question of the need for antibiotic treatment of acute bacterial gastroenterocolitis, i.e. asymptomatic carriage, often arises. The aim of this paper is to provide practical information on the clinical assessment of patients suffering from gastroenteritis in family medicine practice, when and which antibiotic therapy to prescribe, and how to treat cases of asymptomatic carriage.

**Discussion:** According to international and Croatian guidelines, when evaluating any gastroenterocolitis, it is crucial to assess the general condition of the affected patients, the type and severity of symptoms, and hydration through a careful clinical examination. This is accompanied by taking a detailed history, which helps determine the most likely cause of the disease. Routine use of laboratory or specific microbiological tests is not advised, since therapy will not depend on the results. Most often, the only necessary treatment for acute bacterial gastroenterocolitis is symptomatic, with an emphasis on adequate rehydration and the use of probiotics; the disease resolves spontaneously within a few days. Antibiotic therapy in cases of mild to moderate gastroenterocolitis is avoided because of its inability to shorten the duration of the disease and alleviate symptoms. Furthermore, it carries a risk

of developing antibiotic resistance, possible complications of the condition (clostridial diarrhea, hemolytic-uremic syndrome) and prolongation of asymptomatic carriage. If the disease worsens, which is assessed based on the developed symptoms, epidemiological data and risk factors for involvement of distant organs, additional diagnostic workup should be carried out to assess renal function. By determining the causative agent of gastroenterocolitis, empirical antibiotic therapy is replaced by targeted therapy upon arrival of the results of microbiological testing. Asymptomatic carriage of the *Salmonella* genus after overcoming an acute infection usually lasts for about 5 weeks; it most often has no epidemiological significance and is not dangerous for the patient's environment. Chronic carriage can last for over a year. When the carrier has no symptoms of the disease, does not handle food that will not later be thermally processed, is not in contact with immunocompromised persons, and the isolate does not involve typhoid strains, its treatment with antimicrobial drugs is not necessary. Germ control and patient isolation after the acute illness depends on the type of work performed by the patient and local public health regulations.

**Conclusion:** Bacterial gastroenterocolitis that patients seek treatment for in family medicine practices are most commonly diseases with a mild and short clinical course; and, with the exception of a clinical examination, additional diagnostics and antibiotic therapy is not required. Family doctors must assess the patient's condition and risk factors based on antibiotic therapy will be prescribed, taking into account that unjustified antibiotic therapy can have negative consequences for the patient's health and the environment.

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## ■ Pacijentica s hipereozinofilijom u ordinaciji obiteljske medicine

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**Uvod s ciljem:** Eozinofilija je povećani broj eozinofilnih leukocita u perifernoj krvi, a označava ju apsolutni broj eozinofila veći od  $0,5 \times 10^9/L$ . Najčešći uzrok eozinofilije su alergijske bolesti i parazitarne infekcije, no eozinofiliju mogu uzrokovati autoimune, hematološke bolesti i lijekovi. Cilj ovoga rada bio je prikazati važnost otkrivanja etiologije eozinofilije kroz pristup pacijentici s hipereozinofilijom u ordinaciji obiteljske medicine.

**Prikaz slučaja:** Bolesnica u dobi 64 godine dolazi u ordinaciju obiteljske medicine radi uvida u laboratorijske nalaze koji su učinjeni u sklopu redovitog praćenja s obzirom na njezin multimorbiditet. Iz nalaza se izdvaja eozinofilija perifernog krvi (leukociti  $12,4 \times 10^9/L$ , eozinofili 17,0%, apsolutni broj eozinofila  $2,11 \times 10^9/L$ ) koja se u bolesnice prati unatrag 5 godina. Tada provedenom inicijalnom obradom nije nađen uzrok eozinofilije, bolesnica nije bila sklona daljnjoj dijagnostičkoj obradi obzirom da nije imala tegoba. Obiteljska i epidemiološka anamneza bez osobitosti, nema poznatih alergija. Prilikom dolaska u ordinaciju bila je afebrilna, dobrog općeg stanja uz uredan klinički status. Imala je dobar apetit, stolica i mokrenje bili su uredni. Navodi da nije gubila na tjelesnoj masi, negirala pojačano umaranje ili znojenje. U narednim danima učinjena je mikrobiološka obrada stolice koja je bila uredna, osim pozitivnog nalaza stolice na antigen *Helicobacter pylori* zbog kojeg je provedena eradikacijska terapija. U ponovljenoj diferencijalnoj krvnoj slici (DKS) mjesec dana kasnije i dalje perzistira eozinofilija. S obzirom na dugotrajnu umjerenu eozinofiliju nepoznatog uzroka, pacijentici je ponovno predložena dodatna dijagnostička obrada na koju je pristala. U sklopu provedene obrade dobiveni nalaz serologije na crijevne parazite bio je pozitivan na *Echinococcus* spp., *Strongyloides* i *Ascaris lumbricoides*. Pacijentici je nakon ponovljene mikrobiološke obrade

stolice putem infektološke dnevne bolnice indicirana terapija ivermektinom. U početku nije bila sklona uzimanju terapije zbog nuspojava o kojima je čitala, nakon konzultacije u kojoj su razložene prednosti i moguće nuspojave, ipak pristaje na liječenje. Kontrolni nalaz DKS dva mjeseca nakon provedene terapije bio je uredan (leukociti  $11,4 \times 10^9/L$ , eozinofili 3,6%, apsolutni broj eozinofila  $0,41 \times 10^9/L$ ). Pacijentica je upućena da periodično kontrolira DKS i ponovi serologiju na tkivne parazite 6-12 mjeseci od provedene terapije.

**Rasprava:** Infekcija *Strongyloides* i *Ascaris lumbricoides* često je asimptomatska, a posebno kod strongiloidoze eozinofilija može perzistirati i nekoliko desetljeća nakon primarne infekcije s obzirom na njihov autoinfektivni ciklus. Stoga je nekoliko mjeseci nakon provedenog antiparazitskog liječenja potrebno ponoviti serologiju na crijevne i tkivne parazite kako bi se potvrdila eradikacija. Liječnik obiteljske medicine treba ustrajati u otkrivanju etiologije eozinofilije s obzirom na to da i izolirana, asimptomatska eozinofilija perifernog krvi može biti rani znak hipereozinofilnog sindroma, koji može dovesti do teškog oštećenja organa i smrti. U slučaju da se dijagnostičkom obradom na razini primarne zdravstvene zaštite ne otkrije uzrok perzistentne eozinofilije, liječnik obiteljske medicine pacijenta može uputiti na dodatnu obradu u sekundarnu ili tercijarnu zdravstvenu zaštitu.

**Zaključak:** Otkrivanje uzroka eozinofilije važno je radi adekvatnog liječenja. Kontinuirana skrb za pacijente omogućuje liječniku obiteljske medicine da pravovremeno prepozna promjene u njihovu zdravstvenom stanju i započne potrebnu dijagnostičku obradu.

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## ■ Patient with hypereosinophilia at a family physician's office - case report

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**Introduction with aim:** Eosinophilia is defined as an increased number of eosinophil leukocytes in the peripheral blood, and indicates an absolute eosinophil count greater than  $0.5 \times 10^9/L$ . The most common causes of eosinophilia are allergic diseases and parasitic infections, but eosinophilia can also be caused by autoimmune, hematological diseases, and drugs. The aim of this paper was to demonstrate the importance of discovering the etiology of eosinophilia through the approach to a patient with hypereosinophilia in a family physician's office.

**Case report:** A 64-year-old female patient comes to the family physician's office for an insight into her laboratory findings which were made as part of regular follow-up due to her multimorbidity. Peripheral blood eosinophilia (leukocytes  $12.4 \times 10^9/L$ , eosinophils 17.0%, absolute number of eosinophils  $2.11 \times 10^9/L$ ), which has been followed in the patient for 5 years, can be distinguished in her blood count. The initial workup 5 years ago did not find the cause of eosinophilia, and the patient wanted no further diagnostic workup considering that she did not have any complaints. The patient's family and epidemiological history are unremarkable, and she has no known allergies. When the patient arrived at the physician's office, she had no fever, and was in a good general condition. She had a good appetite, stools and urination were regular. She denied losing weight, increased fatigue and sweating. Microbiological examination of her stool was normal. In the repeated differential blood count one month later, eosinophilia still persisted. Regarding the long-term moderate eosinophilia of unknown cause, the patient was offered additional diagnostic workup, to which she agreed to. The serology test for intestinal parasites was positive for *Echinococcus* spp., *Strongyloides* and *Ascaris lumbricoides*. After repeated microbiological stool analysis, the patient was prescribed ivermectin therapy. The patient was initially

against therapy because of the side effects she had read about, but after benefits and possible side effects of the therapy were explained to her, she agreed to the treatment. The differential blood count control results two months after the therapy were normal (leukocytes  $11.4 \times 10^9/L$ , eosinophils 3.6%, absolute number of eosinophils  $0.41 \times 10^9/L$ ). The patient was instructed to periodically control the differential blood count and repeat the serology for tissue parasites 6-12 months after therapy.

**Discussion:** Infection with *Strongyloides* and *Ascaris lumbricoides* is often asymptomatic, and especially in strongyloidiasis, eosinophilia may persist several decades after the primary infection due to its autoinfectious cycle. Therefore, a few months after antiparasitic treatment, it is necessary to repeat serology for intestinal and tissue parasites in order to confirm eradication. A family physician should persist in discovering the etiology of eosinophilia, given that even isolated, asymptomatic peripheral blood eosinophilia can be an early sign of hypereosinophilic syndrome, which can lead to severe organ damage and death. If diagnostic treatment at the level of primary health care does not reveal the cause of persistent eosinophilia, the family physician can refer a patient to secondary or tertiary health care for additional diagnostics.

**Conclusion:** Finding the cause of eosinophilia is important for adequate treatment. Continuous care for patients enables the family physician to recognize changes in their health condition and initiate the necessary diagnostic processing.

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## ■ Klinička inercija u propisivanju novih antidijabetika – praksa, stavovi i iskustva liječnika obiteljske medicine u Hrvatskoj

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**Uvod s ciljem:** Raniji glukocentrični pristup u liječenju dijabetesa tipa 2 (DT2) s primarnim ciljem regulacije glikemije, zadnjih desetljeća nadopunio je sveobuhvatniji, dualni pristup, koji istovremeno stavlja naglasak na smanjenje kardiovaskularnog (KV) rizika. Inhibitori suprijenosnika natrija-glukoze 2 (SGLT2i) i agonisti GLP-1 receptora (GLP-1 RA) posljednjih godina unijeli su revoluciju u liječenje ne samo dijabetesa već i niza drugih metaboličkih i KV poremećaja. Unatoč povoljnim učincima i preporukama smjernica, njihove su razine propisivanja nedovoljne, uglavnom kao posljedica kliničke inercije. Cilj ovog istraživanja je utvrditi povezanost uzroka inercije i razine samopouzdanja liječnika opće/obiteljske medicine (LOM) pri samostalnom propisivanju ovih lijekova.

**Ispitanici i metode:** Istraživanje je provedeno putem samostalno dizajniranog anonimnog upitnika, koji je dostavljen na e-adrese LOM-a na području cijele Hrvatske u digitalnom formatu. Podatke o broju pacijenata s dijagnozom DT2 i propisanim određenim lijekom ispitanici su ispisali iz e-kartona. Pitanja koja su ispitivala razinu samopouzdanja u propisivanju bila su postavljena u obliku Likertove ljestvice, a procjena utjecaja čimbenika inercije na vjerojatnost nižeg samopouzdanja učinjena je bivarijantnom i multivarijantnom logističkom regresijom.

**Rezultati:** Ispitano je 168 LOM, od kojih 66,1% žene, 49,4% specijalisti obiteljske medicine, 67,9% iz gradske sredine. Broj pacijenata s DT2 je 23 036, među kojima najviše onih u dobi 60-80 godina. S obzirom na prevalenciju KV komorbiditeta pacijenata s DT2, udio bolesnika s hipertenzijom iznosi 59,1%, s koronarnom arterijskom bolešću 16,9% te s bubrežnim popuštanjem 13,3%. Udio DT2 bolesnika koji imaju propisan

inhibitor dipeptidil peptidaze 4 (DPP4i) iznosi 33,3%, SGLT2i 18,6% te GLP-1 RA 12,1%. S obzirom na procjenu samopouzdanja, 76,2% ima visoku razinu samopouzdanja za propisivanje SGLT2i, a GLP-1 RA 53,6%. Značajno veće samopouzdanje imaju specijalisti obiteljske medicine. Najizraženiji prediktori nižeg samopouzdanja odnose se na nepoznavanje i kompliciranost smjernica, dok su kao prediktori koji podižu razinu samopouzdanja uočeni detaljna informiranost o nuspojavama lijekova, veći ukupni broj pacijenata te onih s već propisanim istim lijekom.

**Zaključak:** Velik dio populacije pacijenata s DT2 isključivo je u skrbi LOM, stoga je iznimno važno detektirati uzroke inercije s kojima se suočavaju u svrhu optimizacije propisivanja novih antidijabetika te unaprjeđenja skrbi za bolesnike sa šećernom bolesti.

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## ■ Clinical inertia in prescribing novel antidiabetics – practice, attitudes and experiences of GPs in Croatia

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**Introduction with aim:** The earlier glucocentric approach to the type 2 diabetes (T2D) treatment with the primary goal of glycemic control has been complemented in recent decades by a more comprehensive, dual approach, which simultaneously emphasizes the reduction of cardiovascular (CV) risk. Sodium-glucose cotransporter 2 inhibitors (SGLT2i) and GLP-1 receptor agonists (GLP-1 RA) have revolutionized treatment of diabetes and a number of other metabolic and CV disorders in recent years. Despite their beneficial effects and guideline recommendations, their prescribing levels are insufficient, mostly as a result of clinical inertia. The aim of this study is to determine the association between the causes of inertia and the level of general practitioner's (GPs) self-confidence in prescribing these medications.

**Participants and methods:** Research was conducted using a self-designed anonymous questionnaire, which was delivered to the e-mails of GPs throughout Croatia in digital format. Data on the number of patients diagnosed with T2D and prescribed a specific medication were declared by respondents from their e-database. Questions that examined the level of self-confidence in prescribing were asked in the form of a Likert scale, and the assessment of the influence of inertia factors on the probability of lower self-confidence was done using bivariate and multivariate logistic regression.

**Results:** 168 GPs were examined, among which 66.1% were women, 49.4% were family medicine (FM) specialists, and 67.9% were from urban areas. The number of patients with T2D was 23 036, most of whom were aged 60-80 years. Considering the prevalence of CV comorbidities in T2D patients, the proportion of patients with hypertension was 59.1%, with coronary artery

disease 16.9%, and with renal failure 13.3%. The proportion of T2D patients prescribed a dipeptidyl peptidase 4 inhibitor (DPP4i) was 33.3%, SGLT2i 18.6%, and GLP-1 RA 12.1%. Regarding the assessment of self-confidence, 76.2% had a high level of self-confidence in prescribing SGLT2i, and 53.6% GLP-1 RA. FM specialists showed significantly higher self-confidence. The most pronounced predictors of lower self-confidence relate to complexity and unfamiliarity with guidelines, while self-confidence increase in those well informed about medications side effects, and with a larger total number of patients.

**Conclusion:** A large proportion of the T2D patients is solely in GPs care, so it is vastly important to identify the causes of inertia they encounter to optimize the prescribing of novel antidiabetic medications and improve the care of patients with diabetes.

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## Zbrinjavanje sindroma periodične vrućice, aftoznog stomatitisa, faringitisa i cervikalnog adenitisa (PFAPA sindrom) u ordinaciji obiteljske medicine

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**Uvod s ciljem:** Liječnici obiteljske medicine (LOM) se sve češće susreću s pedijatrijskom populacijom pacijenata u svakodnevnom radu. Postoje mnoge razlike u pristupu, dijagnostici, terapijskom zbrinjavanju, ali i u spektru dijagnoza i učestalosti bolesti između pedijatrijske i odrasle populacije. Cilj ovog rada je približiti sindrom periodične vrućice, aftoznog stomatitisa, faringitisa i cervikalnog adenitisa (engl. periodic fever, aphthous stomatitis, pharyngitis and adenitis – PFAPA) LOM kako bi što lakše i učinkovitije zbrinuli pacijente.

**Rasprava:** PFAPA najčešći je sindrom periodične groznice u djece. Uzrok PFAPA-e je nepoznat, smatra se da ga uzrokuje disregulacija imunološkog sustava. Bolest obično počinje prije pete godine života (između 2. i 5. godine života) i završava tijekom adolescencije. Epizode povišene temperature obično traju 3 do 6 dana i ponavljaju se svakih 2-8 tjedana. Sindrom uzrokuje umor, zimicu, povremeno i bolove u trbuhu, artralgiju te glavobolju, groznicu, faringitis, aftozne ulkuse i cervikalnu limfadenopatiju. Dijagnostički kriteriji PFAPA-e odnose se na kliničku sliku:  $\geq 3$  epizode povišene temperature koje traju do 5 dana i javljaju se u pravilnim intervalima kod mlađih od 5 godina; faringitis uz adenopatiju ili aftozne ulkuse; dobro opće stanje između epizoda i normalan rast. Upalni pokazatelji poput C-reaktivnog proteina i sedimentacije eritrocita povišeni su tijekom febrilne epizode, ali ne i između epizoda. Prisutnost neutropenije ili nekih drugih simptoma (npr. osip, proljev, kašalj) upućuju na druge bolesti. Od velike je važnosti isključiti cikličku neutropeniju. Smjernice liječenja nisu usuglašene zbog nedostatka kliničkih studija koje bi potvrdile točnu terapiju. Nesteroidni antireumatici

imaju pozitivan učinak na umanjivanje boli i spuštanje temperature, ne djeluju na učestalost pojave febrilnih epizoda. Prema mnogim studijama, glukokortikoidna terapija (prednizon) u niskim dozama od 0.5 do 2 mg/kg ima najbolji učinak u liječenju akutne febrilne epizode. Profilaktička terapija kolhicinom produžuje vrijeme između ponavljajućih febrilnih epizoda, ali ne dovodi do totalne remisije. Ukoliko terapija kolhicinom djeluje, treba isključiti familijarnu mediteransku vrućicu. Osim kolhicina, u profilaktičkoj terapiji koristi se i cimetidin. Određene studije pokazale su da se cimetidin ne koristi često te da nije dovoljno istraženo koliko je učinkovit. Uporaba anakinre (antagonist IL-1) i vitamina D ukazuju na pozitivno profilaktičko djelovanje, dodatna istraživanja tu činjenicu trebaju potvrditi. Kirurško liječenje poput tonsilektomije i adenotonsilektomije je rijetko, upitnog je učinka te je rizik od kirurških komplikacija veliki. Adenotonsilektomija može biti metoda izbora u izabраних bolesnika koji imaju kratke intervale između febrilnih epizoda te ako glukokortikoidna terapija nije učinkovita.

**Zaključak:** PFAPA je najčešći sindrom periodične groznice u djece mlađe od 5 godina. Iako djeca spontano prerastaju sindrom i nemaju posljedice, sindrom utječe na kvalitetu života djeteta i cijele obitelji. S obzirom na povećani priljev pedijatrijske populacije u ordinacije LOM, od velike je važnosti prepoznati simptome sindroma i pravovremeno djelovati prema recentnim preporukama. Potrebno je provesti dodatna istraživanja o PFAPA sindromu te uvesti jasne smjernice liječenja.

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## ■ Management of periodic fever, aphthous stomatitis, pharyngitis and adenitis- PFAPA syndrome in general medicine practice

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**Introduction with aim:** Family medicine doctors (FMDs) increasingly encounter pediatric patients in their daily practice. There are significant differences in the approach, diagnosis, therapeutic management, as well as in the spectrum of diagnoses and disease prevalence between pediatric and adult populations. This paper aims to familiarize FMDs with periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis syndrome (PFAPA) to facilitate easier and more effective patient management.

**Discussion:** PFAPA is the most common periodic fever syndrome in children. The exact cause of PFAPA is unknown, it is believed to result from immune system dysregulation. The disease typically begins before the age of five (between 2 and 5 years old) and resolves during adolescence. Fever episodes usually last 3 to 6 days and recur every 2 to 8 weeks. The syndrome causes fatigue, chills, occasional abdominal pain, arthralgia, headache, fever, pharyngitis, aphthous ulcers, and cervical lymphadenopathy. The diagnostic criteria for PFAPA are based on clinical presentation:  $\geq 3$  episodes of fever lasting up to 5 days occurring at regular intervals in children under 5 years old; pharyngitis with adenopathy or aphthous ulcers; good general health between episodes and normal growth. Inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate are elevated during febrile episodes but normalize between episodes. The presence of neutropenia or other symptoms (e.g., rash, diarrhea, cough) points to alternative diagnoses, and it is crucial to exclude cyclic neutropenia. There are no standardized treatment guidelines due to the lack of clinical studies confirming specific therapies. Nonsteroidal anti-inflammatory drugs

effectively reduce pain and fever but do not affect the frequency of febrile episodes. According to several studies, glucocorticoid therapy (prednisone) at low doses (0.5 to 2 mg/kg) is the most effective treatment for acute febrile episodes. Prophylactic therapy with colchicine extends the time between recurrent febrile episodes but does not lead to complete remission. If colchicine proves effective, familial Mediterranean fever should be excluded. Cimetidine is also used in prophylactic treatment, but studies suggest it is not commonly used and its effectiveness remains uncertain. The use of anakinra (IL-1 antagonist) and vitamin D has shown promising prophylactic effects, though further research is needed to confirm their efficacy. Surgical treatments, such as tonsillectomy or adenotonsillectomy, are rarely used, with uncertain efficacy, and the risk of surgical complications. Adenotonsillectomy may be considered in selected patients with short intervals between febrile episodes or when glucocorticoid therapy is ineffective.

**Conclusion:** PFAPA is the most common periodic fever syndrome in children under the age of 5. Although children outgrow the syndrome spontaneously without long-term effects, it significantly impacts the quality of life of both the child and their family. Given the increasing number of pediatric patients in FMD practices, it is crucial to recognize the symptoms of PFAPA and act promptly according to the latest recommendations. Further research on PFAPA is needed, along with the establishment of clear treatment guidelines.

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## ■ Što nam govore upalni markeri?

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**Uvod s ciljem.** Reaktanti akutne faze (RAF) su proteini plazme čije se vrijednosti značajno mijenjaju za vrijeme upale u organizmu. RAF mogu biti pozitivni ili negativni što ovisi o njihovim koncentracijama u serumu za vrijeme akutne upale. U svakodnevnoj praksi kod procjene upalnih stanja najviše se služimo pozitivnim RAF poput sedimentacije eritrocita i vrijednostima C reaktivnog proteina. Cilj rada je prikazati značaj upalnih markera i njihovog pravilnog tumačenja.

**Rasprava.** Sedimentacija eritrocita (SE) je indirektni pokazatelj razine proteina akutne faze, točnije fibrinogena. C reaktivni protein (CRP) je protein kojim se direktno mjeri upalni odgovor organizma. Sintetizira se u hepatocitima pod utjecajem citokina, dominantno interleukina-6 (IL-6). Njegove vrijednosti rastu 4-6 sati od početka upale, a vrhunac postižu za 36-50 sati. Vrijednosti SE rastu kasnije, ali ostaju dulje vremena povišene. U bolesnika u kojih su u akutnoj infekciji povišene vrijednosti SE i CRP-a, upotpunjene s ukupnim brojem leukocita, diferencijalnom krvnom slikom i udjelom nezrelih bijelih krvnih stanica možemo utvrditi narav, virulenciju uzročnika, i obrambene sposobnosti organizma. Istražuje se i kinetika CRP-a (eCRPv) kao potencijalnog alata u razlikovanju bakterijskih od virusnih infekcija. Postoji niz čimbenika koji nisu povezani s akutnom ili kroničnom upalom u organizmu, a koji mogu utjecati na vrijednosti SE i CRP-a, što može dovesti do lažno pozitivnih ili lažno negativnih rezultata. CRP i SE su nespecifični upalni markeri koji mogu biti povišen u infektivnim i drugim upalnim stanjima, malignim procesima i ozljedama tkiva. Kao jedan od rizičnih čimbenika za razvoj kardiovaskularnih

bolesti koriste se i vrijednosti visoko osjetljivog C reaktivnog proteina (hsCRP-a). CRP i SE smatramo pozitivnim reaktantima akutne faze, njihove vrijednosti mogu biti u diskrepanciji što može djelovati zbunjujuće. Sve više se istražuju klinički biomarkeri poput prokalcitonina (PCT), IL-6, interleukina-10 (IL-10), udjela neutrofila u olakšavanju rane dijagnoze sepse. Štoviše, vrijednosti PCT, IL-6 i IL-10 pokazuju sposobnost razlikovanja gram negativnih i gram pozitivnih patogena, što je od velikog značenja za adekvatnu primjenu antibiotske terapije. Molekule, poput cinka, bakra, željeza i vitamina D, mogu se ponajviše slično proteinima akutne faze, što dovodi do značajnih promjena u njihovim razinama tijekom akutnog upalnog odgovora.

**Zaključak.** Laboratorijske nalaze je uvijek potrebno sagledati u kontekstu kliničke slike bolesnika i imati na umu komorbiditetna stanja i životne navike koje mogu značajno utjecati na vrijednost, a time i na interpretaciju dobivenih nalaza.

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## ■ What do inflammatory indicators tell us?

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**Introduction and aim.** Acute phase reactants (RAF) are plasma proteins whose values change significantly during inflammation in the body. RAF can be positive or negative depending on their serum concentrations during acute inflammation. In everyday practice, positive RAF, such as erythrocyte sedimentation, and C reactive protein values are mostly used in the assessment of inflammatory conditions. The aim of this paper is to show the importance of inflammatory markers and their correct interpretation.

**Discussion.** Sedimentation of erythrocytes (SE) is an indirect indicator of the level of acute phase proteins, more precisely fibrinogen. On the other hand, C reactive protein (CRP) is a protein that directly measures the body's inflammatory response. It is synthesized in hepatocytes under the influence of cytokines, predominantly interleukin-6 (IL-6). Its values increase 4-6 hours after the onset of inflammation, and reach their peak in 36-50 hours. While SE values increase later, but remain elevated for a longer time. In patients with elevated SE and CRP values in acute infection, complete with the total number of leukocytes, differential blood count and the proportion of immature white blood cells, we can determine the nature and virulence of the causative agent, as well as the body's defense capabilities. The kinetics of CRP (eCRPv) is also being investigated as a potential tool in differentiating bacterial from viral infections. There are various factors unrelated to acute or chronic inflammation in the body that can influence SE and CRP values, potentially leading to false positive or false negative results. CRP and SE are non-specific inflammatory markers that can be elevated in infectious

conditions, but also in other inflammatory, malignant processes and tissue injuries. As one of the risk factors for the development of cardiovascular diseases, high-sensitivity C-reactive protein (hsCRP) values are also used. We consider CRP and SE to be positive reactants of the acute phase, but their values can be discrepant, which can be confusing. Clinical biomarkers such as procalcitonin (PCT), IL-6, interleukin-10 (IL-10), the role of neutrophils in facilitating the early diagnosis of sepsis are increasingly being investigated. Moreover, the values of PCT, IL-6 and IL-10 show the ability to distinguish gram-negative and gram-positive pathogens, which is of great importance for the adequate use of antibiotic therapy. Other molecules, such as zinc, copper, iron, and vitamin D, can exhibit behavior similar to acute-phase proteins, leading to significant changes in their levels during an acute inflammatory response.

**Conclusion.** Laboratory findings must always be seen in the context of the patient's clinical picture and keep in mind comorbid conditions, as well as lifestyle habits that can significantly impact on the value and thus on the interpretation of the obtained findings.

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## ■ Izazovi u dijagnostici novotvorina jajnika: Prikaz slučaja seroznog cistadenofibroma

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**Uvod s ciljem:** Karcinom jajnika je sedmi po učestalosti rak kod žena i osmi uzrok smrti od raka globalno prema podacima Globocana iz 2020. godine. Upravo zbog nespecifičnih simptoma koji se mogu zamijeniti s drugim stanjima, važno je naglasiti potrebu za redovitim ginekološkim kontrolama, edukacijom žena i kontinuiranim pozivanjima na preglede. Cilj rada je prikazati slučaj bolesnice kod koje je, nakon sumnje na ehinokoknu cistu, dokazan serozni cistadenofibrom jajnika.

**Prikaz slučaja:** Pedesetjednogodišnja bolesnica javlja se u ordinaciju obiteljske medicine radi bolova u abdomenu te osjećaja napuhnutosti unazad mjesec dana. Učinjeni laboratorijski nalazi i pretraga stolice na *Helicobacter pylori* bili su uredni. Bolesnici je dodatno učinjen ultrazvuk abdomena gdje je uočena septirana cista i postavljena sumnja na ehinokoknu cistu s rasapom te je upućena infektologu. Serologija na ehinokok je došla negativna, a tumorski marker CA125 povišen (45,3 mU/L). Dodatno je učinjen MR zdjelice koji pokazuje opsežne multicistične tvorbe ovarija; desna tvorba seže do supraumbilikalno, a lijeva ispunjava zdjelicu i potiskuje okolne strukture. Uterus je potisnut ventralno i desno. Objekti tvorbe su dominantno cistične, s diskretnom papilarnom proliferacijom. Vidljiva je manja količina tekućine u zdjelici. Bolesnica je upućena dalje na ginekološki pregled kojim se potvrđuje multicistična septirana tvorba desnog i lijevog ovarija izvan dosega vaginalne sonde. Upućena je na totalnu abdominalnu histerektomiju s obostranom salpingoovarijektomijom te patohistološki nalaz prikazuje da se radi o seroznom cistadenofibromu jajnika.

**Rasprava:** Simptomi novotvorina jajnika su nespecifični i mogu se pripisati bilo kojem drugom poremećaju te ih je jednostavno previdjeti u ranijim fazama. Često se simptomi ne pojavljuju do

kasnog stadija. Najčešće se javljaju osjećaj rane sitosti i nadutost. Također, može se pronaći palpabilna masa u području zdjelice, ascites ili tiši šum disanja zbog pleuralnih izljeva. Transvaginalni ultrazvuk i/ili ultrazvuk abdomena i zdjelice su prva dijagnostička metoda. Ultrazvuk pruža uvid u veličinu, položaj i složenosti mase jajnika. Dodatne slikovne pretrage, kao što su MRI zdjelice, PET skeniranje i/ili CT skeniranje prsnog koša i abdominalne zdjelice koriste se za definiranje širenja tumora. Uz slikovne pretrage, određuju se i serumske razine tumorskog markera CA-125. Većina epitelnih tumora jajnika ima sveukupno povećane razine CA-125, dok samo 50% onih s epitelnim ranim stadijem novotvorina jajnika ima povećanu razinu CA-125. Samo 40% žena koje osjete jedan od nespecifičnih simptoma novotvorina jajnika prvu liječničku pomoć potraži kod ginekologa, stoga iznimno bitnu ulogu imaju liječnici obiteljske medicine kao najčešće osobe prvog kontakta s bolesnicima.

**Zaključak:** Simptomi novotvorina jajnika su nespecifični i često ostaju neprepoznati sve do razvoja uznapredovale bolesti, te je neophodno da žene redovito odlaze na ginekološke preglede. Također, treba istaknuti važnost temeljite anamneze i fizikalnog pregleda u ordinacijama obiteljske medicine kako bi se što ranije postavila sumnja na dijagnozu i pravovremeno započelo liječenje.

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## ■ Challenges in the Diagnosis of Ovarian Neoplasms: A Case Report of Serous Cystadenofibroma

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**Introduction and aim:** Ovarian cancer is the seventh most common cancer among women and the eighth leading cause of cancer-related death globally according to Globocan data from 2020. Due to its nonspecific symptoms, which can be mistaken for other conditions, it is important to emphasize the need for regular gynecological check-ups, educating women, and consistent invitations for examinations. The aim of this paper is to present the case of a patient in whom a serous cystadenofibroma of the ovary was diagnosed after suspicion of an echinococcal cyst.

**Case report:** A 51-year-old female patient presented to the family medicine clinic with abdominal pain and a feeling of bloating for the past month. Laboratory tests and stool analysis for *Helicobacter pylori* were performed, and all values were within normal limits. Additionally, abdominal ultrasound was performed, which revealed a septated cyst and raised suspicion of an echinococcal cyst with dissemination, after which she was referred to an infectious disease specialist. Serology for echinococcus was performed and returned negative. Tumor markers, including CA125, were tested, with elevated values (45.3 mU/L). Additionally, MRI of the pelvis was performed and it showed extensive multicystic ovarian formations, with the right ovary cyst extending supraumbilically and the left ovary filling the pelvis and compressing surrounding structures. The uterus was displaced ventrally and to the right. Both formations were predominantly cystic, with discrete papillary proliferation. A small amount of fluid was visible in the pelvis. The patient was referred for a gynecological examination, which confirmed a multicystic septated mass of the right and left ovaries extending beyond the range of the vaginal probe. She was advised to undergo a total abdominal hysterectomy with bilateral salpingo-oophorectomy.

Pathohistological findings confirmed a serous cystadenofibroma of the ovary.

**Discussion:** The symptoms of ovarian neoplasm are nonspecific, making them easy to overlook in the early stages, as they can be attributed to other conditions. Symptoms often do not appear until the disease reaches an advanced stage. The most common symptoms include early satiety and bloating. Additionally, a palpable mass in the pelvic area, ascites, or diminished breath sounds due to pleural effusions may be found. Transvaginal ultrasound and/or abdominal and pelvic ultrasound are the first diagnostic methods. Ultrasound provides insight into the size, location, and complexity of the ovarian mass. Additional imaging studies, such as pelvic MRI, PET scans, and/or CT scans of the chest and abdomen, are used to define tumor spread. Along with imaging studies, serum levels of the tumor marker CA-125 are determined. Most epithelial ovarian tumors exhibit elevated CA-125 levels overall, although only 50% of early-stage epithelial ovarian neoplasm show increased CA-125 levels. Since only 40% of women who experience one of the nonspecific symptoms of ovarian neoplasm first seek medical attention from a gynecologist, family medicine physicians play an exceptionally important role as they are often the first point of contact.

**Conclusion:** The symptoms of ovarian tumors are nonspecific and often go unrecognized until the disease reaches an advanced stage. Therefore, it is essential for women to attend regular gynecological check-ups. Additionally, the importance of a detailed history and physical examination in family medicine clinics should be emphasized to enable earlier suspicion of a diagnosis and timely initiation of treatment.

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## ■ Skrb o bolesnicima na oralnoj antikoagulantnoj terapiji u ordinaciji obiteljske medicine

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**Uvod s ciljem:** Liječnici obiteljske medicine (LOM) svakodnevno skrbe o bolesnicima koji uzimaju antikoagulantne lijekove te trebaju biti upoznati sa indikacijama, nuspojavama i potencijalnim interakcijama, posebice direktnih oralnih antikoagulantnih lijekova (DOAK lijekova) koji postaju temelj suvremene antikoagulantne terapije. Ciljevi rada bili su: ustanoviti razloge i trend propisivanja DOAK-a odnosu na antagoniste vitamina K, utvrditi najčešće propisivane DOAK-e, doze i zabilježene nuspojave, analizirati jesu li prije uvođenja DOAK-a evidentirani potrebni podaci za određivanje adekvatne doze lijeka, procijeniti kontroliraju li liječnici bubrežnu funkciju te ispitati stavove i razinu znanja LOM o antikoagulantnim lijekovima.

**Ispitanici i metode:** Istraživanje je provedeno u dva dijela. U prvi dio uključeno je 256 ispitanika iz pet ordinacija obiteljske medicine koji su u vrijeme istraživanja uzimali DOAK, a podaci su prikupljeni pojedinačnom analizom podataka iz zdravstvenih kartona ispitanika. U drugom dijelu istraživanja provedena je anketa o znanju i stavovima LOM koju je ispunilo 117 ispitanika.

**Rezultati:** Istraživanjem je utvrđeno češće propisivanje DOAK-a u odnosu na antagoniste vitamina K (>80% ispitanika ima propisan DOAK), manjak evidentiranih podataka bitnih za doziranje DOAK-a (29% ispitanika uključenih u ovo istraživanje nije imalo evidentiran podatak o bubrežnoj funkciji u kompletnoj dostupnoj medicinskoj dokumentaciji u periodu zadnjih 6 mjeseci prije uvođenja DOAK-a, a >90% ispitanika nije imalo evidentiran podatak o tjelesnoj težini prilikom uvođenja apiksabana i edoksabana niti u periodu zadnjih 6 mjeseci), neadekvatno

evidentiranje nuspojava i praćenje bolesnika na terapiji DOAK-om (44% ispitanika nije imalo zadovoljavajući broj kontrola bubrežne funkcije po godini terapije DOAK-om) te manjak znanja o suvremenoj antikoagulantnoj terapiji (91,5% liječnika obiteljske medicine koji su sudjelovali u istraživanju ima nedovoljno znanje o suvremenoj antikoagulantnoj terapiji).

**Zaključak:** Obiteljski liječnici pri propisivanju antikoagulantne terapije trebaju razmotriti indikacije, potencijalne kontraindikacije i individualne karakteristike bolesnika kako bi se svakom bolesniku osigurala sigurna i učinkovita antikoagulantna terapija. Također trebaju više pažnje i vremena posvetiti adekvatnom vođenju medicinske dokumentacije, ranom uočavanju, evidentiranju i prijavljivanju nuspojava, praćenju bolesnika na terapiji DOAK-om te osuvremeniti svoja znanja o antikoagulantnoj terapiji.

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## Care of patients on oral anticoagulant therapy in a family medicine practice

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**Introduction with goals:** Family medicine physicians (FMPs) care for patients taking anticoagulant medications on a daily basis and need to be familiar with the indications, side effects and potential interactions, especially of direct oral anticoagulant medications (DOACs), which are the foundation of modern anticoagulant therapy. The objectives of the study were: to establish the reasons and trend of prescribing DOACs compared to vitamin K antagonists, to determine the most commonly prescribed DOACs, doses and reported side effects, to analyze whether the necessary data for determining the adequate dose of the drug were recorded before the introduction of DOACs, to assess whether physicians monitor renal function and to examine the attitudes and level of knowledge of FMPs about anticoagulant medications.

**Respondents and methods:** The research was conducted in two parts. In the first part, 256 respondents from five family medicine offices who were taking DOACs at the time of the study were included and the data were collected by individual analysis of data from the respondents' health records. In the second part of the research, a survey on FMPs knowledge and attitudes was conducted, which was completed by 117 respondents.

**Results:** The study found more frequent prescription of DOACs compared to vitamin K antagonists (>80% of respondents were prescribed DOACs), a lack of recorded data relevant to DOAC dosing (29% of respondents included in this study did not have recorded data on renal function in the complete available medical documentation in the last 6 months before the introduction of DOACs and >90% of respondents did not have recorded

data on body weight when introducing apixaban and edoxaban or in the last 6 months), inadequate recording of side effects and monitoring of patients on DOAC therapy (44% of respondents did not have a satisfactory number of renal function checks per year of DOAC therapy) and a lack of knowledge about modern anticoagulant therapy (91.5% of family medicine physicians who participated in the study had insufficient knowledge about modern anticoagulant therapy).

**Conclusion:** When prescribing anticoagulant therapy, family physicians should consider indications, potential contraindications and individual patient characteristics to ensure safe and effective anticoagulant therapy for each patient. They should also devote more attention and time to adequate medical record keeping, early detection, recording and reporting of adverse events, monitoring of patients on DOAC therapy and updating their knowledge of anticoagulant therapy.

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## ■ Utjecaj kliničke manifestacije bolesti i terapije na indeks stupnja trajnog oštećenja u oboljelih od sistemskog eritematoznog lupusa

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**Uvod s ciljem:** Sistemski eritemski lupus (SLE) je kronična multisistemska bolest koja predominantno zahvaća žene, dobi 20 do 40 godina. Etiologija bolesti rezultat je djelovanja genetskih, hormonskih, okolišnih, etničkih i imunoloških čimbenika. Patogeneza nije u potpunosti razjašnjena. U raznolikosti kliničke manifestacije najčešće dominiraju opći simptomi uz zahvaćenost kože i zglobova. Cilj istraživanja bio je ispitati povezanost kliničkih manifestacija bolesti i terapije sa stupnjem trajnog oštećenja u bolesnika sa SLE.

**Ispitanici i metode:** Presječno istraživanje s povijesnim podacima (2019. – 2023.g.) uključilo je 73 ispitanika sa SLE iz KBC Osijek. Prikupljeni su sljedeći podatci: spol, dob, dob postavljanja dijagnoze, duljina trajanja bolesti, prisutnost abnormalnih hematoloških pokazatelja, prisutnost karakterističnih protutijela, postojanje sniženih vrijednosti komponenti komplekta C3 i C4, kliničke manifestacije bolesti, podatci o korištenim lijekovima i duljini liječenja glukokortikoidima, indeks aktivnosti bolesti SELENA SLEDAI i indeks oštećenja uzrokovanog bolesti SLICC/ACR.

**Rezultati:** SLE je češća u žena, a najčešća dob pri postavljanju dijagnoze je između 40 i 60 godina. Bolesnici uključeni u istraživanje najčešće su bolovali kraće od 20 godina. Abnormalne hematološke pokazatelje imalo je 30,1 % ispitanika (trombocitopeniju, leukopeniju). ANA protutijelo bilo je pozitivno u 83,6 % ispitanika. Artralgijska i kožni osip bile su najčešće kliničke manifestacije. U liječenju je najviše ispitanika dobivalo glukokortikoide i antimalarike. Uočena je značajno pozitivna povezanost indeksa aktivnosti bolesti

(SELENA SLEDAI) s leukopenijom ( $R = 0,337$ ). Duljina trajanja bolesti je značajno povezana sa indeksom oštećenja SLICC/ACR ( $R = 0,548$ ) pa je tako u ispitanika u kojih bolest traje dulje, indeks oštećenja bio veći.

**Rasprava:** Za postavljanje dijagnoze koriste se EULAR/ACR klasifikacijski kriteriji iz 2019. godine. U osnovnim laboratorijskim nalazima vidljiva je pancitopenija uz posebno izražene neutropeniju i limfopeniju, a neki od specifičnih markera jesu: antinuklearna protutijela (ANA), anti-Ro, anti-Sm i anti-dsDNA protutijela. U terapiji SLE koriste se glukokortikoidi, biološki lijekovi, antimalarici te imunosupresivi. Za procjenu aktivnosti bolesti koristi se SELENA SLEDAI indeks koji boduje prisutnost kliničkih manifestacija bez obzira na težinu dok se pomoću SLICC/ACR indeksa određuje stupanj oštećenja uzrokovanog bolešću.

**Zaključak:** U ispitanika sa SLE postoji značajna povezanost leukopenije sa SELENA SLEDAI indeksom aktivnosti bolesti kao i povezanost duljine trajanja bolesti sa SLICC/ACR indeksom oštećenja. Navedeno je važno imati na umu pri praćenju oboljelih i redovitim laboratorijskim kontrolama u ambulantom obiteljskih liječnika.

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## ■ The influence of the clinical manifestation of the disease and therapy on the index of the degree of permanent damage in patients with systemic lupus erythematosus

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**Introduction with objective:** Systemic lupus erythematosus (SLE) is a chronic multisystemic disease that predominantly affects women, aged 20 to 40 years. The etiology of the disease is the result of genetic, hormonal, environmental, ethnic, and immunological factors. Its pathogenesis has not been fully elucidated. Among the variety of clinical manifestations, general symptoms involving the skin and joints most often dominate. This study aimed to examine the relationship between clinical manifestations of the disease and therapy and the degree of permanent damage in patients with SLE.

**Participants and methods:** A cross-sectional study with historical data (2019 - 2023) included 73 subjects with SLE from University Hospital Centre Osijek. The following data were collected: gender, age, age at diagnosis, duration of disease, presence of abnormal hematological indicators, presence of characteristic antibodies, presence of reduced values of complement components C3 and C4, clinical manifestations of the disease, data on the drugs used and duration of glucocorticoid treatment, activity index SELENA SLEDAI disease, and SLICC/ACR disease damage index.

**Results:** SLE is more common in women, and the most common age at diagnosis is between 40 and 60 years. Patients included in the study were most often ill for less than 20 years. Abnormal hematological indicators (thrombocytopenia and leukopenia) were observed in 30.1% of subjects. ANA antibodies were detected in 83.6% of the subjects. Arthralgia and skin rash were the most frequent clinical manifestations. The most frequent therapy were glucocorticoids and antimalarials. A significant positive correlation

was observed between the disease activity index (SELENA SLEDAI) and leukopenia ( $R = 0.337$ ). Disease duration was significantly related to the SLICC/ACR damage index ( $R = 0.548$ ); therefore, the damage index was higher in subjects whose disease lasted longer.

**Discussion:** The 2019 EULAR/ACR classification criteria are used to establish the diagnosis. In basic laboratory findings, pancytopenia is visible with particularly pronounced neutropenia and lymphopenia, and some of the specific markers are antinuclear antibodies (ANA), anti-Ro, anti-Sm and anti-dsDNA antibodies. Glucocorticoids, biological drugs, antimalarials and immunosuppressants are used to treat SLE. The SELENA SLEDAI index is used to assess disease activity, which scores the presence of clinical manifestations regardless of severity, whereas the degree of damage caused by the disease was determined using the SLICC/ACR index.

**Conclusion:** In participants with SLE, there was a significant correlation between leukopenia and the SELENA SLEDAI disease activity index, as well as a correlation between the duration of the disease and the SLICC/ACR damage index. The previously mentioned points should be considered when monitoring patients and doing routine laboratory tests at family doctor's offices.

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## **6. Prikaz slučaja**

## ■ Benigni paroksizmalni pozicijski vertigo Prikaz slučaja

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**Uvod s ciljem:** Benigni paroksizmalni pozicijski vertigo (BPPV) najčešći je vestibularni poremećaj, poglavito u ljudi starijih od 60 godina, koji se javi zbog degenerativnih procesa ili traume. Nastane kad se otokoniji (mali kristalići kalcija) odlome s normalne lokacije na vrhu utrikula te plutaju u polukružnim kanalčićima unutarnjeg uha. Najčešće se talože u posteriornim polukružnim kanalima gdje se miču kako se miče i glava čovjeka, ali i kad prestane micanje glave stvarajući lažni osjećaj vrtnje glave i tijela. Cilj ovog rada je senzibilizirati liječnike obiteljske medicine na ovaj benigni poremećaj koji se lako liječi u ambulantnim uvjetima bez potrebe upućivanja u sekundarnu zdravstvenu zaštitu te podsjetiti na izvođenje Dix Hallpike ili supine roll testa te Epleyevog zahvata što kod 90% pacijenata rezultira izliječenjem.

**Prikaz slučaja:** Pacijentica u dobi od 58 godina, inače čistačica u školi, dolazi u ordinaciju zbog nagle vrtoglavice pri pogledu ulijevo i pokretu vrata prema straga. Boluje od arterijske hipertenzije pet godina, u terapiji perindopril 4mg + amlodipin 5mg 1x1. Nepušač, alkohol ne konzumira, urednog apetita, redovite stolice, bez dizuričnih tegoba. Negira naglušnost, šum u uhu, dvoslike te glavobolju. Dobrog općeg stanja, eukardna, eupnoična. Urednih vrijednosti tlaka, pulzacija, saturacije. Ždrijelo mirno, bez eksudata. Limfni čvorovi vrata nisu povećani. Otokoskopi obostrano bez hiperemije zvukovoda, vidljivog trokutastog odsjaja. Rinoskopski uredna sluznica. Srce ritmično, tonovi jasni, bez šumova. Nad karotidama nema šumova. Uredan disajni šum. Abdomen mekan, bezbolan na palpaciju i bez organomegalije. Ekstremiteti simetrični, bez edema. Neurološki status neupadan, izokoričnih zjenica sa urednom reakcijom na svjetlost, bez faciopareze, bez lateralizacije, stabilna u Romberg položaju, urednog tandem hoda. Obzirom na uredan status, a karakteristične simptome vrtoglavice pri pokretu uz očuvanje sluha i bez šumova u uhu, postavi se radna dijagnoza BPPV-a. Učini se Dix Hallpike test na kojem se pokaže rotatorni nistagmus nakon desetak sekundi, ali koji se

smanjuje fiksacijom pogleda. Nakon tog provede se Epleyev zahvat. Pacijentica na kontroli za tjedan dana javi potpuni nestanak simptoma.

**Rasprava:** BPPV je kratkotrajan, no nagao i jak napadaj vrtoglavice što može uznemiriti i prestrašiti pacijenta. Sam napadaj traje do 30 sekundi, a pojavi se prilikom pogleda prema gore ili okretanja u postelji. Učestalost je visoka, 20-40% ukupnog broja vrtoglavica u općoj populaciji, a u starijih i preko 50%. S obzirom na dramatičnost simptoma, a relativno lake radne dijagnoze nakon dobro uzete anamneze i fizikalnog statusa, pacijenta se izliječi na razini primarne zdravstvene zaštite izvođenjem repozicijskih postupaka s ciljem postavljanja glave i tijela u određeni položaj kako bi vratili otolite na manje osjetljivo mjesto. Preporuka su Epleyev zahvat, supine roll te vestibularna rehabilitacija Brandt-Daroffovim vježbama kod refraktornih slučajeva ili jače izražene simptomatologije.

**Zaključak:** Obzirom na učestalost simptoma vrtoglavice u općoj populaciji, BPPV sindrom relativno je čest u svakodnevnoj praksi liječnika obiteljske medicine. Kako za samu radnu dijagnozu i liječenje nije potrebna određena specijalistička dijagnostika, vrlo lako se može pacijenta osloboditi straha i neugodnih tegoba koje uzrokuju osjećaj vrtoglavice izvođenjem jednostavnih repozicijskih zahvata u jednom susretu.

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2. Characteristics of assessment and treatment in Benign Paroxysmal Positional Vertigo (BPPV) J Vestib Res. 2020;30(1):55-62.doi: 10.3233/VES-190687

## ■ Benign paroxysmal positional vertigo Case report

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**Introduction and objective:** Benign paroxysmal positional vertigo is the most common vestibular disorder, especially in people over 60 years of age, that occurs due to degenerative processes or trauma. It occurs when otoconies (small calcium crystals) break off from their normal location at the top of the utricles and float in the semicircular canals of the inner ear. They are most often deposited in posterior semicircular canals where they move as the human head moves, but also when the head movement stops, creating a false sensation of spinning the head and body. The aim of this paper is to sensitize family physicians to this benign disorder that is easily treated in an outpatient setting without the need for referral to secondary health care, and to remind them of the Dix Hallpike or supine roll procedure and the Epley maneuver, which completely cures the patient in 90%.

**Case report:** A 58-year-old patient, a cleaning lady at school, comes to the office because of the sudden onset of dizziness when looking to the left and moving the neck to the back. She has been suffering from arterial hypertension for five years, in therapy perindopril 4mg + amlodipine 5mg 1x1. Non-smoker, does not consume alcohol, has a good appetite, regular bowel movements, no dysurical problems. She denies hearing loss, tinnitus, double vision and headaches. Good general condition, eucardic, eupnoic. Regular values of pressure, pulsation, saturation. Throat clear, no exudate. No lymphadenopathy. Otoloscopically on both sides without hyperemia of the ear canal, visible light reflex. Rhinoscopically neat mucosa. Regular rate and rhythm of the heart, no murmurs. There are no bruits above the carotids. Lungs are clear to auscultation. Abodomen is soft, nontender with no organomegaly. Extremities symmetrical, without edema. Neurological status inconspicuous, pupils are equally round and reactive to light, no facioparesis, no lateralization, stable in Romberg position, neat tandem gait. Given the normal status, and the characteristic symptoms of dizziness when moving with hearing preservation and no

tinnitus, a working diagnosis of BPPV is made. A Dix Hallpike test is performed, which shows rotator nystagmus after ten seconds, but which is reduced by fixation of the gaze. After that, the Epley maneuver is carried out. The patient reports a complete disappearance of symptoms at the check-up in a week.

**Discussion:** BPPV is a short-lived, but sudden and severe attack of dizziness that can upset and frighten the patient. The seizure itself lasts up to 30 seconds, and occurs when looking up or turning in bed. The incidence is high, 20-40% of the total number of dizziness in the general population, and in the elderly over 50%. Given the dramatic nature of the symptoms, and the relatively easy working diagnosis after a well-taken medical history and physical status, the patient is cured at the level of primary health care by performing reposition procedures with the aim of placing the head and body in a certain position in order to return the otoliths to a less sensitive place. The recommendation is the Epley maneuver, supine roll and vestibular rehabilitation with Brandt-Daroff exercises in refractory cases or more pronounced symptomatology.

**Conclusion:** Given the prevalence of the dizziness symptoms in the general population, BPPV syndrome is relatively common in the daily practice of family doctors. Since the occupational diagnosis and treatment itself does not require specific specialist diagnostics, it is very easy to relieve the patient of fear and unpleasant problems caused by the feeling of dizziness by performing simple repositioning maneuvers in one encounter.

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## ■ Medikamentozni osip uzrokovan perindoprilom: dijagnostički izazov

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**Uvod s ciljem:** Lijekovi mogu uzrokovati razne nuspojave, pri čemu je koža jedan od najčešće zahvaćenih organa. Medikamentozni osip radi moguće šarolike prezentacije i potrebe za isključenjem diferencijalno dijagnostičkih opcija može predstavljati izazov u praksi obiteljskog liječnika. Cilj ovog rada jest naglasiti važnost detaljne anamneze i promišljanje o nuspojavama lijekova u procesu dijagnosticiranja kožnih promjena u ordinaciji obiteljske medicine.

**Prikaz slučaja:** 82-godišnja pacijentica javila se na pregled u ordinaciju obiteljske medicine radi osipa kože u trajanju od mjesec dana, praćenog jakim svrbežom. Opisivala je pojavu sitnih kožnih promjena crvene boje na prednjoj strani trupa koje su se u posljednja dva dana difuzno proširile uz intenziviranje svrbeža koji joj je otežavao spavanje. Boluje od arterijske hipertenzije, a u kroničnoj terapiji uzima perindopril. Inspekcijom kože uočile su se hiperemične papule i plakovi koji su blijedili na pritisak te prisutnost ekskoriacija. Diferencijalno dijagnostički se, radi noćnog svrbeža i kliničke prezentacije, primarno posumnjalo na svrab te se pacijenticu uputilo na kožni test na *Acarus*. Na kontroli sutradan se, s obzirom na pogoršanje stanja, propisala betametazon krema i bolesnicu uputilo na hitni dermatološki pregled. Anamnestički su dermatolozi saznali o novouvedenom antihipertenzivom lijeku, perindoprilu, propisanom unazad šest tjedana te o povijesti liječenja od oralnog lihenia planusa. Učinila se biopsija kožnih promjena i testiranje na antigene buloznog pemfigoida uz preporuku nastavka propisane lokalne terapije, i ukidanje perindopri-la. Postavila se sumnja na bulozni pemfigoid ili medikamentozni egzantem. Kožnim skarifikatom isključio se svrab, a patohistološkom analizom tkiva potvrdila se dijagnoza reakcije na lijek. S obzirom na nezadovoljavajuću regresiju simptoma po ukidanju perindopri-la, uvela se oralna kortikosteroidna terapija, gastroprotekcija inhibitorom protonske pumpe te antihistaminik što je dovelo do smanjenja simptoma.

**Rasprava:** Dijagnosticiranje dermatoloških nuspojava lijekova prvenstveno se temelji na,

anamnestičkim podacima o vremenskoj korelaciji započinjanja terapije i pojave simptoma te tipu i distribuciji kožnih morfi. U 90% slučajeva, manifestiraju se kao morbiliformni egzantemi no mogu se prikazati i kao lihenoidna erupcija, ekfolijativni dermatitis, urtikariju (s ili bez angioedema) i hipersenzitivni vaskulitis. Kožne promjene diferencijalno dijagnostički predstavljaju veliki izazov u radu liječnika obiteljske medicine. U slučaju pacijentice primarna sumnja bio je svrab, no nisu evidentirana dva ključna podatka dijagnoza oralnog lihenia planusa, koja kao autoimuna bolest može skrenuti pozornost na mogućnost kožnog lihenia ili druge autoimune dermatoze; i nedavno uvedena antihipertenzivna terapija perindoprilom kao mogući uzrok erupcije. Otežavajući faktor je što se osipi kao nuspojave na lijekove ne javljaju uvijek u neposrednom vremenskom intervalu od početka liječenja, već i nekoliko tjedana nakon toga i mogu perzistirati tjednima ili mjesecima nakon ukidanja lijeka koji ga je izazvao. U slučajevima nejasne etiologije, zahvaćenosti velike površine tijela, pojave bula ili ljuštenja kože, postavljanje dijagnoze može zahtijevati biopsiju promjene što podrazumijeva upućivanje pacijenta dermatologu.

**Zaključak:** U ambulanti obiteljske medicine važno je razmotriti nuspojave lijekova kronične terapije, osobito pri konzultacijama vezanima za dermatološka stanja.

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## ■ Drug-induced rash due to perindopril: a diagnostic challenge

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**Introduction and aim:** Medications can cause various side effects, with the skin being one of the most frequently affected organs. A drug-induced rash, due to its potentially diverse presentation and the need to rule out differential diagnostic options, can be a challenge in general practice. The aim of this paper is to highlight the importance of a detailed medical history and consideration of drug side effects in diagnosing skin changes in family medicine practice.

**Case Report:** An 82-year-old female patient presented to a family medicine practice with a skin rash accompanied by severe itching. Over the past month, she noticed small red skin changes on the front side of her torso that spread diffusely over the past two days, causing sleep disturbances. Skin inspection revealed hyperemic papules and plaques that blanched upon pressure, along with excoriations. Based on the nocturnal itching, the primary differential diagnosis was scabies, and the patient was referred for a skin test for *Acarus mites*. At the follow-up visit the next day, due to the worsening condition, beta-methasone cream was prescribed, and the patient was urgently referred to a dermatologist.

During the dermatological examination, it was noted that she had recently started taking anti-hypertensive medication, perindopril, six weeks earlier and had a history of oral lichen planus. A biopsy of the skin lesions and testing for bullous pemphigoid antigens were performed, with a recommendation to continue the prescribed local therapy and discontinue the antihypertensive medication. The working diagnosis included a suspicion of bullous pemphigoid or a drug-induced exanthem. Scabies was ruled out through a skin scraping test and histopathological analysis confirmed a drug reaction. Due to the unsatisfactory regression of symptoms after discontinuing perindopril, oral corticosteroid therapy was introduced, along with gastroprotection and an antihistamine. Over time, the lesions took on a typical urticarial rash appearance.

**Discussion:** Diagnosing dermatological drug reactions is primarily based on clinical observations, patient history, the temporal correlation between therapy initiation and symptom onset, and the type and distribution of skin lesions. Differential diagnosis can be complex, as illustrated in this case. The initial suspicion with this patient was scabies, but due to a busy clinic setting, two key pieces of information were overlooked and only discovered at the dermatological examination. First, the diagnosis of oral lichen planus, which, as an autoimmune disease, should have directed the clinician's attention to the possibility of cutaneous lichen or another autoimmune dermatosis. Second, the recently introduced antihypertensive therapy with perindopril as a potential trigger for the eruption.

A complicating factor is that drug-induced rashes do not always appear immediately after starting medication but may emerge weeks later. Additionally, these rashes can persist for weeks or months after discontinuing the causative drug. In cases of unclear etiology or cutaneous reactions involving large areas of the body, blister formation or skin peeling, biopsy may be required, necessitating referral to a dermatologist.

**Conclusion:** In a family medicine clinic, it is important to consider the side effects of chronic therapy medications, especially during consultations related to dermatological conditions.

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## ■ Ramsay Hunt sindrom u sedamnaestogodišnjakinje – prikaz slučaja

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**Uvod:** Ramsay-Hunt sindrom ili herpes zoster oticus uzrokuje varicella zoster virus (VZV) koji može ostati latentan desetljećima kod osobe koja je u djetinjstvu preboljela vodene kozice. Reaktivacija VZV u retikularnoj formaciji ponsa, gdje se nalaze jezgre facijalnog i vestibulokohlearnog živca, rezultira izbijanjem herpesa zoster, odnosno Ramsay-Huntovog sindroma. Simptomi su izraženi na polovici lica, a manifestiraju se kao paraliza facijalnog živca, otalgija i osip koji zahvaća uho ako je zahvaćen samo facijalni živac, odnosno smetnje sluha i vertigo ako su zahvaćena oba živca. Nakon pojave simptoma, slabost lica obično je naizraženija unutar jednog tjedna. U prikazu pacijenta opisuje se sedamnaestogodišnja pacijentica s manifestacijom Ramsay-Hunt sindroma.

**Cilj:** Podignuti svijest liječnika obiteljske medicine (LOM) o mogućnosti reaktivacije VZV kod mladih pacijenata, kao i prepoznavanje bolesti sličnih manifestacija uključujući Bellovu paralizu, boreliozu, maligni eksterni otitis, akustički neurom ili neuralgiju trigeminusa.

**Prikaz slučaja:** U ambulantu LOM-a dolazi sedamnaestogodišnja djevojka zbog slabosti desne strane lica, bolova u desnom uhu, trnaca, slabosti desne strane lica, oslabljenog okusa i subfebriliteta do 37,5°C koji su počeli tri dana ranije. Iz anamneze saznajemo da je pacijentica preboljela vodene kozice u dobi od pet godina. Uočava se blago hiperemično ždrijelo s uvećanim tonzilama, obostrano palpabilni submandibularni limfni čvorovi uz bolnost desnih. Na desnoj uški vidljive su vezikularne promjene, a tragus je blago osjetljiv. Također, otežano zatvara i otvara desno oko, desni usni kut zaostaje, ne može napuhati obraze i ne može odignuti desnu obrvu. Vrijednosti laboratorijskih nalaza su unutar referentnih vrijednosti. Preporučuje se obrada na klinici za infektivne bolesti zbog sumnje na Ramsay-Hunt sindrom. Brisom desne uške i analizom likvora je detektirana VZV DNA, kojom je sindrom dokazan. Provedeno je liječenje aciklovirom (800mg)

5 puta dnevno tijekom 9 dana, odnosno do prestanka izbijanja vezikula, te metilprednizolonom (1mg/kg) tijekom 5 dana uz gastroprotekciju, kao i fizikalna terapija mimične muskulature. Na kontroli LOM-a nakon deset dana mimika je u potpunosti uredna.

**Rasprava:** Razlog zbog kojeg se VZV reaktivira i utječe na facijalni živac kod ovog sindroma nije poznat, a simptomi također variraju od osobe do osobe. Prednost poznavanja simptoma i znakova u praksi LOM-a došla je do izražaja u zbrinjavanju ove pacijentice obzirom da je zabrinuti otac inzistirao na upućivanju u otorinolaringološku ambulantu, no zahvaljujući poznavanju bolesti i komunikacijskim vještinama liječnika obiteljske medicine, pacijentica je odmah upućena na infektologiju. Pregledom literature je utvrđeno poklapanje simptoma i znakova u prikazane pacijentice s ostalim slučajevima ovog sindroma kod osoba bez komorbiditeta, uz uspješan oporavak.

**Zaključak:** Poznavanje znakova i simptoma može olakšati i ubrzati donošenje odluka, kao i spriječiti obavljanje nepotrebnih dijagnostičkih pretraga. Stoga, detaljno i ciljano uzimanje anamneze i klinički pregled omogućit će pravovremeno i uspješno liječenje pacijenata sa Ramsay-Hunt sindromom.

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## ■ Ramsay Hunt syndrome in a seventeen-year-old girl – a case report

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**Introduction:** Ramsay Hunt syndrome, or herpes zoster oticus, is caused by the varicella-zoster virus (VZV), which can remain latent for decades in individuals who had chickenpox during childhood. Reactivation of VZV in the reticular formation of the pons, where the facial and vestibulocochlear nerve nuclei are located, results in herpes zoster outbreak or leads to the development of Ramsay Hunt syndrome. Symptoms are localized to one side of the face and manifest as facial nerve paralysis, otalgia, and a rash affecting the ear if only the facial nerve is involved. If both nerves are affected, hearing disturbances and vertigo may also be present. After symptom onset, facial weakness typically reaches its peak within one week. This case report describes a seventeen-year-old female patient presenting with Ramsay Hunt syndrome.

**Objective:** To raise awareness among general practitioners (GPs) about the possibility of VZV reactivation in young patients, as well as recognizing diseases with similar manifestations, including Bell's palsy, acoustic neuroma, or trigeminal neuralgia.

**Case Report:** A 17-year-old girl is presented to her GP with right-sided facial weakness, right ear pain, tingling, right-sided facial weakness, impaired taste and low-grade fever up to 37.5°C, which had started three days earlier. The patient's history revealed that she had chickenpox at the age of five. Examination showed mildly hyperemic pharynx with enlarged tonsils, bilaterally palpable submandibular lymph nodes with tenderness on the right side. Vesicular changes were visible on the right auricle, and the tragus was mildly tender. She also had difficulty closing and opening her right eye, lagging of the right corner of her mouth, inability to puff her cheeks and inability to raise her right eyebrow. Laboratory findings were within reference ranges. Referral to an infectious diseases clinic was recommended due to suspected Ramsay Hunt syndrome. VZV DNA was detected via swab of

the right auricle and cerebrospinal fluid analysis, confirming the diagnosis. Treatment included acyclovir (800 mg) five times daily for 9 days, until vesicle eruption ceased, and methylprednisolone (1mg/kg) for 5 days with gastroprotection, as well as physical therapy for facial muscles. At the 10-day follow-up, facial mimicry was fully restored.

**Discussion:** The reason why VZV reactivates and affects the facial nerve in this syndrome remains unknown, and symptoms also vary among individuals. The advantage of recognizing symptoms and signs in GP practice was evident in this case, as the patient's concerned father initially requested a referral to an otorhinolaryngology clinic. However, thanks to the GP's knowledge of the disease and communication skills, the patient was promptly referred to infectious diseases specialists. A literature review confirmed that the symptoms and signs observed in this patient matched other cases of this syndrome in individuals without comorbidities, with successful recovery.

**Conclusion:** Recognizing signs and symptoms can facilitate and fasten decision-making, as well as prevent unnecessary diagnostic tests. Therefore, detailed and targeted history-taking and clinical examination enable prompt and successful treatment of patients with Ramsay Hunt syndrome.

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## ■ Prikaz mladog pacijenta s osteoporozom

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**Uvod s ciljem.** Osteoporoza je progresivna metabolička bolest koja dovodi do smanjene gustoće kostiju. Javnozdravstveni sustav veću pažnju obraća ženama nego muškarcima jer žive duže i u svakoj dobi imaju nižu mineralnu gustoću kostiju. Učestalost osteoporotskih prijeloma raste eksponencijalno s dobi, iako kod muškaraca počinje otprilike deset godina kasnije. Procijenjeno je da će u Europi do 90. godine života svaki osmi muškarac oboljeti od osteoporoze. Cilj rada je ukazati na mogućnost pojave osteoporoze u mlađih muškaraca koji u anamnezi imaju višestruke prijelome kostiju uslijed minimalne traume.

**Prikaz slučaja:** Pacijent u dobi od 28. godine javlja se u ordinaciju obiteljske medicine u listopadu 2019. godine zbog napuknuća 8. rebra tijekom vožnje kartinga. Iste godine u kolovozu zadobio je frakturu prednjeg luka 8. rebra udarcem u prozor, a godinu ranije imao je prijelom kažiprsta kada mu je prijatelj slučajno stao na ruku. U obiteljskoj anamnezi majka boluje od osteoporoze, pacijent negira teže bolesti, ne puši i ne konzumira alkohol. Fizikalni status bio je bez osobitosti, a indeks tjelesne mase 20 kg/m<sup>2</sup> (tjelesna visina 190 cm, tjelesna težina 73 kg). Zbog sumnje na osteoporozu pacijent je upućen na denzitometriju koja pokazuje opsežnu osteoporozu kralježnice s T vrijednosti: -4.9, dok su kuk i vrat bedrene kosti osteopenični, granično s T vrijednosti: -2.4. Učinjena je opsežna endokrinološka obrada u smislu otkrivanja sekundarnog uzroka osteoporoze. Utvrđeno je da je funkcija gonadalnih žlijezda, kore nadbubrežne žlijezde i štitnjače uredna. Gastroenterološkim pregledom nađena je steatoreja koja se nakon uvođenja nadomjesne enzimske terapije povukla. U siječnju 2021. godine je započeta terapija natrij ibandronatom, a u travnju iste godine zamijenjena s denosumabom svakih 6 mjeseci. Od ostale terapije preporučeni su kalcijev karbonat a 1000 mg i D vitamin. Do 2023. godine došlo je do značajnog porasta mineralne koštane mase (BMD) u lumbalnoj kralježnici, ali je zglob kuka i dalje bez promjena. Još uvijek nije otkriven uzrok osteoporoze i steatoreje.

**Rasprava:** Iako je najčešća u postmenopausalnih žena, osteoporoza u muškaraca je nedovoljno prepoznata i dijagnosticirana bolest. Prema istraživanjima, manja je vjerojatnost da će muškarci nakon prijeloma kuka biti dijagnostički obrađeni i primiti odgovarajuću terapiju (4,5 % naspram 49,5 % žena). Njih 20 do 50% neće biti u stanju samostalno živjeti, a svaki treći stariji od 65 godina će umrijeti unutar prve godine. Zbog 20% višeg vrška koštane mase i 30% većih kostiju, muškarcima osteoporoza nastupa otprilike 10 godina nakon žena. U određenim slučajevima, zbog sekundarnih uzroka ili nepostizanja vršne koštane mase, muškarcima mogu ranije nastupiti osteoporotični prijelomi i smanjenje mineralne gustoće kostiju, a njih 2-3% ima dijagnozu odgođenog puberteta, što može dovesti do idiopatske osteoporoze. Dijagnoza idiopatske osteoporoze primjenjuje se za muškarce mlađe od 60 godina u kojih nema drugih mogućih uzroka bolesti, a sekundarna osteoporoza dijagnosticira se u 40-60% kao posljedica kroničnih, endokrinoloških i gastroenteroloških bolesti.

**Zaključak:** Liječnici obiteljske medicine imaju značajnu ulogu u prepoznavanju simptoma osteoporoze. Kod mlađih muškaraca s višestrukim prijelomima važno je posumnjati i na osteoporozu te uputiti pacijenta na dijagnostičku obradu kako bi se pravovremeno uvela terapija i dovelo do bolje prognoze bolesti.

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## ■ Young patient presenting with osteoporosis

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**Introduction and aim.** Osteoporosis is a progressive metabolic disease that causes lower bone density. The public health system brings more attention to women than men because they live longer and have lower bone density in any age. The incidence of osteoporotic fractures grows exponentially with age, although in men it increases 10 years later. It is estimated that in Europe, by the age of 90, every eighth man will be diagnosed with osteoporosis. The aim of this paper is to warn of a possibility of osteoporosis in young men that have had multiple fractures with minimal trauma.

**Case report.** 28-year-old patient reported to his family doctor in October of 2019 for an infraction of the eighth rib during carting after he already had a fracture of that rib that same year by crashing into a window and a year before he suffered a fracture of his index finger after his friend accidentally stepped on his hand. In his family history it is noted that his mother has osteoporosis and the patient suffers from no chronic illnesses. His status showed nothing out of the ordinary, his body mass index was 20 kg/m<sup>2</sup> (body height 190cm, body weight 73 cm). The patient was sent for densitometry in suspicion of osteoporosis and his results showed extensive spine osteoporosis with T-score -4.9, while hip and femur neck were borderline osteopenic with a T-score of -2.4. A detailed analysis by an endocrinologist was performed in order to detect a possible secondary cause for the disease. His gonadal, thyroid and adrenal function was normal. A gastroenterologist discovered steatorrhea which resolved after enzyme replacement therapy. In January of 2021 a course of sodium ibandronate therapy was started and then replaced with denosumab in April every sixth month. He was also recommended 1000 mg of calcium carbonate and vitamin D. By 2023 there has been a substantial increase of mineral bone mass of the lumbar spine, but his hip is still osteopenic. The cause for osteoporosis and steatorrhea has not been found yet.

**Discussion.** Although most often in postmenopausal women, osteoporosis in men doesn't

have enough recognition. According to research, it is less likely that men will be further treated post-fracture (only 4,5% against 49,5% of women). 20-50% men post-fracture will not be able to live alone and every third older than 65 will die within the year. Thanks to their 20% higher bone mass peak and 30% bigger bones, men's osteoporosis appears 10 years after women's. But sometimes, either because of secondary causes or lower bone mass peak, fractures and lower bone density can appear earlier than usual. It must be noted that papers show that 2-3% of those men have a delayed puberty diagnosis, which can lead to idiopathic osteoporosis. The diagnosis of idiopathic osteoporosis is indicated for men younger than 60 when every other cause is excluded. Secondary osteoporosis is diagnosed in 40-60% of men younger than 60 as a result of chronic, endocrine and gastroenterological diseases.

**Conclusion:** Family physicians have an important role in recognizing symptoms of osteoporosis. Younger male patients with multiple fractures must raise a red flag for the doctor and they must be further processed in order to initiate rightful therapy improve disease prognosis.

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## ■ Pacijent sa subarahnoidalnim krvarenjem u ordinaciji obiteljske medicine

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**Uvod s ciljem.** Spontano (netraumatsko) subarahnoidalno krvarenje (SAH) treći je najčešći uzrok svih moždanih udara. Vodeći simptom je izrazito jaka novonastala glavobolja. Cilj ovog rada bio je naglasiti važnost anamneze i kliničkog pregleda u svakodnevnom radu i prepoznavanju po život opasnih stanja poput SAH-a.

**Prikaz slučaja.** Pacijent u dobi od 49 godina dolazi u ambulantu u pratnji supruge. Navodi da od jučer osjeća pritisak u glavi, pulsirajuću glavobolju u području čela i zatiljka. Preznojava se, povraća, do sada je povratio osam puta. Svijest nije gubio. Smeta mu svjetlost i zvukovi. Afebrilan. Osjeća se iscrpljeno. Inače ga nikad ne boli glava. Negira nedavni pad. Uzeo je ibuprofen u dozi od 600 mg, ali bez učinka. Zna da ima malo povišeni krvni tlak, otkriven na sistematskom pregledu pred 4 godine, ali ga ne mjeri i ne uzima terapiju. Pušač, pack year 30. Mokrenje i stolica bez osobitosti. Uvidom u e-zdravstveni karton vidljivo je da ne dolazi često u ambulantu, ima zabilježene tri posjete. Neurološki status bio je bez osobitosti osim kod izvođenja meningealnih testova pri čemu je kočio vrat, što je uz jaku glavobolju jedna od najznačajnijih karakteristika SAH-a, uz javljanje pojačane boli okcipitalno. Somatski status bio je uredan osim izmjerenih povišenih vrijednosti krvnog tlaka, RR 150/90 mmHg. S obzirom na pozitivan znak nadražaja meningi i novonastalu glavobolju, upućen je u hitnu neurološku ambulantu s popratnim uputnim pismom. Slijedeći dan supruga nas telefonski obavještava da je gospodin hospitaliziran zbog subarahnoidalnog i intracerebralnog krvarenja uslijed rupture aneurizme prednje komunikantne arterije (ACoA). Neurokirurško liječenje uključivalo je postavljanje kleme na vrat aneurizme, a boravak u bolnici komplicirao se pneumonijom i dekubitusom na trtici. Nakon završenog neurokirurškog liječenja dezorjentiran prostorno i vremenski premješten je u Krapinske toplice zbog provođenja neurorehabilitacije.

**Rasprava.** Prosječna incidencija SAH-a u Europi je 10-12 na 100 000 stanovnika. SAH se može pojaviti u svakoj životnoj dobi, najčešće oko 50. godine i dva puta je češći kod žena nego muškaraca. Mortalitet u prvih 6 mjeseci iznosi i do 40%. Oko trećina preživjelih imaće trajni neurološki deficit. U 85% slučajeva nastaje rupturam sakularne aneurizme arterije na bazi mozga. Stečeni rizični čimbenici za razvoj aneurizmi su pušenje, hipertenzija i alkoholizam. Nakon rupture aneurizme oko 10% bolesnika umire prije dolaska u bolnicu. Vodeći simptom SAH-a su naglo nastale, vrlo intenzivne, eksplozivne glavobolje. Često ih opisuju poput udara groma, a u usporedbi sa prijašnjim glavoboljama kao jače nego ikad. Ostali simptomi uključuju gubitak svijesti, bol i ukočenost vrata, vrtoglavicu, mučninu, povraćanje i oduzetost (slabost) jedne polovice tijela. U slučaju pritiska aneurizme na treći moždani živac javlja se oftalmoplegija. Neki bolesnici mogu biti pojačano nemirni i konfuzni te njihovo stanje nalikuje psihozi, a kod nekih se javljaju konvulzije. Slikovna dijagnostička obrada SAH-a uključuje CT mozga i angiografiju krvnih žila mozga. Po potrebi se izvodi lumbalna punkcija. Liječenje aneurizmatškog SAH-a uključuje endovaskularno zatvaranje aneurizme (embolizacija, engl. coiling) ili postavljanje kleme na vrat aneurizme (engl. clipping).

**Zaključak.** Liječnik obiteljske medicine najčešće susreće pacijente sa primarnim glavoboljama. Kod naglo nastale glavobolje poput udara groma treba posumnjati na SAH i osobu odmah uputiti u bolnicu.

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## ■ Patient with subarachnoid hemorrhage in a family medicine office

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**Introduction.** Spontaneous (non-traumatic) subarachnoid hemorrhage (SAH) is the third most common cause of all strokes. The leading symptom is an extremely severe acute headache. The aim of this paper was to emphasize the importance of medical history and clinical examination in everyday work and the recognition of life-threatening conditions such as SAH.

**Case report.** The patient at the age of 49 comes to the clinic accompanied by his wife. He states that since yesterday he has been feeling pressure in his head, a throbbing headache in the area of the forehead and the back of his head. He's been sweating, vomiting, and he's vomited eight times so far. He did not lose consciousness. He is bothered by light and sounds. No fever. He feels exhausted. Otherwise, he never has a headache. He denies a recent fall and a blow to the head. He took ibuprofen at a dose of 600 mg for headaches, but with no effect. He knows that he has slightly elevated blood pressure, discovered at a physical examination 4 years ago. He does not measure blood pressure at home and does not take therapy. Smoker, pack year 30. Urination and stool without peculiarities. By inspecting the e-health record, it is evident that he does not come to the clinic often, he has recorded three visits. The neurological status was unremarkable, except for meningitic tests, where the neck was stiff, which, along with a severe headache, is one of the most significant characteristics of SAH, with increased occipital pain. Somatic status normal except for measured elevated blood pressure, RR 150/90 mmHg. Given the positive sign of meningeal irritation and a newly occurring headache, he was referred to the emergency neurology clinic with a referral and a referral letter. The next day, his wife informs us by phone that he has been hospitalized due to subarachnoid and intracerebral hemorrhage due to a rupture of the anterior communicating artery (ACoA) aneurysm. Neurosurgical treatment included placing a clamp on the neck of the aneurysm, and the hospital stay was complicated by pneumonia and pressure ulcers on the coccyx. After completing

neurosurgical treatment, disoriented in space and time, he was transferred to Krapinske Toplice for neurorehabilitation.

**Discussion.** The average incidence of SAH in Europe is 10-12 per 100 000 inhabitants. SAH can occur at any age, most often around the age of 50, it is twice as common in women as men. Mortality in the first 6 months is up to 40%. About a third of the survivors will have a permanent neurological deficit. In 85% of cases, it is caused by the rupture of the saccular aneurysm of the artery at the base of the brain. Acquired risk factors for the development of aneurysms are smoking, hypertension and alcoholism. After an aneurysm rupture, about 10% of patients die before arriving at the hospital. The leading symptom of SAH is sudden, very intense, explosive headache. It is often described as lightning strikes, thunderclap headache. Compared to previous headaches, it's stronger than ever. Other symptoms include loss of consciousness, neck pain and stiffness, dizziness, nausea, vomiting, and paralysis (weakness) of one half of the body. In the case of pressure of the aneurysm on the third cranial nerve, ophthalmoplegia occurs. Some patients may be intensely restless and confused, and their condition resembles psychosis, and some may experience convulsions. Diagnostic imaging methods of SAH include CT of the brain and angiography of the blood vessels of the brain. If necessary, a lumbar puncture is performed. Treatment of aneurysmatic SAH includes endovascular closure of the aneurysm (embolization, coiling) or placement of a clamp on the neck of the aneurysm (clipping).

**Conclusion.** A family doctor most often encounters patients with primary headaches. In the case of a sudden thunderclap headache, SAH should be suspected and the person should be immediately referred to the hospital.

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## ■ Akutna hiponatremija u starijih pacijenata na kombiniranoj diuretskoj terapiji – prikazi slučajeva

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**Uvod s ciljem:** Akutna hiponatremija je hitno stanje koje nastaje zbog naglog smanjenja koncentracije natrija u serumu (<135 mmol/L) te može dovesti do mučnine, povraćanja, kardiorespiratornog distresa i neuroloških poremećaja. Ovi prikazi slučajeva opisuju dvije starije pacijentice koje su razvile akutnu hiponatremiju kao posljedicu kombinirane diuretske terapije.

**Prikaz slučaja:** Pacijentica 1 (P1) ima 85 godina te boluje od arterijske hipertenzije, kroničnog srčanog zatajenja i šećerne bolesti tipa 2. U stalnoj terapiji ima valsartan 160 mg (0-0-1), moksonidin 0,2 mg (0-1-2), dapagliflozin 10 mg (1-0-0), nebivolol 5 mg (1-0-0), torasemid 5 mg (1-0-0), te su prije mjesec dana u terapiju uvedeni urapidil 90 mg (1-0-1) i indapamid 1,5 mg (1-0-0) po preporuci kardiologa. P1 se javlja liječniku obiteljske medicine (LOM) na pregled zbog izrazito otečenih potkoljenica i zaduhe unazad 2 tjedna. Navodi da ostaje bez zraka u minimalnom naporu. U kliničkom statusu su zabilježeni SpO<sub>2</sub> 89%, 60/min, tlak 154/78 mmHg, oslabljen šum disanja i krepitacije obostrano bazalno te tjestasti edemi obje potkoljenice i stopala. Pacijentica je upućena u hitnu službu (HS) zbog sumnje na plućnu kongestiju u sklopu dekompenzacije kroničnog zatajenja srca. U HS je su ordinirane 2 ampule fursemida. P1 se otpušta kući iz HS uz kliničko poboljšanje i preporuku fursemid 40 mg (1-1-0) uz suplementaciju kalija. 7 dana kasnije P1 se javlja LOM-u zbog mučnine i povraćanja. U laboratorijskim nalazima su natrij 128 mmol/L, i kalij 5.3 mmol/L. Savjetovan je pojačan unos soli uz redovitu kontrolu tlaka, a iz terapije su isključeni fursemid na 3 dana te indapamid i torasemid. Kontrolni natrij bio je 132 mmol/L. Pacijentica 2 (P2) ima 82 godine te boluje od arterijske hipertenzije. U stalnoj terapiji koristi perindopril/indapamid/amlodipin 10/2,5/5 mg (1-0-0), moksonidin 0,2 mg (0-2-1), nebivolol 2,5 mg (1-0-0), eplerenon 25 mg (1-0-0) i fursemid 40 mg (1-0-0 SDD). Pacijentica se javlja LOM-u zbog mučnine i proljeva uz subfebrilitet. Savjetovana joj

je simptomatska terapija zbog blago povišenih upalnih parametra. Mjesec dana nakon toga javlja se kćer u ordinaciju jer je P2 dezorijentirana i učestalo pada zbog vrtoglavice. U laboratoriju je natrij bio 111 mmol/L te ja pacijentica upućena u HS. U HS je ordiniran 3% NaCl te je pacijentica otpuštena kući. Iz terapije je ukinut indapamid. Kontrolni natrij za 3 dana bio je 133 mmol/L, a nakon 2 tjedna 134 mmol/L.

**Rasprava:** Kod obje pacijentice hiponatremija je nastala zbog kombiniranog učinka diuretika koji uzrokuju povećanu natriurezu i diurezu. Indapamid je metabolički neutralan tiazidima sličan diuretik, no uz njega su zabilježeni slučajevi hiponatremije u starijih pacijenata. Furosemid povećava natriurezu blokadom reapsorpcije natrija u Henleovoj petlji, dok eplerenon inhibira djelovanje aldosterona, što dodatno smanjuje reapsorpciju natrija u bubrežima.

**Zaključak:** Ovi slučajevi naglašavaju potrebu za opreznim propisivanjem kombinirane diuretske terapije, posebno u starijih pacijenata. Nije preporučena primjena tiazidskih i tiazidima sličnih diuretika u pacijenata koji imaju akutnu ili kroničnu hiponatremiju. Za prevenciju komplikacija obavezna je kontrola koncentracije elektrolita u serumu mjesec dana nakon uvođenja kombinirane diuretske terapije, a zatim jednom godišnje ako su inicijalni nalazi bili uredni. Bitna je pravovremena prilagodba terapije jer je hiponatremija povezana s lošijom prognozom i preživljenjem.

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## ■ Acute Hyponatremia in Elderly Patients on Combined Diuretic Therapy – Case Reports

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**Introduction with aim:** Acute hyponatremia is a medical emergency caused by a sudden decrease in serum sodium concentration (<135 mmol/L) and can lead to nausea, vomiting, cardiorespiratory distress, and neurological disorders. These case reports describe two elderly female patients who developed acute hyponatremia because of combined diuretic therapy.

**Case Presentation:** Patient 1 (P1) is an 85-year-old woman with a history of arterial hypertension, chronic heart failure, and type 2 diabetes. Her regular therapy includes valsartan 160 mg (0-0-1), moxonidine 0.2 mg (0-1-2), dapagliflozin 10 mg (1-0-0), nebivolol 5 mg (1-0-0), and torasemide 5 mg (1-0-0). One month ago, urapidil 90 mg (1-0-1) and indapamide 1.5 mg (1-0-0) were added to her therapy by a cardiologist. P1 visited her family medicine physician (FMP) due to markedly swollen shins and shortness of breath over the past two weeks. She reports experiencing breathlessness even with minimal physical effort. Clinical findings included SpO<sub>2</sub> 89%, heart rate 60/min, blood pressure 154/78 mmHg, diminished breath sounds, bilateral basal crackles, and significant pitting edema of both lower legs and feet. She was referred to the emergency department (ED) with suspected pulmonary congestion as part of a decompensation of chronic heart failure. In the ED, two ampules of furosemide were administered. P1 was discharged home with clinical improvement and a recommendation for furosemide 40 mg (1-1-0) along with potassium supplementation. Seven days later, P1 returned to her FMP due to nausea and vomiting. Laboratory results showed sodium 128 mmol/L, and potassium 5.3 mmol/L. Increased salt intake was advised with regular blood pressure monitoring, and furosemide was discontinued for 3 days along with indapamide and torasemide. Follow-up sodium levels were 132 mmol/L. Patient 2 (P2) is an 82-year-old woman with arterial hypertension. Her regular therapy includes perindopril/indapamide/

amlodipine 10/2.5/5 mg (1-0-0), moxonidine 0.2 mg (0-2-1), nebivolol 2.5 mg (1-0-0), eplerenone 25 mg (1-0-0), and furosemide 40 mg (1-0-0). P2 visited her FMP with nausea, diarrhea, and low-grade fever. Symptomatic therapy was advised due to mildly elevated inflammatory markers. A month later, P2's daughter reported that the patient was disoriented and experiencing frequent falls due to dizziness. Laboratory results showed sodium at 111 mmol/L, and she was referred to the ED. In the ED, 3% NaCl was administered, and P2 was discharged home. Indapamide was discontinued from her therapy. Sodium levels after three days were 133 mmol/L, and after two weeks, 134 mmol/L.

**Discussion:** In both patients, hyponatremia was caused by the combined effect of diuretics, which increased natriuresis and diuresis. Indapamide is a metabolically neutral thiazide-like diuretic, but cases of hyponatremia in elderly patients have been reported. Furosemide increases natriuresis by blocking sodium reabsorption in the Henle's loop, while eplerenone inhibits aldosterone, further reducing sodium reabsorption in the kidneys.

**Conclusion:** These cases highlight the need for caution when prescribing combined diuretic therapy, particularly in elderly patients. The use of thiazide and thiazide-like diuretics is suggested in patients with acute or chronic hyponatremia. To prevent complications, it is essential to monitor serum electrolyte concentrations one month after initiating combined diuretic therapy and then annually if the initial results are normal. Timely adjustment of treatment is crucial, as hyponatremia is associated with poorer prognosis and survival.

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## ■ Muškarac s hipertireozom

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**Uvod s ciljem:** Hipertireoza je stanje povišene razine trijodtironina (T3) i/ili tiroksina (T4). Jedan od najčešćih razloga hipertireoze je Gravesova bolest, autoimuna bolest koju karakterizira tireotoksikoza uzrokovana cirkulirajućim protutijelima klase IgG koji se vežu za TSH receptore na tireocitima te tako oponašaju stimulirajuće djelovanje TSH. Osam puta je češća u žena. Česti simptomi i znakovi koji se pojavljuju kod pacijenata su: razdražljivost, nesanica, malaksalost, gubitak tjelesne mase, pojačano znojenje, nepodnošenje vrućine, učestale stolice, tahikardija, fibrilacija atrijska. Cilj ovog rada je osvijestiti da i muškarci starije životne dobi mogu oboljeti od hipertireoze te naglasiti važnost pravovremenog prepoznavanja simptoma.

**Prikaz slučaja:** Pacijent u dobi od 72 godine javlja se svom LOM-u zbog dispneje u naporu, pojačanog znojenja, osjećaja vrućine, tremora ruku, nenamjernog gubitka tjelesne težine i palpitacija. Negira osjećaj pritiska u prsima i oticanja potkoljenica. Boluje od poremećaja srčanog ritma (supraventrikularnih ekstrasistola, poremećaja AV provođenja u vidu Mobitza II i arterijske hipertenzije, iritabilnog kolona, divertikuloze crijeva te benigne hiperplazije prostate. Kliničkim pregledom nisu utvrđena odstupanja. Preporučeno mu je učiniti ergometriju, holter EKG-a, UZV srca te mu je izdana uputnica za laboratorij, kao i da se u slučaju pogoršanja simptoma javi na hitni prijem. Na kontrolnom pregledu nakon 10 dana pacijent i dalje ima iste simptome. Nalazi ergometrije, holter EKG-a, UZV srca te laboratorijski nalazi bez većih odstupanja. U terapiju uveden alprazolam (0,25mg, prema potrebi) te je postavljena sumnja na bolest štitnjače. Nalazima je utvrđena hipertireoza (povišene razine fT4, fT3 i Anti TPO protutijela uz snižen TSH), uvedena je terapija tiamazolom u dozi od tri puta po dvije tablete te je pacijent upućen endokrinologu. Endokrinološkom obradom dijagnosticirana tireotoksikoza u sklopu Gravesove

bolesti uzrokovana ingestijom joda kojeg je pacijent uzimao tijekom godinu dana (prestaio unatrag dva mjeseca). UZV štitnjače pokazao uvećanje štitnjače, bez drugih patoloških promjena. U terapiju uveden propranolol u dozi od 40mg te je smanjena doza tireostatika i savjetovana kontrola za mjesec dana uz nove nalaze fT4 i TSH. Na drugom kontrolnom pregledu razine fT4 i TSH i dalje visoke, postavlja se sumnja na autoimuni tireoiditis te se savjetuje povećanje doze tireostatika uz nastavak terapije propranololom. Na idućoj kontroli pacijent navodi kako su se simptomi smanjili. Razine fT4 u padu. Savjetovan nastavak terapije tiamazolom i propranololom, uveden je enteralni kalorijski napitak Ensure Compact zbog gubitka 12kg u protekla 2 mjeseca. Tijekom idućih kontrola pacijent biva sve boljeg općeg stanja, razine fT4 i TSH su se vratile na razine referentnih vrijednosti, TR-AK protutijela negativna, tiamazol smanjivan po režimu 3x2; 2x2; 3,0,0 te 1,0,0 u razmacima od dva mjeseca do potpunog ukidanja. Nastavlja se praćenje razina TSH i fT4 svakih 6 mjeseci.

**Rasprava:** U ovom slučaju postavlja se pitanje je li ingestija joda koji je pacijent uzimao svaki dan tijekom godine dana samoinicijativno u post covid razdoblju zaista dovela do tireotoksikoze te povećanih Anti TPO protutijela? Ukoliko se stvarno radilo o Gravesovoj bolesti, kako je dijagnosticirano pri prvom pregledu, kako je moguće da je bolest u potpunosti nestala pola godine nakon uvođenja terapije, uzimajući u obzir da je u literaturi Gravesova bolest navedena kao kronična bolest koja zahtijeva dugoročno liječenje.

**Zaključak:** Gravesova bolest je kronična te iznimno rijetka u muškaraca, češće je viđamo u žena srednje dobi. Uzroci i razlog nastanka i danas su nepoznanica. Iako ingestija veće količine joda može dovesti do hipertireoidizma i povećanja štitnjače, ipak većina ostaje eutireoidna.

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## ■ A Man with Hyperthyroidism

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**Introduction with aim:** Hyperthyroidism is a condition characterized by elevated levels of triiodothyronine (T3) and/or thyroxine (T4). One of the most common causes of hyperthyroidism is Graves' disease, an autoimmune disorder characterized by thyrotoxicosis caused by circulating IgG antibodies that bind to TSH receptors on thyrocytes, thereby mimicking the stimulating effect of TSH. It is eight times more common in women. Common symptoms and signs that appear in patients include: irritability, insomnia, fatigue, weight loss, increased sweating, heat intolerance, frequent stools, tachycardia, and atrial fibrillation. The aim of this paper is to raise awareness that even older men can suffer from hyperthyroidism and to emphasize the importance of timely symptom recognition.

**Case report:** A 72-year-old male patient presented to his GP with complaints of exertional dyspnea, increased sweating, heat intolerance, hand tremors, unintentional weight loss, and palpitations. He denied chest pressure and lower leg swelling. The patient has a history of cardiac arrhythmia (supraventricular ectopic beats, AV conduction disorder in the form of Mobitz II, and hypertension), irritable bowel syndrome, diverticulosis, and benign prostatic hyperplasia. Clinical examination revealed no significant deviations. He was advised to undergo ergometry, Holter ECG, and echocardiography, and was referred to the laboratory. He was also advised to visit the emergency department if his symptoms worsened. After 10 days, the patient returned with the same symptoms. His ergometry, Holter ECG, echocardiography, and laboratory results showed no significant deviations. Alprazolam (0.25mg, as needed) was introduced, and thyroid disease was suspected. Thyroid tests confirmed hyperthyroidism (elevated fT4, fT3, and Anti TPO antibodies, and low TSH), and therapy with thiamazole was initiated (three doses of two tablets). The patient was referred to an endocrinologist. Endocrinological evaluation confirmed thyrotoxicosis due to Graves' disease, which was caused by iodine intake over the past year

(discontinued two months ago). Thyroid ultrasound revealed an enlarged thyroid but no other pathological changes. Propranolol (40mg) was introduced, the dose of thionamide was reduced, and a follow-up was scheduled for one month with new fT4 and TSH tests. During the next visit, fT4 and TSH remained elevated, and autoimmune thyroiditis was suspected. The thionamide dose was increased, and propranolol therapy continued. On the following visit, the patient reported symptom improvement, and fT4 levels were decreasing. He was advised to continue therapy with thiamazole and propranolol, and an enteral caloric supplement (Ensure Compact) was prescribed due to a 12kg weight loss over the past two months. In subsequent visits, the patient's general condition improved, with fT4 and TSH returning to reference levels. TR-AK antibodies were negative, and thiamazole was tapered according to the prescribed regimen 3x2; 2x2; 3,0,0 to 1,0,0 every two months until discontinuation. Follow-up was scheduled for monitoring TSH and fT4 levels every 6 months.

**Discussion:** This case raises the question of whether the iodine intake, which the patient had taken daily for one year on his own initiative during the post-COVID period, truly caused thyrotoxicosis and increased Anti TPO antibodies. If this was indeed Graves' disease, diagnosed at the first visit, how could the disease have completely disappeared six months after therapy initiation, considering that Graves' disease is a chronic condition requiring long-term treatment according to the literature?

**Conclusion:** Graves' disease is a chronic and extremely rare condition in men, more commonly seen in middle-aged women. The causes and mechanisms of its development are still unknown. Although excessive iodine intake can lead to hyperthyroidism and thyroid enlargement, most people remain euthyroid.

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## ■ Rijetki slučaj aortitisa: dijagnoza, terapija i ishod

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**Uvod s ciljem:** Aortitis je upala aorte koja ponekad uzrokuje aneurizmu ili začepljenje. To je rijetka bolest koja se najčešće povezuje sa autoimunim bolestima poput bolesti vezivnog tkiva i vaskulitisa kao što su Takayashu arteritis, gigantocelularni arteritis, te spondiloartropatije povezane sa HLA-B27 i infektivnim stanjima. Infektivne etiologije uključuju tuberkulozu, sifilis, i druge bakterije. Cilj ovoga rada je naglasiti važnost sveobuhvatnog diferencijalnodijagnostičkog pristupa pacijentima koji se prezentiraju nespecifičnim simptomima.

**Prikaz slučaja:** 68-godišnji pacijent inicijalno se javio liječnici obiteljske medicine zbog nespecifičnih tegoba u vidu nelagode u donjem dijelu abdomena, afebrilan i bez znakova probavnih smetnji. Pacijent se kontrolira kod gastroenterologa zbog cističnih tvorbi gušterače te kod kardiologa zbog angine pectoris i nesigifikantne stenozе LAD. Prilikom fizikalnog pregleda ustanovljeno je da je abdomen mekan i osjetljiv na palpaciju suprapubično. Učinjena je kompletna krvna slika (Leu  $13,4 \times 10^9/L$ ) uz biokemijske parametre (C-reaktivni protein, CRP 112,5mg/L) te sediment urina (Eritrociti 17st/v.p.). Obzirom na kliničku sliku i laboratorijsku analizu postavljena je dijagnoza urinarne infekcije te se pacijenta uputi učiniti urinokulturu. U terapiju je uveden antibiotik, klavulonska kiselina 875mg + amoksicilin 125mg/7dana, uz preporuku kontrole laboratorijskih nalaza (kompletna krvna slika, CRP, kreatinin, elektroliti) za 2 dana. Učinjeni kontrolni laboratorijski nalazi pokazali su dodatno povećanje upalnih parametara (CRP 237.2mg/L) uz daljnju perzistenciju istih simptoma te se pacijent upućuje na objedinjeni hitni bolnički prijem. Učinjena je hitna CT angiografija pri čemu je prikazan zadebljani, trombozirani segment aortalne stijenke duljine 7cm kranijalno od aortne bifurkacije te se postavlja dijagnoza infektivnog aortitisa. Obzirom na dijagnozu učinjena je resekcija abdominalne aorte s rekonstrukcijom, formiranjem aortobilijačne prenosnice. Tijekom operativnog postupka uzeti su višestruki uzorci tkiva koji su poslani na mikrobiološku analizu. Po prispjeću nalaza u jednom uzorku ustanovljen je pozitivan nalaz na *Stafilococcus aureus*, dok su ostali uzorci

bili sterilni. Pacijentu su tijekom 12 tjedana preporučeni peroralni antibiotici sulfometoksazol trimetoprim+ rifampicin uz dogovorenu kontrolnu CT angiografiju. Po provedenoj terapiji pacijent se u potpunosti oporavio.

**Rasprava:** Aortitis predstavlja izazov pri postavljanju ispravne i pravovremene dijagnoze zbog raznolikosti u kliničkoj prezentaciji koja varira od blage nelagode, boli u leđima ili abdomenu pa sve do teških komplikacija kao što su aneurizma i disekcija. Razmatranje širokog spektra diferencijalnih dijagnoza (cistitis, ginekološka patologija, aneurizma aorte, aortitis, kolecistitis) uz laboratorijske parametre i slikovne dijagnostičke metode ključno je u pravovremenom uspostavljanju dijagnoze i prevenciji potencijalno smrtnog ishoda.

**Zaključak:** Aortitis je rijetko, ali životno ugrožavajuće stanje čije je prepoznavanje često otežano zbog nespecifičnih simptoma kojima se pacijenti prezentiraju. Važno je pažljivo razmotriti bilo koji od simptoma razmišljajući i o mogućoj prisutnosti aortitisa ukoliko su laboratorijskom analizom krvi povišeni upalni parametri.

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## ■ Rare case of aortitis: diagnosis, treatment and outcomes

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**Introduction with aim:** Aortitis is an inflammation of the aorta that can sometimes lead to aneurysm or obstruction. It is a rare condition most commonly associated with autoimmune diseases, such as connective tissue disorders and vasculitis, including Takayasu arteritis, giant cell arteritis, and HLA-B27-associated spondyloarthropathies, as well as infectious causes. Infectious etiologies include tuberculosis, syphilis, and other bacterial infections. The diagnosis of aortitis is challenging due to its highly variable clinical presentation, ranging from back or abdominal pain to acute severe aortic insufficiency. The aim of this report is to emphasize the importance of a comprehensive differential diagnostic approach in patients presenting with nonspecific symptoms.

**Case Report:** A 68-year-old male initially presented to his primary care physician with nonspecific discomfort in the lower abdomen, without fever or digestive problems. The patient had a history of pancreatic cystic lesions monitored by a gastroenterologist and angina pectoris with nonsignificant LAD stenosis followed by a cardiologist. Physical examination revealed a soft but tender abdomen on suprapubic palpation. Laboratory tests, including a complete blood count (WBC  $13.4 \times 10^9/L$ ), biochemical parameters (CRP 112.5 mg/L), and urine sediment analysis (RBC 17), were performed. Based on clinical presentation and laboratory findings, a urinary tract infection was diagnosed, and the patient was advised to perform a urine culture. Antibiotic therapy with amoxicillin/clavulanic acid (2x1gr for 7 days) was initiated, with a follow-up recommendation for blood count, creatinine, and electrolytes in two days. Follow-up tests showed further elevation of inflammatory markers (CRP 237.2 mg/L) with persistent symptoms, leading to referral for an emergency hospital admission. Urgent CT angiography revealed a thickened, thrombotic aortic wall segment measuring 7 cm cranial to the aortic bifurcation, confirming a diagnosis of infectious aortitis. Given the diagnosis, the patient underwent resection of the abdominal aorta with reconstruction using an aortobifemoral bypass. Multiple tissue samples

were obtained intraoperatively and sent for microbiological analysis. One sample tested positive for *Staphylococcus aureus*, while the others were sterile. The patient was prescribed oral antibiotics (trimethoprim-sulfamethoxazole + rifampin) for 12 weeks, with a scheduled follow-up CT angiography. After completing therapy, the patient fully recovered.

**Discussion:** Aortitis poses a diagnostic challenge due to its highly variable clinical presentation, ranging from mild discomfort to severe complications such as aneurysm and dissection. A broad differential diagnosis—including cystitis, gynecological pathology, aortic aneurysm, aortitis, and cholecystitis—should be considered. Laboratory markers and imaging modalities play a crucial role in early diagnosis and prevention of potentially fatal outcomes.

**Conclusion:** Aortitis is a rare but life-threatening condition that is often difficult to recognize due to its nonspecific symptoms. Careful evaluation of symptoms and consideration of aortitis as a potential diagnosis, especially in cases with elevated inflammatory markers, are essential for timely diagnosis and appropriate management.

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## ■ Dijagnostički izazov atipične urtikarije u pacijentice s višestrukim komorbiditetima: pristup paraneoplastičnom NSCLC i važnost multidisciplinarnog tima

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**Uvod s ciljem:** Paraneoplastični sindromi često se javljaju u oboljelih od raka pluća i mogu prethoditi dijagnozi ili se manifestirati u ranijim fazama bolesti, recidivima ili prisutnim metastazama. To su rijetki poremećaji u kojima malignitet uzrokuje sistemske učinke koji nisu izravno povezani s invazijom ili metastazama tumora. Cilj ovog rada je naglasiti važnost pravovremenog prepoznavanja ranih, nespecifičnih simptoma maligniteta.

**Prikaz slučaja:** 65-godišnja pacijentica, dolazi u ambulatnu svom liječniku obiteljske medicine (LOM) u siječnju 2024. s atipičnim eflorescencijama oko očiju, čela, prsnog koša i ruku, praćenim peckanjem i svrbežom. Pacijentica je preboljela inferiorni infarkt miokarda i ima ugrađene premosnice, boluje od hipotireoze i hipertenzije, a u kroničnoj terapiji koristi levotiroksin. Obzirom na simptome i kliničku sliku primjenjen je Solu Medrol amp 1x40 mg/ml no bez značajnijeg poboljšanja te se pacijentica uputi specijalisti dermatologu. Po provedenoj obradi postavi se dijagnoza dermatomiozitisa uz preporuku primjene momectan masti na što ne dolazi do poboljšanja. Zbog novonastalih simptoma u vidu otečenosti lica, otežanog disanja i gutanja, što se shvatilo kao posljedica smanjenja doze eplerenona s 50mg na 25mg, te se terapija ukida. Zbog svega navedenoga pacijentica je hospitalizirana u travnju 2024. godine radi opsežnije dijagnostičke obrade. Učinjen CT toraksa, abdomena i zdjelice, pokazao je tumorski proces u plućima, a bronhoskopijom se nađe submukozna infiltracija distalnog dijela glavnog bronha, s krvarenjem pri endoskopskom kontaktu. Patohistološki nalaz potvrdio je NSCLC (rak pluća nemalih stanica) stadij T4N2M0 te se započinje kemoterapija prema protokolu CE (karboplatin + etoposid). Nakon pet ciklusa, kontrolnim CT-om u srpnju 2024., zabilježena je parcijalna regresija tumorskog procesa. U razdoblju od 20. kolovoza do 5. rujna 2024. godine pacijentica je primila radioterapiju (13 frakcija), a kontrolni CT u listopadu 2024. godine

pokazuje daljnju regresiju tumora s progresijom retikularnih lezija plućnog parenhima što može ukazivati na postradijacijske promjene. U studenom 2024. godine praćenje lokalno uznapredovalog NSCLC pokazuje stabilizaciju tumorskog procesa uz blagu progresiju perifokalnog infiltrata donjeg lijevog plućnog režnja te blagu anemiju i trombocitopeniju. Nastavlja se daljnje liječenje pod nadzorom LOM-a i redovitim kontrolama imunologa i onkologa s terapijom koja uključuje metilprednizolonsukcinat, perindopril, pantoprazol, levotiroksin, enoksaparinatrij, betametazona, diazepam, amlodipin, D-vitamin i imunoglobulin IgG.

**Rasprava:** Paraneoplastički sindrom predstavlja značajan dijagnostički izazov, a pojava kronične spontane urtikarije (KSU) kao jednog od njegovih simptoma može otežati dijagnozu osnovne bolesti. Rezultati brojnih istraživanja pokazali su da je Omalizumab lijek izbora u liječenju KSU. Paraneoplastični sindromi mogu zahvatiti različite organske sustave, uključujući živčani, endokrini, dermatološki, reumatološki i hematološki sustav, a njihova klinička slika varira od blagih simptoma poput umora i mučnine do teških neuroloških ili endokrinih disfunkcija. Najčešće su povezani s karcinomom pluća, dojke, jajnika i limfomima. Hematološke manifestacije mogu uključivati eritrocitozu i trombocitozu, što dodatno komplicira dijagnostički proces. Ključno je proširiti dijagnostički pristup i ne podcjenjivati stanja refraktorna na terapiju. Unapređenje suradnje među stručnjacima i osnivanje multidisciplinarnih timova, uz podršku države u financiranju i edukaciji, moglo bi smanjiti broj pretraga i ubrzati početak terapije.

**Zaključak:** Atipični simptomi i multimorbidni pacijenti predstavljaju izazov u radu zdravstvenih djelatnika što zahtijeva usku suradnju liječnika obiteljske medicine s ostalim specijalnostima kao dio multidisciplinarnog tima.

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## ■ Diagnostic Challenge of Atypical Urticaria in a Patient with Multiple Comorbidities: Approach to Paraneoplastic NSCLC and the Importance of a Multidisciplinary Team

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**Introduction and aim:** Paraneoplastic syndromes often accompany lung cancer, potentially preceding diagnosis or emerging in early disease stages, recurrence, or metastasis. These rare disorders cause systemic effects unrelated to tumor invasion or spread. Clinical manifestations range from mild fatigue and nausea to severe neurological or endocrine dysfunction, complicating diagnosis due to their subtle, nonspecific nature. This paper highlights the importance of recognizing early malignancy symptoms and ensuring timely referral for further evaluation and treatment.

**Case report:** A 65-year-old female patient presented to her primary care physician in January 2024 with atypical skin eruptions around the eyes, forehead, chest, and arms, accompanied by burning and itching. Her medical history includes an inferior myocardial infarction with coronary bypass grafting, hypothyroidism, and hypertension, for which she is on chronic levothyroxine therapy. Given her symptoms, Solu-Medrol amp 1x40 mg/mL was administered throughout February 2024, but with no significant improvement, prompting a referral to a dermatologist. Following an extensive workup, dermatomyositis was diagnosed, and Momecutan ointment was prescribed, but symptoms persisted. Subsequently, facial swelling, dyspnea, and dysphagia developed, initially attributed to dose reduction of eplerenone from 50 mg to 25 mg, leading to treatment discontinuation. Due to worsening symptoms, she was hospitalized in April 2024 for further diagnostic evaluation. A CT scan of the thorax, abdomen, and pelvis revealed a pulmonary tumor, and bronchoscopy identified submucosal infiltration of the distal main bronchus with bleeding upon endoscopic contact. Histopathology confirmed non-small cell lung cancer (NSCLC), stage T4N2M0, and chemotherapy with the CE protocol (carboplatin + etoposide) was initiated. After

five cycles, a follow-up CT in July 2024 showed partial regression of the tumor. From August 20 to September 5, 2024, she underwent radiotherapy (13 fractions), with an October 2024 CT scan revealing further tumor regression but progression of reticular pulmonary parenchymal lesions, suggestive of post-radiation changes. In November 2024, follow-up of locally advanced NSCLC showed stabilization of the tumor with mild progression of perifocal infiltration in the lower left lung lobe, as well as mild anemia and thrombocytopenia. Treatment continues under the supervision of her primary care physician, with regular follow-ups by an immunologist and oncologist. Her current therapy includes methylprednisolone succinate, perindopril, pantoprazole, levothyroxine, enoxaparin sodium, betamethasone, diazepam, amlodipine, vitamin D, and IgG immunoglobulin.

**Discussion:** Paraneoplastic syndrome is a significant diagnostic challenge, and chronic spontaneous urticaria (CSU) can further obscure malignancy detection. Studies show omalizumab as the preferred CSU treatment. These syndromes affect the nervous, endocrine, dermatologic, rheumatologic, and hematologic systems, often linked to lung, breast, ovarian cancers, and lymphomas. Hematologic signs like erythrocytosis and thrombocytosis complicate diagnosis. Expanding diagnostic strategies and recognizing therapy-resistant cases are vital. Strengthening interdisciplinary collaboration and establishing multidisciplinary teams, with government support, could streamline diagnostics and accelerate treatment.

**Conclusion:** Atypical symptoms and multimorbid patients pose a significant challenge for healthcare professionals, necessitating close collaboration between primary care physicians and specialists as part of a multidisciplinary team.

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## ■ Periferna arterijska bolest donjih ekstremiteta

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**Uvod s ciljem:** Periferna arterijska bolest je djelomična ili potpuna opstrukcija jedne ili više perifernih arterija s prevalencijom od 1,52%, a koja raste s dobi (14,91% u dobi od 80-84 godine). Rizična populacija za obolijevanje su dijabetičari mlađi od 50 godina koji imaju neki od dodatnih čimbenika rizikaza nastanak ateroskleroze poput pušenja, dislipidemije, hipertenzije, potom osobe u dobi od 50-69 godina koji su pušači ili imaju šećernu bolest, te stariji i oni kod kojih je već poznata ateroskleroza drugog vaskularnog područja (karotidna, koronarna, renalna). Cilj ovog rada je ukazati na rizičnu populaciju i simptome kojima se prezentira bolest.

**Prikaz slučaja:** Pacijent u dobi od 88 godina dolazi u ordinaciju obiteljske medicine radi pojave nagle boli desne noge unazad 2 dana koja se javljala kod kretanja. Pacijent je samostalno pokretan, hoda usporeno i dobrog je općeg stanja. Hodna pruga mu je 40 metara. Prije 25 godina prebolio je infarkt miokarda, nakon kojeg mu je ugrađen STENT. Boluje od hipertenzije i hiperlipidemije, a u redovnoj terapiji koristi nebivolol 1x2.5mg, felodipin 1x2.5mg, ramipril 1x2.5mg, simvastatin 1x20mg i acetylsalicilnu kiselinu 1x100mg. Urednih je vrijednosti krvnoga tlaka i lipidograma. Puši lulu unatrag 50-tak godina. Prilikom fizikalnog pregleda desna noga bila je lividnija u odnosu na lijevu, hladnija na dodir, a koža nape-tija. Nije bio prisutan edem, a Homanov znak bio je negativan. Pulsacije a.tibialis i dorsalis pedis nisu bile palpabilne. Obzirom na anamnezu i fizikalni status te prisutne čimbenike rizika, pacijent je upućen na color doppler arterija desne noge te konzilijarni pregled vaskularnog kirurga. Color dopplerom arterija nogu nalazi se promijenjen bifazičan do monofazičan spektar sniženih brzina u proksimalnoj polovici a.femoralis superficialis, a distalnije se protok nije uspio prikazati. Dalje se učinila MSCT angiografija arterija zdjelice i nogu s ciljem anatomske lokalizacije okluzije i pripreme za revaskularizaciju. Pacijent je potom podvrgnut kirurškom zahvatu.

**Rasprava:** Periferna arterijska bolest može biti asimptomatska (20-50%), prezentirati se atipičnim simptomima (40-50%), intermitentnim klaudikacijama (10-35%), kritičnom ishemijom ekstremiteta (bolovi u mirovanju, ulceracije, nekroza/gangrena 1-2%) te akutnom ishemijom ekstremiteta. Simptomi obuhvaćaju utrnulost i slabost zahvaćenog ekstremiteta, intermitentne klaudikacije kod hodanja, promjenu boje kože, hladnoću na dodir, pojavu rana, sjajnu kožu, gubitak dlaka i sporiji rast noktiju. Imajući na umu da se bolest u 20-50% slučajeva manifestira asimptomatski, važno je prepoznati rizičnu populaciju i ukoliko je moguće odrediti engl. ankle-brachial indeks (ABI). Atipični simptomi poput otežanog hodanja ili hoda uz pomoć pomagala u starijoj populaciji često se pripisuju drugim bolestima i to najčešće lokomotornog sustava. Detaljna anamneza i fizikalni pregled pomažu nam u otkrivanju osobe rizične za obolijevanje od periferne arterijske bolesti. Klasifikacija bolesti prema stupnjevima određuje daljnji dijagnostički i terapijski protokol.

**Zaključak:** Obzirom na visok broj oboljelih u svijetu nužno je staviti naglasak na prepoznavanje rizičnog pacijenta i adekvatnu kontrolu čimbenika rizika za obolijevanje od periferne arterijske bolesti što je jedna od najvažnijih uloga liječnika obiteljske medicine. Pravovremena dijagnoza omogućuje optimalno konzervativno i/ili kirurško liječenje bez posljedica komplikacija odnosno potrebe za amputacijom zahvaćenog ekstremiteta.

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## ■ Peripheral arterial disease of the lower extremities

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**Introduction with aim:** Peripheral arterial disease (PAD) is the partial or complete obstruction of one or more peripheral arteries. Global prevalence is 1.52%, increases with age (14.91% in those aged 80-84 years). The at-risk population includes diabetics under the age of 50 who have at least one risk factor for the development of atherosclerosis (smoking, dyslipidemia, hypertension), patients aged 50-69 who are smokers or have diabetes, individuals over 70 years of age, and those with pre-existing atherosclerosis of another vascular area (carotid, coronary, renal). The aim of this paper is to identify the at-risk population and symptoms of the PAD.

**Case report:** An 88-year-old patient presented to the family medicine office due to sudden pain in his right leg that had persisted for the past two days. The pain occurred during movement. The patient was mobile, walking slowly and in good general condition. His walking distance was 40 meters. Twenty-five years ago, he had a myocardial infarction, after which he had a STENT implanted. Since then, he has been receiving treatment for hypertension and hyperlipidemia: nebivolol 1x2.5mg, felodipine 1x2.5mg, ramipril 1x2.5mg, simvastatin 1x20mg and acetylsalicylic acid 1x100mg. He had normal values of blood pressure and lipid profile. He has been smoking a pipe for 50 years. On examination, it was evident that the right leg was more livid than the left, colder, and the skin was taut without edema. Homan's sign was negative. Pulsations of the a. tibialis and dorsalis pedis were not palpated. Based on these findings, the patient was referred for a Color Doppler (CD) ultrasound of the arteries of the right leg and a vascular surgeon consultation. CD imaging revealed a biphasic-to-monophasic spectrum with reduced velocities in the proximal half of the superficial femoral artery, while more distally blood flow could not be visualised. Subsequently, MSCT angiography of the pelvic and leg arteries was performed to

determine the anatomical location of the occlusion and prepare for revascularization. The patient then underwent surgical treatment.

**Discussion:** The PAD can be asymptomatic (20-50%), present with atypical symptoms (40-50%), intermittent claudication (10-35%), or progress to critical limb ischemia (pain at rest, ulceration, necrosis/gangrene 1-2%) and acute limb ischemia. Symptoms include numbness and weakness of the affected limb, intermittent claudication while walking, skin discoloration, coldness to the touch, sores, shiny skin, hair loss, and slower nail growth. Considering that the disease manifests asymptotically in 20-50% of cases, it is important to recognize the risk population and refer these patients for at least an ankle-brachial index measurement. Atypical symptoms such as mobility impairment and walking with an aid in older people are often attributed to other diseases, most commonly of the musculoskeletal system. A well-taken medical history and physical examination help identify risk patients and symptoms of peripheral arterial disease. The classification of the disease severity determines the further diagnostic and therapeutic protocol.

**Conclusion:** Given the high number of patients worldwide, it is necessary to emphasize the recognition of PAD risk patients and adequate control of risk factors, which is one of the most important roles of family medicine doctors. Timely diagnosis enables optimal conservative and/or surgical treatment without further complications or the need for amputation of the affected limb.

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## **7. Slobodne teme**

## ■ Zdjelična bol kod žena – uloga obiteljskog liječnika u dijagnostici i liječenju

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**Uvod:** Zdjelična bol (ZB) složen je klinički simptom s mogućim ginekološkim, urološkim, gastrointestinalnim, neurološkim i psihosomatskim poremećajima u pozadini. Prema Europskom medicinskom časopisu (European Medical Journal), 25% žena reproduktivne dobi i 15% svih žena u svijetu pati od kronične ZB s godišnjom prevalencijom od 38 %. Precizna dijagnoza zahtijeva temeljitu procjenu simptoma i često multidisciplinarni pristup. Cilj ovog rada je prikazati dijagnostičke i terapijske pristupe bolovima u zdjelici u okviru obiteljske medicine, uključujući multidisciplinarnu suradnju i upotrebu suvremenih dijagnostičkih metoda.

**Rasprava:** ZB se klasificira, ovisno o trajanju i etiologiji, kao akutna ili kronična. Akutna ZB koja je posljedica ektopične trudnoće, upalne bolesti zdjelice, torzije jajnika ili akutnog cistitisa zahtijeva brzu evaluaciju i hitno liječenje. Kroničnu ZB karakterizira trajanje od četiri do šest mjeseci s često multifaktorijskom etiopatogenezom koja može uključivati stanja poput endometrioze, intersticijskog cistitisa, miofascijalnih poremećaja i sl. Pri početnoj procjeni ZB, liječnik obiteljske medicine (LOM) treba uzeti ciljanu anamnezu. Važno je ispitati karakteristike boli (lokalizacija, intenzitet, trajanje, čimbenici koji pogoršavaju ili olakšavaju simptome), prisutnost drugih simptoma (npr. dismenoreje, dispareunije, disurije, gastrointestinalnih tegoba) te psihosocijalne čimbenike, uključujući utjecaj na kvalitetu života pacijentice. Svako pacijentici reproduktivne dobi potrebno je isključiti moguću trudnoću. Fizikalni pregled uključuje procjenu abdomena, zdjelice i muskulature, pri čemu se pažnja posvećuje mogućim znakovima upale, tumora ili adhezivnih promjena. Laboratorijski testovi (CRP, FSH, LH, β-hCG) i slikovne metode, poput transvaginalnog ultrazvuka, MRI-a ili CT-a zdjelice, ključni su za potvrdu dijagnoze, a u objektivizaciji intenziteta boli pomažu upitnici (npr. indeks boli u zdjelici). Uloga LOM-a je razlikovanje hitnih stanja od manje hitnih, kroničnih uzroka ZB. Znakovi

upozorenja su omaglica, iznenadni gubitak svijesti, izrazito nizak krvni tlak, vaginalno krvarenje nakon menopauze, povišena tjelesna temperatura ili zimica, iznenadna jaka bol praćena mučninom, povraćanjem, pretjeranim znojenjem ili nemir. Liječenje funkcionalnih i psihosomatskih uzroka ZB, poput sindroma iritabilnog crijeva, miofascijalnih poremećaja zdjelice muskulature te psihosomatskih poremećaja povezanih sa stresom ili anksioznošću, u domeni je LOM-a. Blage urološke i gastrointestinalne bolesti liječe se na razini primarne zdravstvene zaštite. Kronična zdjelica bol nepoznatog uzroka također ostaje u nadležnosti LOM-a, uz odgovarajuću diferencijalnu dijagnozu i multidisciplinarnu suradnju. Kod kroničnih bolova, LOM koordinira daljnju dijagnostiku i terapiju, uključujući farmakološko i nefarmakološko liječenje (fizioterapija, kognitivno-bihevioralna terapija). S druge strane, akutni ginekološki hitni slučajevi, uključujući izvanmaterničnu trudnoću, torziju jajnika i teške upale zdjelice, zahtijevaju hitnu ginekološku obradu. Kronična ginekološka stanja poput endometrioze, koja često zahtijeva napredne dijagnostičke metode poput laparoskopije, te adenomioze ili mioma maternice koji uzrokuju bol i obilne menstruacije, spadaju u skrb ginekologa. Postoperativne komplikacije i adhezivna bolest zdjelice, osobito kod pacijentica s poviješću zdjelčnih operacija, zahtijevaju ginekološku evaluaciju. Također, kronični cervicitis, vaginitis ili infekcije koje ne reagiraju na standardnu terapiju trebaju biti upućeni ginekologu. Cjelovita skrb se osigurava multidisciplinarnim pristupom, a ključna je i edukacija pacijentice o prirodi boli, mogućnostima liječenja i važnosti promjena životnih navika.

**Zaključak:** LOM ima ključnu ulogu u prepoznavanju simptoma bolova u zdjelici, razlikovanju uzroka i koordinaciji daljnje obrade. Individualizirana skrb i multidisciplinarni pristup omogućuju ranu dijagnozu, smanjenje rizika od kronifikacije boli te poboljšanje kvalitete života.

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## ■ Pelvic pain in women - the role of the family medicine physician in diagnosis and treatment

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**Introduction:** Pelvic pain (PP) is a complex clinical symptom with potential gynecological, urological, gastrointestinal, neurological, and psychosomatic causes. According to the European Medical Journal, 25% of women of reproductive age and 15% of all women suffer from chronic PP, with an annual prevalence of 38%, which is higher than asthma. Diagnosis requires a thorough assessment of symptoms and a multidisciplinary approach. The aim of this paper is to present diagnostic and therapeutic approaches in family medicine.

**Discussion:** PP is classified as acute or chronic. Acute PP, caused by ectopic pregnancy, pelvic inflammation, ovarian torsion, or acute cystitis, requires urgent treatment. Chronic PP lasts longer than four months and may be associated with conditions such as endometriosis, irritable bowel syndrome, or myofascial disorders. In assessing PP, a family medicine physician (FMP) takes a medical history, analyzes pain characteristics, and evaluates other symptoms. Psychological and social factors, as well as the patient's quality of life, are also assessed. A physical examination includes an evaluation of the abdomen and pelvis, while laboratory tests and imaging methods (ultrasound, MRI, CT) are key for diagnosis. The role of the FMP is to differentiate emergency conditions, such as ectopic pregnancy or acute pelvic inflammation, from chronic causes. Warning signs include dizziness, sudden loss of consciousness, low blood pressure, fever, and severe pain with nausea and vomiting. The treatment of functional and psychosomatic causes of PP remains within the FMP's domain, while mild urological and gastrointestinal conditions are managed at the primary care level. Chronic PP of unknown origin requires differential diagnosis

and multidisciplinary collaboration. For chronic pain, the FMP coordinates diagnostics and therapy, including pharmacological and non-pharmacological treatments. Chronic gynecological conditions such as endometriosis, adenomyosis, and uterine fibroids fall under specialist care. Postoperative complications, adhesive pelvic disease, and therapy-resistant infections require gynecological evaluation. Comprehensive care is ensured through a multidisciplinary approach, along with patient education on the nature of pain and treatment options.

**Conclusion:** The FMP plays a key role in recognizing PP symptoms, distinguishing causes, and coordinating further evaluation. Individualized care and a multidisciplinary approach enable early diagnosis, reduce the risk of chronic pain development, and improve quality of life.

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## ■ Razumijevanje, dijagnoza i pristup pacijentu s umorom u obiteljskoj medicini

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**Uvod s ciljem:** Umor je stanje značajne fizičke, mentalne i emocionalne iscrpljenosti i jedan od učestalijih simptoma koji se javlja s prevalencijom od jedan na svakih 15 pacijenata koji se jave obiteljskom liječniku. Oko 24% pacijenata ističe umor kao veliki problem. Prevalencija je veća kod žena (28%) u usporedbi s muškarcima (19%). Istraživanja su pokazala da se preko 100 različitih bolesti mogu češće javiti kod pacijenata s umorom. S obzirom na to, treba dodatno ispitati razlog sve veće prevalencije umora. Cilj ovog rada je pokazati mogućnosti dijagnosticiranja i zadovoljavajućeg liječenja umora u obiteljskoj medicini.

**Rasprava:** Umor je čest simptom koji se može javiti uz veliki broj bolesti, ali može i utjecati na njih. Većina pacijenata s takvim problemom prvo se javlja liječniku obiteljske medicine (LOM). Umor se može klasificirati prema duljini trajanja na akutni i kronični ili prema etiologiji na fiziološki ili umor drugog uzroka. Akutni umor traje do mjesec dana, dok kronični traje dulje od šest mjeseci. Umor drugog uzroka najčešće je posljedica neke osnovne kronične bolesti, dok fiziološki umor može biti povezan s promjenama u spavanju, prehrani ili životnim okolnostima. Zbog svoje širine kao simptoma, važno je imati strukturiran pristup. Murtagh predlaže koristan pristup dijagnozi umora kroz tri kategorije: vjerojatne dijagnoze (anksioznost, stress, virusna infekcija, poremećaj spavanja), ozbiljne bolesti koje se ne smiju propustiti (anemije, karcinomi, srčane aritmije) i dijagnostičke zamke (početno kongestivno zatajenje srca, hemokromatoza, celijska, Addisonova bolest, Parkinsonova bolest, metabolički disbalans, apstinencija od droga). Uz to, kao razlog, treba razmotriti i nuspojave lijekova, osobito kod kroničnih bolesnika. Umor je često povezan s mentalnim poremećajima poput depresije i anksioznosti, što naglašava važnost holističkog pristupa bolesniku. Osim što je to ozbiljan problem za pacijenta, umor zna biti skup simptom za zdravstveni sustav. Istraživanja pokazuju da su za pacijenta najkorisnije osnovne

i jeftine pretrage, poput kompletne krvne slike i biokemije. Nakon 12 mjeseci mnogi pacijenti s umorom kao simptomom i dalje nemaju postavljenu dijagnozu. I kod onih koji imaju dijagnozu, gotovo 50% njih ima samo "umor" kao dijagnozu. Za pacijenta su najbolji učestaliji i opsežniji klinički pregledi tijekom kojih se razgovara i upoznaje ga s mogućim uzrocima umora, ali se također saznaje što za pacijenta predstavlja pojam umora. Metode liječenja mogu biti medikamentne i nemedikamentne. Ne medikamentne metode su terapija vježbanjem i pravilna higijena spavanja uz praćenje dnevnika spavanja. Medikamenta terapija se daje tek ukoliko ništa drugo ne pomogne, najčešće antihistaminici.

**Zaključak:** LOM kao prvi kontakt, uz pomoć svjetskih smjernica i algoritama, može najbolje djelovati na pacijentove probleme povezane s umorom.

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## ■ Understanding, Diagnosis, and Approach to Patients with Fatigue in Family Medicine

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**Introduction:** Fatigue is a condition of significant physical, mental, and emotional exhaustion and is one of the most frequent symptoms, occurring with a prevalence of one in every 15 patients visiting a family medicine physician. About 24% of patients find fatigue as a major problem. Its prevalence is higher among women (28%) compared to men (19%). Research has shown that over 100 different diseases are more likely to occur in patients experiencing fatigue. Considering this, it is essential to further investigate the reasons behind the increasing prevalence of fatigue. The aim of this paper is to highlight the possibilities for diagnosing and adequately treating fatigue in family medicine

**Discussion:** Fatigue is a common symptom that can occur alongside many diseases but can also influence their progression. Most patients with such complaints first consult their family medicine physician (FMP). Fatigue can be classified based on duration as acute or chronic, or by etiology as physiological or fatigue caused by other factors. Acute fatigue lasts up to one month, while chronic fatigue persists for more than six months. Fatigue due to other causes is most often a result of an underlying chronic illness, while physiological fatigue may be associated with changes in sleep, diet, or life circumstances. Given its broad nature as a symptom, a structured approach is crucial. Murtagh proposes a useful approach to diagnosing fatigue through three categories: probable diagnoses (anxiety, stress, viral infection, sleep disorders), serious diseases that must not be missed (anemia, cancer, cardiac arrhythmias), and diagnostic pitfalls (early congestive heart failure, hemochromatosis, celiac disease, Addison's disease, Parkinson's disease, metabolic imbalances, drug withdrawal). Additionally, medication side effects should be considered, especially in patients with chronic conditions. Fatigue is often associated with mental health disorders such as depression and anxiety, emphasizing the importance of a holistic approach to the patient. In addition to being a significant issue for

the patient, fatigue can be a costly symptom for the healthcare system. Research shows that the most beneficial tests for patients are basic and inexpensive ones, such as complete blood counts and biochemistry panels. After 12 months, many patients with fatigue as a symptom still lack a definitive diagnosis. Even among those with a diagnosis, almost 50% have "fatigue" as their sole diagnosis. The best outcomes for patients are achieved through frequent and comprehensive clinical examinations, during which the physician discusses and explores the probable causes of fatigue with the patient while also understanding what fatigue means to them. Treatment methods can be both pharmacological and non-pharmacological. Non-pharmacological methods include exercise therapy and proper sleep hygiene, supported by sleep diaries. Pharmacological therapy is considered only when other methods fail, with antihistamines being the most prescribed.

**Conclusion:** As the first point of contact, the family medicine physician, using global guidelines and diagnostic algorithms, can best address the patient's fatigue-related issues.

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## ■ 10 najčešćih ranih simptoma kronične bubrežne bolesti koje ne smijemo propustiti prepoznati

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**Uvod:** Kronična bubrežna bolest (KBB) jedan je od vodećih globalnih zdravstvenih problema, povezan s visokim rizikom od komplikacija i povećanom smrtnošću. Pravovremeno postavljanje dijagnoze KBB predstavlja izazov za liječnike obiteljske medicine (LOM) jer su rani stadiji, uslijed nespecifičnih simptoma, često neprepoznati. Cilj ovog rada je identificirati i istaknuti najčešće rane simptome KBB koje LOM ne smije propustiti.

**Rasprava:** Simptomatologija KBB, posebno u ranom stadiju, nije tipična. Najčešće se na KBB posumnja na temelju patoloških laboratorijskih nalaza. Simptomi i klinički znakovi KBB obično postaju izraženiji s napredovanjem bolesti. Oni su uzrokovani narušenjem bubrežne funkcije, uključujući zadržavanje viška tekućine, nakupljanje otpadnih tvari (uremijski sindrom), glomerularno oštećenje i elektrolitski disbalans. Dugotrajna KBB, kroz različite mehanizme, uključujući nedostatno izlučivanje hormona eritropoetina, doводи do anemije kronične bolesti.

LOM trebaju razmotriti mogućnost KBB kod visokorizičnih pacijenata, posebno onih s dijabetesom, hipertenzijom, kardiovaskularnim bolestima, pretiulošću ili kod pušača. Na KBB mogu ukazivati simptomi i znakovi poput: 1) perifernih edema, 2) kroničnog umora i slabosti, 3) povišenog arterijskog tlaka, 4) poteškoća s mokrenjem, 5) boli u donjem dijelu leđa, 6) nesanice, 7) mučnine i gubitka apetita, 8) svrbeža kože, 9) grčeva u mišićima i 10) zaduhe. Periferni edemi najčešće se pojavljuju na nogama i gležnjevima, a nekada i periorbitalno. Bol u leđima bubrežnog porijekla nastaje uslijed opstrukcije, zadržavanja tekućine ili upalnog procesa. Hipertenzija i KBB usko su povezane: hipertenzija može biti posljedica KBB, ali je istovremeno i jedan od najčešćih uzroka njenog nastanka. Poteškoće s mokrenjem mogu uključivati pjenušavu mokraću (znak albuminurije), tamnu mokraću (prisutnost krvi), učestalo mokrenje, osobito noću (nikturija), ili

smanjeno mokrenje, što je češće u kasnijim stadijima bolesti.

Prisutnost komorbiditeta može dodatno otežati dijagnozu KBB, jer se navedeni simptomi mogu javiti kod mnogih drugih akutnih ili kroničnih stanja. Stoga LOM trebaju uvijek uzeti u obzir mogućnost prisutnosti KBB, posebno kod visokorizičnih pacijenata. Probir jednom godišnje preporučuje se naročito tim skupinama pacijenata.

**Zaključak:** LOM imaju ključnu ulogu u probiru, ranom prepoznavanju simptoma KBB i adekvatnoj intervenciji. Upravo pravovremeno dijagnosticanje i učinkovito upravljanje KBB presudni su za sprječavanje progresije bolesti, smanjenje rizika od ozbiljnih komplikacija te značajno poboljšanje prognoze pacijenata.

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## ■ The 10 Most Common Early Symptoms of Chronic Kidney Disease That Must Not Be Overlooked

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**Introduction:** Chronic kidney disease (CKD) is one of the leading global health challenges, associated with a high risk of complications and increased mortality. Timely diagnosis of CKD poses a significant challenge for family physicians (FPs) as early stages often go unrecognized due to nonspecific symptoms. The aim of this paper is to identify and highlight the most common early symptoms of CKD that FPs must not overlook.

**Discussion:** The symptomatology of CKD, especially in its early stages, is not typical. CKD is most often suspected based on pathological laboratory findings. Symptoms and clinical signs of CKD usually become more pronounced as the disease progresses. They result from impaired kidney function, including fluid retention, accumulation of waste products (uremic syndrome), glomerular damage, and electrolyte imbalances. Prolonged CKD, through various mechanisms, including insufficient secretion of erythropoietin hormone, leads to anaemia of chronic disease.

FPs should consider the possibility of CKD in high-risk patients, particularly those with diabetes, hypertension, cardiovascular diseases, obesity, or those who smoke. Symptoms and signs indicative of CKD may include: 1) peripheral oedema, 2) chronic fatigue and weakness, 3) elevated blood pressure, 4) urinary difficulties, 5) lower back pain, 6) insomnia, 7) nausea and loss of appetite, 8) itchy skin, 9) muscle cramps, and 10) shortness of breath. Peripheral oedema most commonly appears in the legs and ankles and sometimes around the eyes (peri-orbital). Kidney-related back pain may result from obstruction, fluid retention, or inflammation. CKD and hypertension are closely linked: hypertension can be a consequence of CKD but is also one of its most common causes. Urinary difficulties may include foamy urine (indicative of albuminuria), dark urine (presence of blood), frequent urination, especially at night (nocturia), or reduced

urination, which is more common in advanced stages of the disease.

The presence of comorbidities can further complicate the diagnosis of CKD, as these symptoms may also occur in many other acute or chronic conditions. Therefore, FPs should always consider the possibility of CKD, especially in high-risk patients. Annual screening is particularly recommended for these patient groups.

**Conclusion:** FPs play a crucial role in screening, early recognition of CKD symptoms, and appropriate intervention. Timely diagnosis and effective management of CKD are essential for preventing disease progression, reducing the risk of severe complications, and significantly improving patient outcomes.

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## ■ Prepoznavanje i liječenje zdravstvene anksioznosti u ordinaciji obiteljskog liječnika

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**Uvod s ciljem:** Poremećaj zdravstven anksioznosti ili anksiozni poremećaj zbog bolesti (eng. illness anxiety disorder, IAD) novouvedeni je poremećaj prema najnovijem izdanju „Dijagnostičkog i statističkog priručnika za mentalne poremećaje“ (DSM-5), zamjenjujući time dijagnozu hipohondrije iz DSM-IV. Zdravstvena anksioznost (ZA) može se shvatiti kao kontinuum bolesti koji varira od blagih do izrazito teških oblika, pri čemu se IAD nalazi na samom kraju spektra. Obilježen je intenzivnim strahom od toga da osoba ima ili bi mogla dobiti ozbiljnu medicinsku bolest, poput raka, srčanih bolesti ili drugih bolesti. Cilj ovog rada je ukazati na značajke pacijenta sa ZA u ordinaciji liječnika obiteljske medicine (LOM-a) te ulogu LOM-a u skrbi za takvog pacijenta.

**Rasprava:** Prevalencija ZA u općoj odrasloj populaciji značajno varira prema različitim istraživanjima i procjenjuje se na između 2,1% i 13,1%. Naime, dokazano da je prevalencija viša u pacijenata koji posjećuju zdravstvene ustanove, poput ordinacije LOM-a ili bolničke ustanove, pri čemu se tada kreće od 7% do 19,9%, u usporedbi s općom populacijom. Prema DSM-5 ZA se dijagnosticira samo ako osoba ima blage tjelesne simptome ili ih uopće nema, a pri tom je izrazito usredotočena na svoje zdravstveno stanje, što često dovodi do niza neprilagođenih ponašanja, poput stalnog pregledavanja tijela u potrazi za simptomima bolesti, pretjeranog traženja zdravstvenih informacija na internetu i učestalih odlazaka u medicinske ustanove, u trajanju šest mjeseci ili duže. Takve pacijente možemo svrstati u dvije skupine: oni koji prečesto traže medicinsku skrb kao oblik uvjerenja u bolest i oni koji često izbjegavaju medicinsku skrb zbog snažnog straha i anksioznosti od ozbiljne bolesti. Prema jednom istraživanju o prevalenciji ovih skupina

dokazano je da prvoj skupini pripada oko 25% ispitanika, drugoj 14%, a najveći dio ispitanika zapravo je pokazao da varira između traženja i izbjegavanja zdravstvene skrbi. LOM bi trebao posumnjati na ZA kada je osoba pretjerano zabrinuta oko mogućnosti da ima ozbiljnu bolest iako je provedena detaljnija procjena da se isključivo svi tjelesni poremećaji. Uz to, prisutnost depresije ili drugih poremećaja mentalnog zdravlja bi trebala biti procjenjena budući da to mogu biti predisponirajući čimbenici. Definitivnu dijagnozu LOM konačno postavlja kada zabrinutost traje šest mjeseci ili dulje, unatoč tome što osoba nema simptome ili ima samo blage simptome. Njavažniji aspekt u liječenju dugoročno je uspostavljanje odnosa povjerenja s pacijentom. Komunikacija bi trebala biti usmjerena na empatiju i otvoren dijalog pri čemu pacijentu treba dati do znanja da iako ne postoji specifično liječenje za njegove neobjašnjive simptome koji nisu opasni po život, liječnik ostaje predan pružanju podrške i rada na pacijentovom oporavku. Idući korak je uputiti pacijenta na psihoterapiju, odnosno kognitivno-behavioralnu terapiju koja se smatra prvom linijom liječenja. Nadalje psihotropni lijekovi, kao što su inhibitori ponovne pohrane serotonina, mogu biti učinkoviti u liječenju anksioznosti i depresija u pacijenata sa ZA.

**Zaključak:** Rano prepoznavanje i izradnja otvorenog odnosa LOM-a s pacijentima koji boluju od ZA ključna je ne samo za njihovo zdravlje i oporavak, već i za optimizaciju resursa zdravstvenog sustava. Takav pristup smanjuje nepotrebne pretrage i troškove, istovremeno osiguravajući kvalitetnu i empatičnu skrb usmjerenu na stvarne potrebe takvog pacijenta.

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## ■ The Recognition and Treatment of Health Anxiety Disorder in the Family Medicine Office

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**Introduction with aim:** Health Anxiety Disorder or Illness Anxiety Disorder (IAD) is identified in the latest "Diagnostic and Statistical Manual of Mental Disorders" (DSM-5), which replaces hypochondriasis from the previous edition. This disorder represents the severe end of a continuum of health anxiety issues, manifesting as an intense fear of having or acquiring serious diseases such as cancer or heart disease. The aim of this paper is to highlight the patient with IAD in the family medicine doctor's office and their role in caring for such a patient.

**Discussion:** The prevalence of health anxiety varies widely, with estimates ranging from 2.1% to 13.1% in the general adult population, but it is higher among those visiting medical facilities—between 7% and 19.9%. According to DSM-5, IAD is diagnosed in individuals who have either no or mild physical symptoms but exhibit excessive health-related behaviors. These include frequent checks for symptoms, obsessive health research, and regular medical visits lasting over six months. Patients typically fall into two categories: those who seek constant medical reassurance and those who avoid medical care due to fear of discovering a serious illness. Research shows that about 25% of patients actively seek medical reassurance, 14% avoid it, and the majority fluctuate between these behaviors. The family medicine doctor should suspect IAD when a person is overly concerned about the possibility of having a serious illness despite a detailed assessment to rule out all physical disorders. Additionally, the presence of depression or other mental health disorders should be assessed since these can be predisposing factors. The family medicine doctor finally makes the definitive diagnosis when the concern lasts six months or longer, despite the person having no symptoms or only mild

symptoms. The most important aspect of treatment is establishing a long-term trusting relationship with the patient. Communication should be focused on empathy and open dialogue, informing the patient that although there is no specific treatment for their unexplained symptoms that are not life-threatening, the doctor remains committed to providing support and working on the patient's recovery. The next step is to refer the patient to psychotherapy, specifically cognitive-behavioral therapy, which is considered the first line of treatment. Furthermore, psychotropic drugs, such as serotonin reuptake inhibitors, can be effective in treating anxiety and depression in patients with IAD.

**Conclusion:** Early recognition and the development of an open relationship with patients suffering from IAD by the family medicine doctor is crucial not only for their health and recovery but also for optimizing healthcare system resources. Such an approach reduces unnecessary examinations and costs while ensuring quality and empathetic care focused on the real needs of such a patient.

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## ■ Upalna križobolja u ordinaciji obiteljske medicine

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**Uvod s ciljem:** Križobolja je jedan od najčešćih razloga dolaska liječniku obiteljske medicine (LOM). Iako je prevalencija upalnih križobolja (UK) oko 1%, izuzetno je važna rana dijagnoza. Aksijalni spondiloartritis (SpA) karakterizira negativni RF uz upalu kralježnice, SI zglobova i enteza, te često i izvanzglobna obilježja (uveitis, psorijaza i UBC). Cilj je rada podsjetiti na ulogu LOM-a u ranom prepoznavanju i pravovremenom početku liječenja upalne križobolje.

**Rasprava:** UK uključuje prvi simptom u dobi < 40 godina, postepeni „podmukao“ razvoj križobolje, poboljšanje vježbanjem, izostanak poboljšanja mirovanjem i odmorom, prisutnost noćne boli (poboljšanje nakon ustajanja) uz trajanje duže od tri mjeseca. Prisutnost minimalno četiri navedena obilježja upućuju na UK. Glavno kliničko obilježje SpA je jutarnja ukočenost s bolovima u križima koji se šire u gluteuse ili stražnji dio bedara ako su zahvaćeni SI zglobovi, te često umor. U fizikalnom pregledu dominira smanjena pokretljivost lumbalne kralježnice u svim smjerovima (Schoberov test između druge i treće točke normalno > 5 cm; lateralna fleksija normalno > 10 cm), bolnost SI zglobova (Mennel test pozitivan) i zahvaćenost enteza (hvatište m. gluteus medius na veliki trohanter). U laboratorijskom nalazu se nalazi povišena SE i CRP (u 35- 50% bolesnika), anemija (potrebno odrediti i fekalni kalprotektin radi probira upalne bolesti crijeva (UBC)). HLA-B27 je pozitivan u 70 - 90 % bolesnika. Aksijalni SpA dijelimo u dvije skupine: prvu čini ankilozantni spondilitis s radiografski vidljivim oštećenjima SI zglobova ili kralježnice, a drugu neradiografski aksijalni SpA, uz manje izražene upalne promjene koji je češći u žena. Dijagnostički kriteriji za aksijalni SpA su: sakroileitis uz jedan ili više SpA obilježja ili HLA B27 uz dva ili više SpA obilježja (upalna križobolja, artritis, entezitis, uveitis, daktilitis, psorijaza, UBC, dobar odgovor na nesteroidne antireumatike (NSAR), obiteljska anamneza SpA, HLA-B27, povišen CRP). Prva slikovna metoda je RTG zdjelice s analizom SI zglobova (erozije, ankiloza, suženje zglobne pukotine, skleroza) i kukova (destruktivna artropatija). Uz izostanak RTG znakova,

indiciran je MR SI zglobova (prikazuje upalne promjene, edem subhondralne kosti, masnu metaplaziju, erozije i ankilozu). Uz uredan MR SI te visoku sumnju na SpA, indiciran je MR kralježnice. UZV je indiciran u dijagnostici entezitisa. Diferencijalno dijagnostički treba razlikovati mehaničke križobolje, fibromijalgije, infekcije, lumbalnu erozivnu osteohondrozu, kompresijski prijelom. Nefarmakološke mjere liječenja uključuju edukaciju, promjenu stila života, regulaciju tjelesne težine i vježbanje. Farmakološke mjere u prvoj liniji uključuju NSAR tijekom dva do četiri tjedna, potom po potrebi. Uz visoku aktivnost bolesti i neučinkovitost dva NSAR preporuka su biološki lijekovi (blokatori TNF-a i antagonisti IL-17), a glukokortikoidi nisu indicirani. Fizikalna terapija značajno usporava progresiju bolesti.

**Zaključak:** Liječenje i praćenje UK je prvenstveno u domeni reumatologa i fizijatra, ali LOM ima ključnu ulogu u ranom prepoznavanju, početnom liječenju i pravovremenom upućivanju.

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## ■ Inflammatory back pain in primary care

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**Introduction:** Low back pain is one of the most common reason for visiting a family doctor (FD). Although the prevalence of inflammatory back pain (IBP) is about 1%, early diagnosis is extremely important. Axial spondyloarthritis (SpA) is characterized by negative RF with inflammation of the spine, SI joints and entheses, and often extra-articular features (uveitis, psoriasis and inflammatory bowel disease (IBD)). The aim is to remain of the importance early recognition in GP office and timely initiation of treatment of IBP.

**Discussion:** IBP includes the first symptom at the age < 40 years, gradual “insidious” development of low back pain, improvement with exercise, lack of improvement with rest, presence of nocturnal pain (improvement after standing) with a duration last for three months and more. The presence of at least four of the listed features indicates IBP. The main clinical feature of SpA is morning stiffness with low back pain that spreads to the gluteus or posterior thigh if the SI joints are affected, and often fatigue. Physical examination is dominated by reduced mobility of the lumbar spine in all directions (Schober test normally > 5 cm; lateral flexion normally > 10 cm), SI joint tenderness (Mennel test positive) and involvement of the entheses (the attachment of the muscle gluteus medius to the greater trochanter). Laboratory tests show elevated SE and CRP (in 35-50% of patients), anemia (fecal calprotectin should also be determined for screening of IBD). 70-90% patients have positive HLA-B27. Axial SpA is divided into two groups: the first is ankylosing spondylitis with radiographically visible damage to the SI joints or spine, and the second is non-radiographic axial SpA, with less pronounced inflammatory changes, which is more common in women. Diagnostic criteria for axial SpA are: sacroiliitis with one or more SpA features or HLA B27 with two or more SpA features (inflammatory low back pain, arthritis, enthesitis, uveitis, dactylitis, psoriasis, IBD, good response to nonsteroidal anti-rheumatic drugs (NSAIDs), family history of SpA, HLA-B27, elevated CRP). The first imaging method is an X-ray of the pelvis with analysis of the SI joints (erosions,

ankylosis, joint space narrowing, sclerosis) and hips (destructive arthropathy). In the absence of X-ray signs, an MRI of the SI joints is indicated (shows inflammatory changes, subchondral bone edema, fatty metaplasia, erosions and ankylosis). With normal MRI of the SI joints but a high suspicion of SpA, an MRI of the spine is indicated. Ultrasound is indicated in the diagnosis of enthesitis. Differential diagnosis encompasses mechanical back pain, fibromyalgia, infections, lumbar erosive osteochondrosis and compression fracture. Non-pharmacological treatment measures include education, lifestyle changes, weight control, and exercise. The initial pharmacological measures include NSAIDs during two to four weeks, then as needed. With high disease activity and ineffectiveness of two NSAIDs, biological drugs (TNF- $\alpha$  blockers and IL-17 antagonists) are recommended, and glucocorticoids are not indicated. Physical therapy significantly slows down the progression of the disease.

**Conclusion:** Treatment and follow-up of IBP is primarily a domain of rheumatologists and psychiatrists, but FD has very important part in early recognition, initial treatment and timely referral.

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## ■ Što može učiniti LOM kad simptomi i znakovi upućuju na seksualnu disfunkciju?

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**Uvod i cilj:** Rijetko koji obiteljski liječnik se upušta u probleme seksualnog zdravlja svojih pacijenata iako je seksualna funkcija, uz disanje, hranjenje, potrebe za vodom i izlučivanje, jedna od osnovnih životnih funkcija. Najčešće se ne osjeća dovoljno educirano za takav razgovor ili mu razgovor o ovoj temi samom stvara nelagodu. S druge strane, većini pacijenata koji imaju probleme iz domene seksualnosti, može se pomoći jednostavnim savjetovanjem koje mogu obavljati svi liječnici, pa i drugi zdravstveni profesionalci (medicinske sestre, psiholozi...). Obiteljski liječnik koji ima izgrađeni odnos povjerenja sa svojim pacijentom je sigurno najbolji izbor. Cilj ovog rada je prikazati kako može liječnik obiteljske medicine (LOM), koji nije posebno educiran u domeni seksualnog zdravlja, pomoći svom pacijentu koji ima simptome i znakove seksualne disfunkcije, a kada pacijenta treba uputiti savjetniku za seksualno zdravlje ili seksualnom terapeutu.

**Rasprava:** Seksualno zdravlje je prema definiciji WHO (World Health Organization)- Svjetska zdravstvena organizacija iz 2002.godine stanje fizičkog, emocionalnog, mentalnog i socijalnog blagostanja vezanog za seksualnost; nije samo nedostatak bolesti, disfunkcije ili nemoći. Ono ne podrazumijeva samo reproduktivno zdravlje i zaštitu od spolno prenosivih bolesti, već i pozitivan i poštujući pristup seksualnosti i seksualnom odnosu kao i sposobnost za siguran i uživajući seksualni doživljaj, oslobođen diskriminacije, nasilja ili prisile. Model PLISSIT kojeg je još 1974. godine razvio Annon je akronim engleskih riječi P- permissio (dati dopuštenje), LI- limited information (ograničene informacije), SS- specific suggestions (specifični prijedlozi), IT- intensive therapy (intenzivna terapija), provodi se u savjetovanju i liječenju seksualnih problema. Većini pacijenata trebat će samo prva dva koraka koja mogu provoditi obiteljski liječnici i drugi zdravstveni profesionalci koji nemaju posebnu edukaciju iz domene seksualnog zdravlja. Ako seksualni problem traje dulje od 6 mjeseci, javlja se barem u 75% spolnih odnosa i stvara značajnu patnju paru, radi se o seksualnoj disfunkciji ili poremećaju. Mnoge od njih seksualni terapeuti i

savjetnici za seksualno zdravlje uspješno liječe, kao što su: smanjena ili odsutna seksualna želja muškaraca i žena, anorgazmija kod žena, erektilna disfunkcija muškaraca, preuranjena i odgođena ejakulacija kod muškaraca, bolan seksualni odnos muškaraca i žena (dispareunija, vulvodinija).

**Zaključak:** Bez obzira na vlastite stavove u domeni seksualnosti, obiteljski liječnik bi trebao biti spreman za konzultaciju u domeni seksualnog zdravlja na osnovnoj razini. Pri tom ne smije nametati svoje stavove, već samo dati znanstveno utemeljene informacije. Mora poštivati stavove i afinitete pacijenta koji se tiču seksualnosti.

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## ■ What can a GP do when symptoms and signs indicate sexual dysfunction?

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**Introduction with aim:** A GP doesn't often deal with sexual problems of his/her patients, even though sexual function is one of the basic functions of life. Mostly he/she does not feel educated enough in this field or talking about it brings discomfort. Nevertheless, most patients who have sexual problems can be helped by simple counseling at the GP practice, as well as by other healthcare professionals (nurses, psychologists, etc.). A GP who has a relationship built on trust with his patient is certainly the best choice. The aim of this paper is to show how a GP, without any special education in the domain of sexual health, can help his patient who has symptoms and signs of sexual dysfunction, and recognize when the patient should be referred to a sexual health counselor or a sex therapist.

**Discussion:** According to the WHO (2002) sexual health is a state of physical, emotional, mental and social well-being related to sexuality; it is not merely the absence of disease, dysfunction or infirmity. It requires a positive and respectful approach to sexuality and sexual relationships, as well as the ability of having pleasurable and safe sexual experiences, free from discrimination, violence or coercion. The PLISSIT model (Annon in 1974) is an acronym of the English words P- permission, LI- limited information, SS- specific suggestions, IT- intensive therapy and is used in the counseling and treatment of sexual problems. Most patients need the first two steps, which can be performed by a GP without special education in sexual health. If the sexual problem lasts longer than 6 months, occurs in at least 75% of sexual intercourses and creates significant suffering for the couple, it becomes a sexual dysfunction or disorder. Many of them are successfully treated by sex therapists and sexual health counselors, such as: reduced or absent sexual desire in men and women, anorgasmia in women, erectile dysfunction, premature and delayed ejaculation in men and painful sexual intercourse (dyspareunia, vulvodynia).

**Conclusion:** Regardless of one's own stance in the domain of sexuality, a GP should be prepared

for a consultation in the domain of sexual health at a basic level. He/she must respect the patient's attitudes and affinities regarding sexuality, not imposing his/her views, but only providing scientifically based information.

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## ■ Simptomi i znakovi srčanog zatajivanja – specifičnosti pri postavljanju dijagnoze

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**Uvod:** Srčano zatajivanje (SZ) je klinički sindrom karakteriziran tipičnim simptomima (zaduha, edemi potkoljenica, umor, ...) koji su praćeni kliničkim znacima (vlažni hropci, obostrani edem potkoljenica, srčani šum, nabrekle vratne vene, lateralni pomak apeksa srca), uzrokovanom strukturno i/ili funkcionalno bolesnim srcem, a koje rezultira oslabljenim srčanim izgonom i/ili porastom vrijednosti tlakova u srcu u mirovanju ili u naporu. Prevalencija SZ je otprilike 1-2% odrasle populacije u razvijenim zemljama, a raste na  $\geq 10\%$  kod starijih od 70 godina. U prosječnoj ordinaciji obiteljske medicine (OOM) u Hrvatskoj može se očekivati više od 20 bolesnika sa SZ. Kod starijih od 65 godina koji se jave obiteljskom liječniku zbog nedostatka zraka u naporu, jedan od šest imaće neprepoznato SZ. Cilj ovog rada je prikaz simptoma i znakova SZ koji mogu povećati vjerojatnost postavljanja dijagnoze u OOM.

**Rasprava:** Simptomi SZ su često nespecifični i mogu se podijeliti u tri skupine; simptomi prekomjernog nakupljanje tekućine (zastoj unatrag), simptomi vezani uz kompenzaciju ili adaptaciju, te simptomi koji su posljedica smanjene dopreme kisika tkivima (zastoj unaprijed). Potonje je posebno teško prepoznati jer su nespecifični (npr. blago kognitivno oštećenje, umor, usporen oporavak nakon tjelesnog napora,...). Ovi, ali i svi ostali, simptomi mogu biti prolazni, posebno u ranoj fazi SZ. Ukoliko bolesnik zbog drugih razloga (npr. hipertenzije) ima u terapiji od ranije propisan diuretik, znaci zastoja tekućine ne moraju biti evidentni. Galopni ritam koji je specifičan za ZS rijetko se nalazi kod nehospitaliziranih pacijenata. Pomak apeksa srca prema lateralno u položaju na lijevom boku ili tahikardija, kao znaci adaptacije, su češći nalaz, ali ih je teže otkriti. Manje tipičan simptom, a relativno čest u OOM je nalaz psikanja (engl. wheezing), a nalazi se kod 35% bolesnika s akutnim ZS. Osobito je

teško prepoznati i protumačiti znakove u pretilih, starijih i bolesnika s kroničnom plućnom bolešću. U usporedbi sa starijim, mlađi bolesnici često imaju drugačiju etiologiju, kliničku sliku i ishod. Za bolesnike koji se prvi put javljaju sa simptomima ili znakovima, vjerojatnost SZ najprije treba procijeniti temeljem bolesnikove prethodne kliničke povijesti (npr. koronarna bolest srca, arterijska hipertenzija, primjena diuretika), prisutnih simptoma (npr. ortopneja), fizikalnog pregleda (npr. bilateralni edemi, povećani jugularni venski tlak, pomaknuti apikalni puls) i EKG-a u mirovanju. Ukoliko nema odstupanja u niti jednom od navedenog, SZ je malo vjerojatno i potrebno je razmotriti druge dijagnoze. Uz prisutan ijedan patološki pokazatelj potrebno je izmjeriti natriuretske peptide u plazmi, kako bi se identificirali oni pacijenti kojima je potrebna ehokardiografija. Ona je indicirana uz vrijednosti iznad referentnih, ali i uz nemjerljive razine. Akutno SZ odnosi se na brzu pojavu ili pogoršanje simptoma i/ili znakova bolesti srca. Klinička klasifikacija može se temeljiti na fizikalnom pregledu kako bi se otkrila prisutnost kliničkih simptoma/znakova kongestije ('mokri' naspram 'suh') i/ili periferne hipoperfuzije ('hladni' naspram 'topli'). Ova klasifikacija može biti korisna za usmjeravanje terapije u početnoj fazi i nosi prognostičke informacije.

**Zaključak:** SZ je kompleksna bolest čija incidencija i prevalencija stalno rastu. Liječenje podrazumijeva multidisciplinarnu skrb, a od liječnika obiteljske medicine probiranje visoko rizičnih, pravovremeno dijagnosticiranje i stalnu redovitu kontrolu progresije SZ te koordiniranje skrbi.

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## ■ Signs and symptoms of heart failure Special features when establishing a diagnosis

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**Introduction:** Heart failure (HF) is a clinical syndrome characterized by typical symptoms (shortness of breath, calf edema, fatigue, ...) accompanied by clinical signs (rales, bilateral calf edema, heart murmur, swollen jugular veins, lateral displacement of the cardiac apex), caused by a structurally and/or functionally diseased heart, which results in impaired cardiac output and/or increased cardiac pressures at rest or during exercise. The prevalence of HF is approximately 1-2% of the adult population in developed countries, and increases to  $\geq 10\%$  in those over 70 years of age. In an average family medicine practice (FPP) in Croatia, more than 20 patients with HF can be expected. Among those over 65 years of age who present to their family doctor due to shortness of breath during exercise, one in six will have unrecognized HF. The aim of this paper is to present the symptoms and signs of HF that may increase the likelihood of diagnosing HF in FP.

**Discussion:** Symptoms of CHF are often non-specific and can be divided into three groups; symptoms of excessive fluid accumulation (backward failure), symptoms related to compensation or adaptation, and symptoms that are a consequence of reduced oxygen delivery to the tissues (forward failure). The latter is particularly difficult to recognize because they are non-specific (e.g. mild cognitive impairment, fatigue, slow recovery after physical exertion, ...). These, as well as all other, symptoms may be transient, especially in the early stages of CHF. If the patient has previously been prescribed a diuretic for other reasons (e.g. hypertension), signs of fluid retention may not be evident. The gallop rhythm that is specific to CHF is rarely found in non-hospitalized patients. Lateral displacement of the apex of the heart in the left lateral position or tachycardia, as signs of adaptation, are more common findings, but are more difficult to detect.

A less typical symptom, and relatively common in FPP, is wheezing, which is found in 35% of patients with acute CHF. Signs are particularly difficult to recognize and interpret in the obese, elderly, and patients with chronic lung disease. Younger patients often have a different etiology, clinical presentation, and outcome than older patients. For patients presenting with symptoms or signs of HF for the first time, the likelihood of HF should be assessed based on the patient's previous clinical history (e.g., coronary artery disease, hypertension, diuretic use), presenting symptoms (e.g., orthopnea), physical examination (e.g., bilateral edema, elevated jugular venous pressure, displaced apical pulse), and resting ECG. If none of these are abnormal, HF is unlikely and other diagnoses should be considered. If any pathological markers are present, plasma natriuretic peptides should be measured to identify patients who require echocardiography. Echocardiography is indicated for patients with values above the reference range but also in case of undetectable levels. Acute HF refers to the rapid onset or worsening of symptoms and/or signs of cardiac disease. Clinical classification can be based on physical examination to detect the presence of clinical symptoms/signs of congestion ('wet' vs. 'dry') and/or peripheral hypoperfusion ('cold' vs. 'warm'). This classification can be useful to guide therapy in the initial phase and carries prognostic information.

**Conclusion:** HF is a complex disease with a constantly increasing incidence and prevalence. Treatment involves multidisciplinary care, with screening of at-risk patients, timely diagnosis and ongoing regular monitoring of the progression of heart failure, and coordination of care by a family physician.

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## ■ Dugotrajni bolovi uz negativne nalaze, što dalje? Prikaz slučaja

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**Uvod s ciljem:** Sindrom juvenilne fibromialgije (JFMS) je kronični bolni sindrom koji se očituje difuznim muskuloskeletnim bolovima uz odsutnost bolesti u podlozi te osjetom boli pri palpaciji višestrukih tipičnih bolnih točaka na tijelu, dulje od 3 mjeseca. Dodatne karakteristike su umor, kronične glavobolje, poremećaji raspoloženja i subjektivni dojam otekline zglobova. Bolest se najčešće dijagnosticira u adolescentica, a dijagnoza se temelji na anamnezi i kliničkom pregledu. Promijenjena percepcija boli u JFMS rezultat je pojačane ekscitabilnosti nociceptivnih neuronskih krugova središnjeg živčanog sustava te promjena u živčanim vlaknima na periferiji. Cilj ovog prikaza slučaja je prikazati pacijenta koji ima intenzivne i dugotrajne simptome koji su neobjašnjivi dijagnostičkim pretragama.

**Prikaz slučaja:** Pacijentica je djevojčica od 11 godina. Zbog muskuloskeletnih bolova kojima ne prethodi ozljeda prvi se put javila u ordinaciju u 1. mj. 2021. g. Tada navodi bol u lijevom, a povremeno i u desnom gležnju koja se intenzivirala pri fizičkoj aktivnosti. Rendgenom zglobova isključeno je postojanje prijeloma. Laboratorijski nalazi krvne slike i upalnih parametara pokazali su normalne vrijednosti. Pacijentica je upućena dječjem ortopedu, a zatim imunoreumatologu i na MR lijevog gležnja. MR-om je ustanovljen manji zglobni izljev u donjem nožnom zglobu te plantarna ganglion cista za koje dječji ortoped tvrdi da ne mogu biti uzrokom tegoba koje pacijentica osjeća. Učinjene dodatne pretrage (ANA, RF, anti-CCP, feritin, IgM, IgG, IgA i HLA tipizacija) bile su uredne osim pozitivnog HLA B7 lokusa. Pacijentici je preporučena poštuda od tjelesne aktivnosti, vođenje dnevnika tegoba i uvođenje NSAR u terapiju. Pri primjeni NSAR intenzitet bolova joj se smanjivao no imala je potrebu za

korištenjem terapije većinu dana u godini. Kako su se tegobe ponavljale, početkom 2023. g. učinjene su troetapna scintigrafija skeleta, čiji nalaz ide u prilog dijagnozi kompleksnog regionalnog bolnog sindroma, te artroskopska toaleta lijevog nožnog zgloba. U 6. mj. 2023. g. pacijentica se po prvi put javlja s bolovima u svim zglobovima gornjih i donjih udova koji se pojavljuju na par dana, a zatim regresiraju. Jačina boli dovodi ju do plača. U periodu 2022. – 2024. g. pacijentica povremeno osjeća bolove zbog kojih se ne može osloniti na noge te zbog toga ima povećani broj izostanaka iz škole i veći se broj puta javlja u pedijatrijsku hitnu ambulantu te je u nekoliko navrata i hospitalizirana na odijelu reumatologije. Konačnu dijagnozu sindroma juvenilne fibromialgije postavlja reumatolog krajem 2024. g. temeljem pacijentične medicinske dokumentacije i fizikalnog pregleda. Pacijentici su savjetovani psihoterapija, redovna aerobna fizička aktivnost, hidroterapija i akupunktura.

**Rasprava:** Od prvog javljanja pacijentice u ambulantu do postavljanja dijagnoze prošlo je oko 3 godine što je u skladu s literaturom prema kojoj pacijenti osjećaju tegobe tijekom više godina prije nego dijagnoza JFMS bude postavljena. Tijekom tog vremena pacijentica je prošla brojne pretrage i hospitalizacije koje za rezultat nisu imale smanjenje tegoba. Mogućnosti liječenja zasad su ograničene, a temelje se na redovnoj tjelesnoj aktivnosti i kognitivno-bihevioralnoj terapiji (KBT) koja dokazano poboljšava funkcioniranje oboljelih.

**Zaključak:** Liječnici bi se trebali više osloniti na klinički pregled te uz pomoć osnovne dijagnostičke obrade i prije nego se odluče za invazivne dijagnostičke pretrage.

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## ■ Chronic pain with negative findings: what's next? A case report

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**Introduction with aim:** Juvenile fibromyalgia syndrome (JFMS) is a chronic pain syndrome characterized by diffuse musculoskeletal pain without an underlying disease, along with tenderness upon palpation of multiple typical tender points for more than three months. Additional features include fatigue, chronic headaches, mood disturbances, and a subjective feeling of joint swelling. The syndrome predominantly affects adolescent girls, and the diagnosis is based on medical history and clinical examination. Altered pain perception in JFMS results from increased excitability of nociceptive neuronal circuits in the central nervous system and changes in peripheral nerve fibers. The aim of this case report is to present a patient with severe and persistent symptoms that remain unexplained despite extensive diagnostic evaluations.

**Case report:** The patient is an 11-year-old girl who first visited a general practice office in January 2021 due to musculoskeletal pain without a preceding injury. She reported pain in her left ankle, occasionally affecting the right ankle, which worsened with physical activity. X-rays excluded fractures. Laboratory tests, including complete blood count and inflammatory markers, were within normal ranges. The patient was referred to a pediatric orthopedist, followed by an immunorheumatologist, and underwent MRI of the left ankle. MRI revealed a minor joint effusion in the subtalar joint and a plantar ganglion cyst, which the pediatric orthopedist deemed insufficient to explain the symptoms. Additional tests (ANA, RF, anti-CCP, ferritin, IgM, IgG, IgA, and HLA typing) were normal, except for a positive HLA-B7 locus. Recommendations included rest from physical activity, maintaining a symptom diary, and introducing NSAIDs. While

NSAIDs reduced the intensity of her pain, the patient required them most days of the year. As symptoms persisted, in early 2023, a three-phase skeletal scintigraphy was performed, supporting the diagnosis of complex regional pain syndrome, followed by arthroscopic debridement of the left ankle. In June 2023, the patient reported, for the first time, pain in all joints of the upper and lower extremities, lasting a few days and then subsiding. The pain's intensity led her to tears. Between 2022 and 2024, she intermittently experienced pain so severe that she was unable to walk, resulting in frequent school absences and numerous visits to pediatric emergency services, with multiple hospitalizations in rheumatology departments. A definitive diagnosis of juvenile fibromyalgia syndrome was established by a rheumatologist in late 2024, based on her medical history and physical examination. The patient was advised to begin psychotherapy, regular aerobic physical activity, hydrotherapy, and acupuncture.

**Discussion:** Approximately three years elapsed between the patient's initial presentation and the diagnosis, consistent with literature indicating that patients endure symptoms for several years before receiving a JFMS diagnosis. During this time, the patient underwent numerous investigations and hospitalizations, none of which alleviated her symptoms. Treatment options remain limited and rely on regular physical activity and cognitive-behavioral therapy (CBT), which have been proven to improve patient functioning.

**Conclusion:** Physicians should place greater reliance on clinical examination and basic diagnostic workup to establish a diagnosis early, rather than opting for invasive diagnostic procedures.

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## ■ Od Parkinsonove bolesti do glioblastoma – važnost prepoznavanja simptoma i znakova

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**Uvod s ciljem.** Parkinsonova bolest (PB) neurodegenerativna je bolest koja se javlja u 1-2% starije populacije. Glioblastom je najagresivniji i najčešći zloćudni tumor mozga u odraslih ljudi. Koinkidencija ovih bolesti rijetka je i slabo opisana u literaturi. Cilj ovog rada je prikazati slučaj pacijentice s PB-om kojoj je uslijed pogoršanja osnovne bolesti neočekivano dijagnosticiran maligni tumor mozga.

**Prikaz slučaja.** Sedamdesetšestogodišnja bolesnica javila se u ordinaciju obiteljske medicine u pratnji supruga zbog dizurije i suprapubične boli. Inače boluje od PB-a i redovito uzima terapiju. U anamnezi pacijentica se požalila na pogoršanje stanja, navodeći otežan govor i kretanje, disfagiju i gubitak apetita. Kliničkim pregledom utvrđena je suprapubična bol i gubitak tjelesne mase. Neurološkim pregledom utvrđena je izraženija bradikinezija u odnosu na posljednji kontrolni pregled, pogoršanje hoda vrlo sitnim koracima uz izraženiji akinetski tremor i rigor desne strane. S obzirom na pogoršanje stanja pacijentice, liječnica obiteljske medicine konzultirala je neurologa koji je preporučio hitnu radiološku obradu. CT pretragom mozga otkrivena je tumorska tvorba, zbog čega je pacijentica hitno hospitalizirana te je učinjena dodatna obrada. MR-om mozga potvrđena je lijevostrana temporalna supkortikalna solidno-cistična lezija veličine 36x33 mm, s perifokalnim edemom koji se širio prema hipokampusu i bazalnim ganglijima. Tjedan dana kasnije učinjena je kraniotomija s maksimalnom redukcijom tumorskog tkiva. Pacijentica je otpuštena kući u dobrom općem stanju i upućena na daljnje onkološko liječenje. Patohistološka analiza potvrdila je tumor glioblastoma multiforme.

**Rasprava.** Opisani slučaj sadrži nekoliko posebitosti. Naime, PB i glioblastom imaju naizgled suprotne patofiziološke mehanizme - dok PB

nastaje neurodegeneracijom neurona u bazalnim ganglijima, glioblastom nastaje prekomjernom i nezaustavljivom proliferacijom tumorski promijenjenih glijalnih stanica. Međutim, istraživanja ukazuju na značajnu ulogu mitohondrijske disfunkcije i oksidativnog stresa u nastanku obiju bolesti, kao i na postojanje inverzno reguliranih zajedničkih genetskih puteva. Nadalje, zanimljivo je da neka istraživanja pokazuju pozitivnu korelaciju između PB-a i razvoja određenih tipova tumora, posebice melanoma i tumora mozga. S druge strane, za većinu ostalih tipova tumora dokazana je negativna korelacija, odnosno protektivni učinak PB-a na razvoj tumora, što se naziva „inverse cancer comorbidity“. Razlozi za ovu pojavu nisu posve jasni, ali spominju se genetski i okolišni čimbenici, kao i primjena nekih lijekova (npr. levodope) te učestalije radiološke pretrage mozga u pacijenata s PB-om. Konačno, klinički simptomi ovise o lokalizaciji glioblastoma. U ovome slučaju tumor je bio lociran u temporalnom režnju, no perifokalni edem proširio se sve do hipokampusa i bazalnih ganglija izazivajući simptome nalik onima u PB-u. Kod ove bolesnice su, osim glavobolje, izostali simptomi i znakovi tipični za tumore mozga (kao što su povraćanje, epileptički napadaji i poremećaji stanja svijesti), budući da nije došlo do povišenja intrakranijalnog tlaka, čime je dodatno otežano postavljanje dijagnoze.

**Zaključak.** Iako drugačijeg mehanizma nastanka, PB i glioblastom mogu se klinički manifestirati istim ili sličnim simptomima i znakovima. Ovim prikazom slučaja želi se naglasiti važnost pažljive procjene novonastalih ili naglo progredirajućih simptoma u neuroloških pacijenata. Pravovremena dijagnoza i odgovarajuća terapija mogu značajno utjecati na prognozu i kvalitetu života bolesnika.

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## ■ From Parkinson's Disease to Glioblastoma – The Importance of Recognizing Symptoms and Signs

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**Introduction with aim.** Parkinson's disease (PD) is a neurodegenerative disease that occurs in 1-2% of the elderly population. Glioblastoma is the most aggressive and most common malignant brain tumor in adults. The co-occurrence of these diseases is a rare phenomenon, poorly described in the literature. The aim of this paper is to present the case of a PD patient unexpectedly diagnosed with a malignant brain tumor due to worsening of the underlying disease.

**Case report.** A 76-year-old patient visited a family medicine practice with her husband, complaining of dysuria and suprapubic pain. She had a history of PD and was taking medication regularly. In medical history, the patient complained that her condition had worsened, reported difficulties with speaking and moving, dysphagia and loss of appetite. Clinical examination revealed suprapubic pain and weight loss. Neurological assessment showed increased bradykinesia compared to her last check-up, worsening of short-stepped gait, and more pronounced akinetic tremor and rigidity on the right side. Given the deterioration of patient's condition, the family medicine physician consulted a neurologist who recommended urgent radiological assessment. Brain CT scan showed a mass, leading to her urgent hospitalization for further evaluation. Brain MRI confirmed a left temporal subcortical solid-cystic lesion measuring 36x33 mm, with perifocal edema extending to the hippocampus and basal ganglia. A craniotomy with maximum tumor reduction was performed a week later. The patient was discharged in good general condition and sent home for further oncological treatment. Pathohistological examination revealed a glioblastoma multiforme tumor.

**Discussion.** This case presents several specific features. Namely, PD and glioblastoma have

seemingly opposite pathophysiological mechanisms – PD results from neurodegeneration of basal ganglia neurons, whereas glioblastoma arises from an excessive and uncontrolled proliferation of tumor-altered glial cells. However, research suggests that mitochondrial dysfunction and oxidative stress play significant roles in the development of both diseases. Studies also indicate the existence of inversely regulated common genetic pathways. Furthermore, some studies interestingly show a positive correlation between PD and the development of certain tumors, particularly melanoma and brain tumors. Conversely, PD appears to have a protective effect against most other cancers, which is known as "inverse cancer comorbidity". The underlying causes remain unclear, but genetic and environmental factors are suggested, as well as certain medications (e.g. levodopa), and increased radiological brain assessments in PD patients. Finally, clinical symptoms depend on glioblastoma localization. In this case, the tumor was located in the temporal lobe, but perifocal edema extended to the hippocampus and basal ganglia, inducing symptoms resembling PD. Apart from headache, the patient exhibited no typical brain tumor symptoms (such as vomiting, seizures or impaired consciousness), as intracranial pressure was not elevated, further complicating the diagnostic process.

**Conclusion.** Although PD and glioblastoma have distinct pathophysiological mechanisms, they can clinically present with the same or similar symptoms and signs. This case report highlights the importance of a careful evaluation of new or rapidly progressive symptoms in neurological patients. Timely diagnosis and adequate treatment can significantly impact prognosis and patient's quality of life.

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## ■ Pyoderma gangrenosum Prikaz slučaja

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**Ključne riječi:** pyoderma gangrenosum; leg ulcer; leg dermatoses

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**Uvod s ciljem:** Pyoderma gangrenosum je reaktivna neinfektivna upalna dermatozna koja spada u spektar neutrofilnih dermatozna. Osnovni uzrok nije poznat, ali poznato je da se podliježeća sustavna bolest nalazi u do 50% slučajeva, stoga je potrebna šira obrada pacijenta. U ovom prikazu slučaju, riječ je o 42-godišnjoj pacijentici, prethodno zdravoj, s novonastalim bolnim ulceracijama potkoljenica. Postavljena je sumnja na pyoderma gangrenosum, učinila se biopsija kožne promjene te se dijagnoza potvrdila. Cilj je ovog rada osvijestiti liječnika obiteljske medicine da se pravovremeno posumnja na dijagnozu pyoderme gangrenosum koja je poprilično nespecifična, učiniti biopsiju rane, a nikako opežan debridman kožne promjene jer to može dovesti do pogoršanja iste.

**Prikaz slučaja:** 42-godišnja pacijentica je došla na pregled zbog kožnih promjena desnog gležnja. Prije 9 mjeseci naglo nastala manja ulceracija u području lijeve potkoljenice. Redovno se činila toaleta rane, ali je primjećeno da se pri agresivnijem čišćenju rane i učinjenom debridmanu pogorša lokalni status. Ipak, nakon 2 mjeseca, ulkus je postupno zacijelio. Sada ponovno naglo nastale kožne promjene desnog gležnja, promjene ne svrbe, osjeća blažu bolnost. Dosada zdrava, ne troši kronične terapije. U dermatološkom statusu isticali su se eritematozne papule desnog gležnja, palpabilno induracije, tamnija pigmentacija središta promjena, bez znakova kronične venske/arterijske insuficijencije. Bio je konzultiran dermatovenerolog te je dogovorno pacijentica upućena njemu radi biopsije kože. Isto se učinilo i preporučila se opširnija obrada (fekalni kalprotektin, autoantitijela, tumorski biljezi). Na kontrolnom pregledu su kožne promjene bile u pogoršanju, bol se pojačala, formirala se jasna ulceracija u medijalnom dijelu gležnja s podminiranim rubom

te okolnom hiperemičnom zonom. PHD nalaz postavlja sumnju na pyoderma gangrenosum. Iz laboratorijskih nalaza se izdvajala vrijednost fekalnog kalprotektina (153 µg/g). Ordinirao se prednizon 40 mg 1x dnevno uz gastroprotekciju, uz postepeno snižavanje doze, ovisno o lokalnom kožnom statusu.

**Rasprava:** Kod ove pacijentice su prethodno nastale kožne lezije postupno zarasle primjenom lokalne toaleta rane. Ponovna pojava lezija ukazuje na recidivističku prirodu bolesti. Obzirom da je riječ o naglo nastaloj bolnoj ulceraciji, pyoderma gangrenosum je svakako spadala u diferencijalnu dijagnozu, a potvrdila se kožnom biopsijom. Inače se prezentira iznimno bolnim eritematoznim promjenama, kasnije i ulceracijama, no u ovom slučaju nije bilo jake bolnosti. Lezija može biti precipitirana manjom traumom, fenomenom poznatim kao "patergija". Pyoderma gangrenosum ostaje klinička dijagnoza, iako biopsija kože može biti suportivna i govoriti u prilog bolesti, glavna vrijednost biopsije kože je isključivanje drugih uzroka kožnih ulceracija.

**Zaključak:** Do sada nema validiranih dijagnostičkih kliničkih ili patoloških kriterija za dijagnosticiranje pyoderme gangrenosum, kao niti nacionalnih ili internacionalnih smjernica za liječenje pa se uvelike oslanjamo na vlastito iskustvo, mišljenje eksperata i stupnju zahvaćenosti kože. Jednom kad se potvrdi dijagnoza, započne se liječenje sistemskim kortikosteroidima uz tendenciju smanjivanja doze ovisno o lokalnom kožnom statusu. Zaključno, nama kao liječnicima obiteljske medicine je posebno važno prepoznati pacijenta sa sumnjom na pyoderma gangrenosum, pravovremeno uputiti dermatovenerologu radi biopsije kože zbog potvrde dijagnoze, a nikako ne činiti ekstenzivni debridman rane jer će to dovesti do pogoršanja lokalnog statusa.

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## ■ Pyoderma gangrenosum Case report

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**Introduction with aim:** Pyoderma gangrenosum is a reactive non-infectious inflammatory dermatosis that belongs to the spectrum of neutrophilic dermatoses. The underlying cause is unknown, but it is known that an underlying systemic disease is present in up to 50% of cases, therefore a broader workup of the patient is necessary. In this case report, we are talking about a 42-year-old female patient, previously healthy, with newly developed painful ulcerations of the lower legs. Surgical excision of the lesion was performed, after which the local status deteriorated and new skin lesions appeared on the lower legs. Pyoderma gangrenosum was suspected, a biopsy of the skin lesion was performed, and the diagnosis was confirmed. The aim of this paper is to raise awareness among family physicians to promptly suspect the diagnosis of pyoderma gangrenosum, which is quite non-specific, to perform a biopsy of the wound, and not to perform extensive debridement of the skin lesion, as this can lead to its worsening.

**Case report:** A 42-year-old female patient came for an examination due to skin lesions on her right ankle. 9 months ago, an ulceration suddenly appeared in the area of her left calf. Wound care was performed regularly, but it was noted that more aggressive wound cleaning and debridement worsened the local status. However, after 2 months, the ulcer gradually healed. Now, skin lesions on her right ankle suddenly appeared again, the changes do not itch, she feels mild pain. So far, she is healthy, does not use chronic therapies. In the dermatological status, erythematous papules of the right ankle stood out, palpable induration, darker pigmentation of the center of the changes, without signs of chronic venous/arterial insufficiency. A dermatovenerologist was consulted and the patient was referred to him for a skin biopsy. A biopsy of the skin lesions was performed and more extensive diagnostic work-up was recommended (fecal calprotectin, autoantibodies, tumor markers). At the follow-up examination, the skin changes were

worsening, the pain intensified, a clear ulceration formed in the medial part of the ankle with an undermined edge and a surrounding hyperemic zone. The biopsy finding is more specific this time and raises the suspicion of pyoderma gangrenosum. The value of fecal calprotectin (153 µg/g) was increased. Prednisone 40 mg once a day was prescribed with gastroprotection, with a gradual lowering of the dose, depending on the local skin status.

**Discussion:** In this patient, previously occurring skin lesions gradually healed with the use of local wound dressings. The recurrence of lesions indicates the recurrent nature of the disease. Given that it is a sudden onset of painful ulceration, pyoderma gangrenosum was certainly a differential diagnosis, and was confirmed by skin biopsy. It usually presents with extremely painful erythematous changes, later ulcerations, but in this case there was no severe pain. The lesion may be precipitated by minor trauma, a phenomenon known as "pathergy". Pyoderma gangrenosum remains a clinical diagnosis, although skin biopsy can be supportive and suggestive of the disease, the main value of skin biopsy is the exclusion of other causes of skin ulceration.

**Conclusion:** To date, there are no validated diagnostic clinical or pathological criteria for the diagnosis of pyoderma gangrenosum, nor are there any national or international treatment guidelines, so we rely heavily on our own experience, expert opinion and the degree of skin involvement. Once the diagnosis is confirmed, treatment with systemic corticosteroids is initiated with a tendency to reduce the dose depending on the local skin status. In conclusion, it is especially important for us as general practitioners to recognize a patient with suspicion of pyoderma gangrenosum, promptly refer them to a dermatovenerologist for a skin biopsy to confirm the diagnosis, and not to perform extensive debridement of the wound, as this will lead to a worsening of the local status.

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## ■ Moja dementna baka

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**Uvod s ciljem:** Promjene koje ukazuju na pojavu demencije najprije uoče članovi obitelji. Suživot starijih i mlađih članova obitelji ima velikih prednosti i po koji nedostatak. Dugogodišnji zajednički život omogućuje fino uočavanje promjena, ali ima i opasnost da se na promjene privikne, pa ih se ne uzima za ozbiljno. Cilj rada je istaknuti pozitivne elemente suživota sa dementnom osobom u ranom otkrivanju i svakodnevnom funkcioniranju.

**Rasprava:** Odrasla sam u obitelji čiji je baka član, koji ima svoje mjesto i značaj. Kao najmlađa unuka razvila sam poseban odnos povjerenja, pa sam preuzela ulogu člana koji baki može komunicirati simptome demencije i načine svakodnevnog „suživota“ s bolesti. Dementna osoba se ne smije izolirati, potrebno je da se i dalje osjeća kao važan član obitelji. Stalno treba procjenjivati mogućnosti i pred nju postavljati realne zahtjeve i očekivanja.

Intervencija: najčešće komunikacijske epizode mogu se dogoditi na različite načine.

1. Ne smiješ izlaziti iz kuće da se ne izgubiš / Idemo zajedno u šetnju
2. Stalno gubiš stvari, ne možemo stalno zbog tebe biti u stresu / Svima se dogodi da nešto izgube, pronaći ćemo
3. Moraš nositi ovu SOS ogrlicu oko vrata da bi te kontrolirali / Poklanjam ti ovu narukvicu kao znak ljubavi. Ako me zatrebaš, stisni ovu tipku
4. Zašto nam danas deseti puta pričaš o djedu / Hajde mi ispričaj ono o djedu, zaboravila sam detalje
5. Što će ti te križaljke, ionako ništa ne znaš / Hajde mi pomoz da riješim ovu križaljku
6. Ne kontaktiraj sa susjedima da ne misli da si poludjela / Zovi na kavu prijateljicu iz mladosti

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## ■ My demented grandmother

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**Introduction with aim:** Changes that indicate the onset of dementia are first noticed by family members. The coexistence of older and younger family members has great advantages and some disadvantages. Living together for many years allows for fine observation of changes, but there is also the danger of he gets used to the changes, so he doesn't take them seriously. The goal of the work is to highlight positive elements coexistence with a demented person in early detection and daily functioning.

### Discussion:

I grew up in a family of which my grandmother is a member, which has its own place and significance. As the youngest granddaughter, I developed a special relationship of trust, so I took on the role of a member of the grandmother can communicate the symptoms of dementia and ways of daily "coexistence" with the disease. A demented person should not be isolated, it is necessary for him to continue to feel like an important member of the family. It is necessary to constantly evaluate the possibilities and set realistic demands and expectations before it. Intervention: the most common communication episodes can happen in different ways.

1. You must not leave the house to avoid getting lost / Let's go for a walk together.

2. You keep losing things, we can't always be stressed because of you / Everyone loses something, we will find.

3. You have to wear this SOS necklace around your neck to be controlled / I'm giving you this bracelet as a sign of love. If you need me, press this button.

4. Why are you telling us about grandfather for the tenth time today / Come on, tell me about grandfather, I forgot details.

5. What do you do with crosswords, you don't know anything anyway / Come on, help me solve this crossword.

6. Don't contact your neighbors so they don't think you've gone crazy / Invite a friend from youth.

7. Do nothing, because you can't do it / Bake us the cookies you do best, I'll prepare them mixture according to your recipe.

**Conclusion:** It is important to recognize the key person in the family who has the role of the one who has dementia recognizes and communicates about the disease in the right way. Specific knowledge is required for this they go beyond the framework of family care and empathy. It is recommended that every family be educated about signs of dementia, coexistence with demented persons and possible complications. It's good to recognize a key family member who will approach the demented member in a positive way, acquire trust and propose solutions and decisions, which are not always simple or easy.

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## ■ Prikaz pacijenta s dubokom venskom trombozom gornjih ekstremiteta

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**Uvod s ciljem:** Duboka venska tromboza gornjih ekstremiteta (DVT) čini 4-10% svih slučajeva DVT-a, a klasificira se kao primarna te sekundarna, češća, koja je najčešće posljedica ozljede endotela centralnim venskim kateterom, srčanim elektrostimulatorom ili uslijed intravenske zloupotrebe droga. Cilj je ovog rada prikazati složenost pravovremenog prepoznavanja te otkrivanja uzroka i liječenja pacijenta s DVT-om gornjih ekstremiteta.

**Prikaz slučaja:** Pacijent u dobi od 69 godina javio se u ambulantu obiteljske medicine zbog oticanja desne ruke unatrag tjedan dana, što povezuje s pojačanom fizičkom aktivnosti. Nije bio febrilan niti primjetio crvenilo na području ekstremiteta, oticanje je prvotno krenulo u području podlaktice te se potom širilo proksimalno, popraćeno bolovima. Zaduho, pritisak u prsima i krize svijesti nije manifestirao. Liječi se od hiperlipidemije (rosuvastatin 20 mg 1x1) te je 2022. učinjena radikalna prostatektomija zbog karcinoma prostate. Kliničkim pregledom ustanovljen je povećan opseg desne nadlaktice (>3 cm u odnosu na lijevu), uredne periferne pulzacije, osjet i motorika, lokalizirana osjetljivost duž toka dubokih vena te vidljive kolateralne nevarikozne vene. U statusu eupnoičan, eukardan, RR 128/85 mm Hg, EKG: fibrilacija atrijska (FA), frekvencija 90/min, lijeva električna osovina, bez znakova akutne ishemije i hipertrofije. Pacijent je upućen na hitni prijam gdje je obradom (d-dimeri 3,51 mg/L, doppler vena) potvrđena dijagnoza te je hospitaliziran zbog duboke venske tromboze v.brachialis desno i tromboflebitisa v.basilice te FA nepoznatog trajanja. Dodatnom obradom u svrhu razjašnjenja etiologije DVT-a zaključeno je da se radi o DVT-u provociranom fizičkim naporom. U sklopu obrade FA učinjen je ultrazvuk srca kojim se verificirala dijastolička disfunkcija I. stupnja, reducirana kontraktilna sposobnost (EF 40-50%) uz laboratorijski nalaz povišenog NT-proBNP-a. Započeto je liječenje direktnim oralnim antikoagulantom (DOAK), a u kratkotrajnoj anesteziji učinjena je uspješna sinkronizirana elektrokonverzija, nakon koje se pratio sinus ritam. Pacijent je otpušten s terapijom: rivaroksaban 15 mg 2x1

tri tjedna, potom 20 mg 1x1, perindopril 2 mg 1x1, bisoprolol 2,5 mg 1x1, dapagliflozin 10 mg 1x1 te rosuvastatin/ezetimib 20 mg 1x1.

**Rasprava:** Primarna duboka venska tromboza gornjih ekstremiteta u 80% slučajeva povezana je s intenzivnom fizičkom aktivnosti gornjeg dijela tijela, pretežno hiperabdukcijom. Diferencijalnodijagnostički u obzir dolazi akutni celulitis, limfangitis, ruptura mišića, varikozne vene i površinski tromboflebitis. Prema Wellsovoj ljestvici, pacijent ima veliku vjerojatnost za DVT te je preporuka učiniti D-dimere, a s obzirom na povišene vrijednosti, sljedeći je korak doppler vena radi potvrde dijagnoze. Preboljela maligna bolest nije bila uključena u Wellsove kriterije zbog završenog liječenja prije dvije godine, no učinjene su pretrage u svrhu isključenja paraneoplastičnog sindroma. U liječenju se koriste DOAK-i, a moguće ga je prekinuti nakon tri mjeseca, s obzirom na provocirajući uzrok koji nije više prisutan, što u ovom slučaju neće biti moguće zbog novootkrivene FA. Prilikom odabira lijeka važno je razmotriti kontraindikacije, komorbiditete te moguće nuspojave.

**Zaključak:** Ovaj rad naglašava važnost pravovremenog prepoznavanja i dijagnostike rjeđih kliničkih entiteta DVT-a u ambulanti obiteljske medicine. Rana dijagnostika važna je kako bi se spriječile moguće komplikacije plućne embolije i posttrombotskog sindroma, a u suradnji s bolničkim specijalistima nastavlja se dijagnostika, liječenje i praćenje pacijenta.

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## ■ Case of a patient with deep venous thrombosis of the upper extremities

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**Introduction with aim:** Deep Venous Thrombosis of the Upper Extremities (DVT) accounts for 4-10% of all DVT cases and is classified into primary and secondary, the latter being more common and usually resulting from endothelial injury due to a central venous catheter, a cardiac pacemaker, or intravenous drug abuse. The aim of this paper is to highlight the complexity of timely recognition, identifying the causes, and treating a patient with upper extremity DVT.

**Case report:** A 69-year-old patient presented to the family medicine clinic with swelling in the right arm for the past week, which he linked to increased physical activity. He was not febrile and did not notice redness in the area of the extremity. The swelling initially occurred in the forearm and then spread proximally, accompanied by pain. He did not experience shortness of breath, chest pressure, or episodes of confusion. He was being treated for hyperlipidemia (rosuvastatin 20 mg once daily) and had undergone radical prostatectomy in 2022 for prostate cancer. Clinical examination revealed an increased circumference of the right upper arm (>3 cm compared to the left), normal peripheral pulses, sensation, and motor function, localized tenderness along the deep vein course, and visible collateral non-varicose veins. The patient was in a eupneic state, normal heart rate, with blood pressure 128/85 mm Hg, EKG showing atrial fibrillation (AF) with a heart rate of 90/min, left electrical axis, no signs of acute ischemia or hypertrophy. The patient was referred for emergency admission, where diagnosis was confirmed through testing (D-dimers 3.51 mg/L, Doppler venous ultrasound), and he was hospitalized due to deep venous thrombosis of the right brachial vein and thrombophlebitis of the basilic vein, along with AF of unknown duration. Further testing to clarify the etiology of the DVT concluded that it was induced by physical exertion. As part of the AF evaluation, an echocardiogram revealed first-degree diastolic dysfunction, reduced contractility (EF 40-50%), and elevated NT-proBNP levels. Treatment with direct oral anticoagulants (DOACs) was initiated, and successful synchronized electrical cardioversion

was performed under short-term anesthesia, after which sinus rhythm was restored. The patient was discharged with the following therapy: rivaroxaban 15 mg twice daily for three weeks, then 20 mg once daily, perindopril 2 mg once daily, bisoprolol 2.5 mg once daily, dapagliflozin 10 mg once daily, and rosuvastatin/ezetimibe 20 mg once daily.

**Discussion:** Primary deep venous thrombosis of the upper extremities is associated with intense upper body physical activity in 80% of cases, particularly hyperabduction. Differential diagnoses include acute cellulitis, lymphangitis, muscle rupture, varicose veins, and superficial thrombophlebitis. According to the Wells score, the patient has a high probability of DVT, and it is recommended to perform D-dimer testing. Due to elevated values, the next step is Doppler venous ultrasound to confirm the diagnosis. The patient's past cancer was not considered in the Wells criteria because treatment was completed two years ago; however, tests were done to exclude a paraneoplastic syndrome. Direct oral anticoagulants (DOACs) are used in treatment, and it may be discontinued after three months if the provoking cause is no longer present, which in this case is not possible due to the newly diagnosed AF. When selecting medication, it is important to consider contraindications, comorbidities, and potential side effects.

**Conclusion:** This paper emphasizes the importance of timely recognition and diagnosis of rarer clinical entities of upper extremity DVT in the family medicine setting. Early diagnosis is crucial to prevent potential complications such as pulmonary embolism and post-thrombotic syndrome, and in collaboration with hospital specialists, the diagnosis, treatment, and monitoring of the patient continue.

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## ■ Akutna intermitentna porfirija otkrivena u 38. Godini

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**Uvod s ciljem.** Porfirija je rijetka metabolička bolest koja nastaje zbog disfunkcije u biosintezi hema, ključne molekule za funkciju hemoglobina. Ovisno o vrsti porfirije, simptomi mogu biti vrlo različiti i mogu obuhvatiti neurološke, kožne ili oba tipa simptoma. Porfirija može biti nasljedna ili stečena, a simptomi često počinju u odrasloj dobi. Ovaj slučaj prikazuje dijagnozu porfirije kod muškarca u 38. godini života, nakon što su uobičajeni medicinski tretmani za bolove u abdomenu i neurološke simptome bili neučinkoviti. Cilj prikaza je predstaviti dijagnostički proces i terapijske opcije kod akutne intermitentne porfirije (AIP), te podići svijest o važnosti ranog prepoznavanja rijetkih bolesti.

**Prikaz slučaja.** Muškarac, 38 godina, bez ozbiljnih bolesti u anamnezi, javlja se liječniku obiteljske medicine jer unatrag godinu dana trpi bolove u abdomenu, utrnulost i slabost u ekstremitetima, tremor, promjene raspoloženja i primjećuje kožne lezije u vidu crvenih bolnih mrlja. Iako su standardne pretrage bile uredne, pronađeni su povišeni porfirini u krvi i urinu. Dijagnoza porfirije je potvrđena genetskim testiranjem. Terapija je uključivala izbjegavanje okidača (alkohol, izlaganje stresu, sunčanje), pravilnu hidrataciju, simptomatsko liječenje (analgetici, antiepileptici), te psihološku potporu.

**Rasprava.** Ovaj slučaj ističe važnost razmatranja rijetkih bolesti, poput porfirije, čak i kada su standardni nalazi uredni. Kasno otkrivanje može otežati liječenje, stoga je ključno uvažiti pacijentovo stanje i povijest simptoma. U literaturi se naglašava kako rano prepoznavanje AIP-a može značajno poboljšati prognozu, smanjiti rizik od napada i time poboljšati kvalitetu života.

**Zaključak.** Prikazani slučaj ukazuje na važnost pažljivog pristupa pacijentima s nespecifičnim simptomima, te potrebu za sveobuhvatnim dijagnostičkim postupkom. Ključni aspekt uspješnog liječenja uključuje izbjegavanje okidača, praćenje metaboličkih parametara, kao i psihološku potporu za pacijente koji se suočavaju s

kroničnom bolešću. Ranom dijagnozom i pravilnim liječenjem moguće je smanjiti učestalost i intenzitet simptoma, čime se poboljšava kvaliteta života pacijenata.

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## ■ Acute intermittent porphyria diagnosed at the age of 38

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**Introduction with aim.** Porphyria is a rare metabolic disorder caused by dysfunction in the biosynthesis of heme, a critical molecule for hemoglobin function. Depending on the type of porphyria, symptoms can vary significantly and may include neurological, dermatological, or a combination of both types of symptoms. Porphyria can be hereditary or acquired, with symptoms often beginning in adulthood. This case report describes the diagnosis of porphyria in a 38-year-old man after conventional medical treatments for abdominal pain and neurological symptoms proved ineffective. The aim of this report is to present the diagnostic process and therapeutic options for acute intermittent porphyria (AIP) and to raise awareness of the importance of early recognition of rare diseases.

**Case Report.** A 38-year-old patient with no significant medical history, consulted his primary care physician due to a year-long history of abdominal pain, numbness, and weakness in the extremities, tremors, mood changes, and the appearance of red, painful skin lesions. Although standard tests yielded normal results, elevated porphyrins were detected in his blood and urine. The diagnosis of porphyria was confirmed through genetic testing. Treatment included avoiding triggers (alcohol, stress, sun exposure), ensuring proper hydration, symptomatic management (analgesics, antiepileptics), and psychological support.

**Discussion.** This case highlights the importance of considering rare diseases such as porphyria, even when standard test results are normal. Delayed diagnosis can complicate treatment; therefore, it is crucial to evaluate the patient's condition and symptom history thoroughly. The literature emphasizes that early recognition of AIP can significantly improve prognosis, reduce the risk of attacks, and enhance quality of life.

**Conclusion.** The presented case underscores the importance of a meticulous approach to patients with nonspecific symptoms and the need for a

comprehensive diagnostic process. Key aspects of successful treatment include avoiding triggers, monitoring metabolic parameters, and providing psychological support for patients coping with a chronic condition. Early diagnosis and proper management can reduce the frequency and severity of symptoms, thereby improving patients' quality of life.

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## ■ Nesanica

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**Uvod s ciljem.** Poremećaj nesanicе se definira kao prevladavajuće nezadovoljstvo kvantitetom ili kvalitetom spavanja, uz poteškoće u uspjavanju, održavanju spavanja ili preranom jutarnjem buđenju, koje uzrokuju klinički značajne poteškoće u dnevnom funkcioniranju unatoč odgovarajućim mogućnostima i okolnostima za spavanje, a traje najmanje tri puta tjedno kroz tri mjeseca. Način na koji konceptualiziramo nesanicu (bilo kao simptom ili poremećaj), može značajno utjecati na stope prevalencije, koje variraju od oko 10% kada se promatra kao poremećaj do 30% kada se promatra kao simptom. Liječenje nesanicе predstavlja izazov jer se često prepisuju lijekovi poput benzodiazepina i sedativnih antidepresiva, koji su učinkoviti za kratkotrajnu uporabu, ali mogu uzrokovati ovisnost i nuspojave pri duljem uzimanju. Cilj prikaza slučaja je razumjeti pravilne metode liječenja nesanicе kako bi se izbjegla nepotrebna ili dugotrajna upotreba lijekova koji mogu uzrokovati ovisnost i nuspojave.

**Prikaz slučaja:** Pacijent, rođen 1997. godine, dosada zdrav, javio se zbog kronične nesanicе praćene intenzivnom tjeskobom i depresivnim simptomima koji su započeli nakon gubitka posla. Žalio se na poteškoće s uspjavanjem i s učestalim noćnim buđenjima u trajanju od dulje od tri mjeseca. Ove poteškoće rezultirale su izraženim osjećajem umora i iscrpljenosti tijekom dana, što je utjecalo na njegovo raspoloženje i sposobnost obavljanja svakodnevnih aktivnosti. Pacijentu je, u pokušaju ublažavanja simptoma nesanicе, preporučeno diazepam u dozi 5 mg, no nakon mjesec dana je dobio za nuspojavu palpitacije, te je lijek isključen. Potom je uključen zolpidem u dozi 10 mg, no nije zamijećeno kliničkog poboljšanja. Upućen je u ambulantu za poremećaje spavanja. Nakon uzimanja anamnestičkih podataka je određen indeks težine nesanicе, koji je iznosio 23 (klinička nesanicа). Preporučeno je započeti kognitivno-bihevioralnom terapijom za nesanicu (CBT-I). Nakon osam provedenih terapijskih tretmana, pacijent prijavljuje značajno poboljšanje

kvalitete spavanja, skraćanje latencije uspjavanja i preranog buđenja, smanjenje anksioznosti i depresivnih simptoma te bolje sveukupno funkcioniranje. Više ne koristi farmakoterapiju.

**Rasprava.** Prikazani slučaj pacijenta s nesanicom, tjeskobom i depresijom jasno ilustrira kako emocionalni stresori, poput gubitka posla, mogu pokrenuti začarani krug nesanicе i negativnih emocija. Liječenje nesanicе zahtijeva razlikovanje primarne nesanicе od one povezane s komorbiditetima poput anksioznosti i depresije. Farmakoterapija, poput benzodiazepina i sedativnih antidepresiva, ograničena je zbog rizika od ovisnosti i nuspojave te pruža samo kratkotrajno ublažavanje simptoma. Preporuke za dijagnostiku nesanicе uključuju klinički pregled s anamnezom spavanja, korištenje upitnika i dnevnika spavanja, dok se polisomnografija koristi kod sumnje na druge poremećaje spavanja. Europske smjernice ističu CBT-I kao prvu liniju liječenja kronične nesanicе, uživo ili digitalno. Za kratkotrajno liječenje (do 4 tjedna) mogu se koristiti benzodiazepini, agonisti benzodiazepinskih receptora, daridoreksant i sedativni antidepresivi, dok se dugotrajna primjena razmatra oprezno. Antagonisti oreksinskih receptora i melatonin s produljenim otpuštanjem mogu se koristiti u određenim slučajevima, dok se lijekovi poput antihistaminika, antipsihotika i fitoterapeutika ne preporučuju.

**Zaključak.** Brojni su izazovi u liječenju nesanicе, posebno kada je povezana s tjeskobom i depresijom. Farmakološki tretmani često nisu učinkoviti dugoročno, dok se kognitivno-bihevioralna terapija (CBT-I) pokazala kao uspješna metoda za rješavanje temeljnih uzroka nesanicе. Edukacija pacijenata i smanjenje oslanjanja na lijekove ključni su za trajno poboljšanje kvalitete sna i života.

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## ■ Insomnia

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**Introduction with aim.** Insomnia is defined as a persistent dissatisfaction with the quantity or quality of sleep, characterized by difficulty falling asleep, maintaining sleep, or waking up too early in the morning. These difficulties must cause clinically significant impairments in daytime functioning despite adequate opportunities and circumstances for sleep and persist at least three times a week for three months. The way insomnia is conceptualized—whether as a symptom or a disorder—can significantly influence prevalence rates, which range from approximately 10% when viewed as a disorder to 30% when regarded as a symptom. Treating insomnia poses a challenge because medications such as benzodiazepines and sedative antidepressants, although effective for short-term use, can lead to dependency and side effects with prolonged usage. The aim of this case report is to understand proper methods for treating insomnia to avoid unnecessary or prolonged use of medications that may cause dependency and adverse effects.

**Case report.** A patient born in 1997, previously healthy, presented with chronic insomnia accompanied by intense anxiety and depressive symptoms following job loss. He reported difficulties falling asleep and frequent nighttime awakenings lasting over three months. These issues resulted in pronounced fatigue and exhaustion during the day, affecting his mood and ability to perform daily activities. To alleviate the symptoms of insomnia, the patient was initially prescribed diazepam at a dose of 5 mg. However, after a month, he experienced palpitations as a side effect, and the medication was discontinued. Subsequently, zolpidem at a dose of 10 mg was introduced, but no clinical improvement was observed. The patient was referred to a sleep disorder clinic. Following an anamnesis, the Insomnia Severity Index was determined to be 23 (clinical insomnia). Cognitive-behavioral therapy for insomnia (CBT-I) was recommended. After eight therapy sessions, the patient reported significant improvements in sleep quality, a reduction in sleep onset

latency and early awakenings, decreased anxiety and depressive symptoms, and better overall functioning. He no longer uses pharmacotherapy.

**Discussion.** This case of a patient with insomnia, anxiety, and depression clearly illustrates how emotional stressors, such as job loss, can initiate a vicious cycle of insomnia and negative emotions. Treating insomnia requires distinguishing primary insomnia from insomnia associated with comorbidities such as anxiety and depression. Pharmacotherapy, including benzodiazepines and sedative antidepressants, is limited by risks of dependency and side effects and provides only short-term symptom relief. Recommendations for diagnosing insomnia include clinical evaluation with a sleep history, the use of questionnaires and sleep diaries, while polysomnography is utilized when other sleep disorders are suspected. European guidelines emphasize CBT-I as the first-line treatment for chronic insomnia, whether delivered in-person or digitally. For short-term treatment (up to four weeks), benzodiazepines, benzodiazepine receptor agonists, daridorexant, and sedative antidepressants can be used, while long-term use is approached with caution. Orexin receptor antagonists and extended-release melatonin may be used in certain cases, while medications such as antihistamines, antipsychotics, and phytotherapeutics are not recommended.

**Conclusion.** There are numerous challenges in treating insomnia, particularly when associated with anxiety and depression. Pharmacological treatments are often not effective long-term, whereas cognitive-behavioral therapy (CBT-I) has proven to be a successful method for addressing the underlying causes of insomnia. Patient education and reducing reliance on medications are crucial for achieving lasting improvements in sleep quality and overall quality of life.

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## ■ Tinnitus ili nešto više

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**Uvod s ciljem:** Tinnitus je čest poremećaj uzrokovan mnogim čimbenicima. Otološki problemi, posebice gubitak sluha, najčešći su uzroci subjektivnog tinitusa. Objektivni tinnitus obično je uzrokovan vaskularnim abnormalnostima karotidne arterije ili jugularnog venskog sustava. Početna procjena tinitusa obuhvaća temeljitu anamnezu, pregled glave i vrata i audiometrijsko testiranje kako bi se utvrdila temeljna etiologija. Jednstrani ili pulsirajući tinnitus može biti uzrokovan ozbiljnijim patološkim procesima i obično zahtijeva specijalizirano audiometrijsko testiranje i radiološke studije. Intrakranijalne aneurizme su lokalne dilatacije u cerebralnim arterijama koje dominantno zahvaćaju Willisov krug. Javljaju se u otprilike 2-5% odraslih osoba i sklone su rupturama, što može dovesti do subarahnoidalnog krvarenja (SAH), vrste hemoragičnog moždanog udara. Zbog ranog početka i loše prognoze, SAH čini > 25% izgubljenih godina za sve žrtve moždanog udara mlađe od 65 godina. Cilj prikaza je ukazati na važnost uzimanja dobre anamneze, detaljnog fizikalnog pregleda, zajedno s odgovarajućim slikovnim metodama za utvrđivanje temeljnog uzroka tinitusa, te usmjerenog pristupa prema pacijentu u rješavanju problema s ciljem otklanjanja ozbiljnih patoloških procesa.

**Prikaz slučaja:** Pacijentica u dobi 40 godina dolazi u ordinaciju obiteljske medicine u rujnu 2024. godine zbog osjećaja pulsiranja u lijevom uhu u trajanju od jedan dan. Do sada nije teže bolovala, bivši je pušač, alkohol ne konzumira. Afebrilna, negira sekreciju iz uha, bolnost uha i tegobe sa sluhom. Nos je prohodan, ne curi i negira glavobolju. U kliničkom statusu otoskopski nalaz je uredan, ždrijelo je mirno, na palpaciju oba temporomandibularna zgloba su bezbolna. Akcija srca je ritmična, tonovi jasni, šumove ne čujem. Auskultatorno na plućima uredan šum disanja. Nad karotidama bez prisutnih patoloških šumova. Vrijednost tlaka je bila 125/90 mm Hg, puls 90/min, EKG nalaz je uredan. Pacijenticu se upućuje na pregled neurologu uz preporuke redovite evidencije tlaka, pulsa i tegoba. Neurolog preporučuje MR mozga s TOF angiografijom intrakranijskih krvnih žila kojim se utvrđuje aneurizma oftalmičke grane lijeve ACI, veličine 4x3 mm i preporučio je daljnju obradu. Neuroradiolog je indicirao endovaskularni zahvat

embolizacije aneurizme. Pacijentica je tražila mišljenje neurokirurga o eventualnom operativnom zahvatu za koji se trenutno ne odlučuje. Tijekom hospitalizacije radi liječenja asimptomatske aneurizme, liječnici su konzilijarno donijeli odluku za praćenje aneurizme s kontrolnom MR mozga s TOF angiografijom intrakranijskih krvnih žila u periodu od 6-12 mjeseci uz kontrole čimbenika rizika.

**Rasprava:** Retrospektivne studije pokazuju da stope intrakranijalnih aneurizmi i arteriovenskih malformacija u skupini s pulsirajućim tinitusom sugeriraju da bi vaskularne lezije mogle biti slučajni nalazi, a ne uzroci pulsirajućeg tinitusa, te su pokazale da su bile usporedive s onima u normalnoj populaciji. Preporučuje se evaluacija učinkovitosti novih smjernica Nacionalnog instituta za zdravlje i izvrsnost skrbi u ispitivanju pulsirajućeg tinitusa. Druge studije su pokazale da su osobe s jednim ili više oboljelih srodnika u prvom koljenu s aneurizmatiskim subarahnoidalnim krvarenjem i pacijenti s autosomno dominantnom policističnom bubrežnom bolešću kandidati za probir na nerupturirane intrakranijalne aneurizme. Druga skupina osoba koja može imati koristi od probira su osobe ≥35 godina koje puše i imaju hipertenziju, ali prevalencija nerupturiranih intrakranijalnih aneurizmi u takvih osoba i učinkovitost i isplativost probira u ovoj skupini još nije poznata. Potrebna su daljnja istraživanja kako bi se identificirale osobe s niskim ili visokim rizikom razvoja i rupture aneurizme unutar do sada identificiranih skupina u svrhu poboljšanja učinkovitosti probira.

**Zaključak:** Tinnitus je simptom koji se pojavljuje u 10-15 % populacije. Vrlo je čest razlog posjete ordinacijama obiteljske medicine. S obzirom na brojne uzorke tinitusa, važno je napomenuti kako je potrebno napraviti liječničku evaluaciju u slučaju simptoma upozorenja kao što su jednostrani ili pulsirajući tinnitus, te prisutnost neuroloških simptoma. Ako se utvrdi da je tinnitus povezan s postojanjem aneurizme, ključno je pacijenta pravovremeno uputiti radi procjene rizika od rupture aneurizme te donošenje odluke o odgovarajućem liječenju, s obzirom na visoku prevalenciju smrtnosti i stope invaliditeta nakon rupture.

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## ■ Tinnitus or something more

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**Introduction with aim:** Tinnitus is a common disorder caused by many factors. Otologic problems, especially hearing loss, are the most common causes of subjective tinnitus. Objective tinnitus is usually caused by vascular abnormalities of the carotid artery or jugular venous system. The initial evaluation of tinnitus includes a thorough history, head and neck examination, and audiometric testing to determine the underlying etiology. Unilateral or pulsatile tinnitus can be caused by more serious pathological processes and usually requires specialized audiometric testing and radiological studies. Intracranial aneurysms are local dilatations in the cerebral arteries that predominantly affect the circle of Willis. They occur in approximately 2-5% of adults and are prone to rupture, which can lead to subarachnoid hemorrhage (SAH), a type of hemorrhagic stroke. Due to its early onset and poor prognosis, SAH accounts for > 25% of years lost for all stroke victims under the age of 65. The goal of the case report is to point out the importance of taking a good medical history, a detailed physical examination, together with appropriate imaging methods to determine the underlying cause of tinnitus, and a directional approach to the patient in solving problems with the aim of eliminating serious pathological processes.

**Case report:** A 40-year-old female patient presents to the family medicine office in September 2024 due to a feeling of pulsation in her left ear lasting one day. So far, she has not been seriously ill, she is a former smoker, she does not consume alcohol. Afebrile, denies ear discharge, ear pain and hearing problems. The nose is passable, does not leak and negates the headache. In the clinical status, the otoscopic findings are normal, the pharynx is calm, and both temporomandibular joints are painless on palpation. The action of the heart is rhythmic, the tones are clear, I do not hear any murmurs. Auscultation sound of breathing on the lungs is normal. Over the carotids without pathological murmurs present. The blood pressure value was 125/90 mm Hg, pulse 90/min, ECG results were normal. The patient is referred for examination by a neurologist with recommendations for regular records of blood pressure, pulse and complaints. The neurologist recommended MR of the brain with TOF angiography of intracranial blood vessels, which determined the aneurysm of the ophthalmic branch of the left ACI, size 4x3 mm, and recommended further treatment.

The neuroradiologist indicated an endovascular procedure for embolization of the aneurysm. The patient sought the opinion of a neurosurgeon about a possible surgical intervention, which is currently not decided upon. During the hospitalization for the treatment of an asymptomatic aneurysm, the doctors made a conciliatory decision to monitor the aneurysm with control MR of the brain with TOF angiography of intracranial blood vessels for a period of 6-12 months with control of risk factors.

**Discussion:** Retrospective studies show that rates of intracranial aneurysms and arteriovenous malformations in the pulsatile tinnitus group suggest that vascular lesions may be incidental findings rather than causes of pulsatile tinnitus, and have been shown to be comparable to those in the normal population. An evaluation of the effectiveness of the new guidelines from the National Institute for Health and Care Excellence in the examination of pulsatile tinnitus is recommended. Other studies have shown that individuals with one or more affected first-degree relatives with aneurysmal subarachnoid hemorrhage and patients with autosomal dominant polycystic kidney disease are candidates for screening for unruptured intracranial aneurysms. Another group of people who may benefit from screening are people ≥35 years of age who smoke and have hypertension, but the prevalence of unruptured intracranial aneurysms in such people and the efficiency and cost-effectiveness of screening in this group are not yet known. Further research is needed to identify individuals at low or high risk of aneurysm development and rupture within the groups identified so far in order to improve the effectiveness of screening.

**Conclusion:** Tinnitus is a symptom that occurs in 10-15% of the population. It is a very common reason for visiting family medicine offices. Considering the numerous patterns of tinnitus, it is important to note that it is necessary to make a medical evaluation in case of warning symptoms such as unilateral or pulsatile tinnitus, and the presence of neurological symptoms. If it is determined that tinnitus is associated with the existence of an aneurysm, it is crucial to refer the patient in a timely manner to assess the risk of rupture of the aneurysm and to make a decision on the appropriate treatment, considering the high prevalence of mortality and disability rates after rupture.

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## ■ Vrućica nepoznatog uzroka i metastatski karcinom prostate

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**Uvod s ciljem:** Sindrom vrućice nepoznatog uzroka (VNU) karakterizira kod bolesnika vrućicu od 38,3 C koja se javlja u nekoliko prigoda u trajanju od najmanje tri tjedna, a čija je etiologija nepoznata unatoč poduzetim dijagnostičkim postupcima. Uzroci tog sindroma mogu biti infektološke bolesti, reumatološke bolesti i maligne bolesti te heterogena skupina bolesti od kojih su u toj skupini najčešće sarkoidoza i vrućica zbog upotrebe psihoaktivnih tvari ili droga. Jedan od čestih uzroka iz skupine malignih bolesti su limfom, leukemija i karcinom bubrega. Sindrom vrućice nepoznatog uzroka, iako rjeđe, može se javiti i kod drugih malignih stanja poput kolorektalnog karcinoma, hepatocelularnog karcinoma, glioblastoma, karcinoma jajnika, karcinoma gušterače i karcinoma pluća te metastatske bolesti. Cilj ovog prikaza slučaja je upoznati liječnike s jednim od malignih uzroka vrućice nepoznatog uzroka.

**Prikaz slučaja :** 71-godišnji bolesnik javlja se liječniku obiteljske medicine početkom 2024. godine zbog gubitka tjelesne težine i opće slabosti. Prethodno je u nekoliko navrata imao blago povišenu tjelesnu temperaturu. Inače boluje od šećerne bolesti tip 2, dislipidemije i hiperplazije prostate te redovito uzima propisanu terapiju. Otac mu je umro od karcinoma prostate, a majka od karcinoma pluća. Bolesnikov fizikalni nalaz je bio neupadan te su učinjeni laboratorijskih nalazi, koji su pokazali povišenu razinu C-reaktivnog proteina (67,4 mg/L) uz porast leukocita s blagim skretanjem u lijevo i trombocitozom koja je iznosila  $578 \times 10^9/L$  te gama glutamil transferazom (GGT) (79 U/L) dok biokemijska analiza urina pokazala je akutnu upalu mokraćnog mjehura zbog čega je ordiniran antibiotik. Bolesnik je imao i sideropeničnu anemiju (hemoglobin 125 g/L, hematokrit 0,383 L/L, željezo 4,7 uml/L) uz negativan test na okultno krvarenje. Na kontrolnom pregledu, unatoč provedenoj antibiotskoj terapiji nije došlo do pada upalnih parametara, već do porasta C-reaktivnog proteina (82,4 mg/L) uz to bile su povišene vrijednosti prostata

- specifičnog antigena (PSA) (51,40 ug/L) te je upućen na daljnju urološku obradu koja je dokazala metastatsku bolest karcinoma prostate.

**Rasprava:** Kod karcinoma prostate s metastatskom bolesti jedan od prvih znakova može biti vrućica nepoznatog uzroka zbog sistemskog upalnog odgovora. U literaturi je do sada opisano svega nekoliko takvih slučajeva. PSA može biti povišen kod maligne bolesti kao i u akutnom prostatitisu. Digitorektalni pregled prostate u tom slučaju može nam biti od koristi u postavljanju sumnje na moguću dijagnozu. Svakako je potrebno učiniti detaljnu obradu kod takvih bolesnika.

**Zaključak:** Kod bolesnika sa simptomima upale mokraćnih puteva uz pojavu vrućice i povišenog PSA treba uvijek pratiti tijek bolesti kako bi se pravovremeno postavilo dijagnozu i isključilo mogućnost da se radi o malignoj bolesti.

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## ■ Fever of unknown origin and metastatic prostate cancer

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**Introduction with aim:** Fever of unknown origin (FUO) is characterized by a fever of 38.3 °C in patients, which occurs on several occasions lasting at least three weeks, and whose etiology is unknown despite the diagnostic procedures undertaken. The causes of this syndrome can be infectious diseases, rheumatological diseases and malignant diseases, as well as a miscellaneous group of diseases, of which the most common are sarcoidosis and fever due to the use of psychoactive substances or drugs. One of the frequent causes from the group of malignant diseases is lymphoma, leukemia and kidney cancer. Fever syndrome of unknown origin, although less common, can also occur in other malignant conditions such as colorectal cancer, hepatocellular carcinoma, glioblastoma, ovarian cancer, pancreatic cancer, lung cancer, and metastatic disease. The goal of this case report is to familiarize doctors with one of the malignant causes of fever of unknown origin.

**Case report:** 71-year-old patient presented to a family medicine doctor at the beginning of 2024 due to weight loss and general weakness. Previously, he had a slightly elevated body temperature on several occasions. Otherwise, he suffers from type 2 diabetes, dyslipidemia and prostatic hyperplasia and regularly takes the prescribed therapy. His father died of prostate cancer, and his mother died of lung cancer. The patient's physical findings were unremarkable, and laboratory findings were performed, which showed an elevated level of C-reactive protein (67.4 mg/L) with an increase in leukocytes with a slight shift to the left and thrombocytosis, which was 578 x10<sup>9</sup>/L, and gamma glutamyl transferase (GGT) (79 U/L), while the biochemical analysis of urine showed acute inflammation of the urinary bladder, for which an antibiotic was prescribed. The patient also had sideropenic anemia (hemoglobin 125 g/L, hematocrit 0.383 L/L, iron 4.7 uml/L) with a negative test for occult bleeding. At the follow-up examination, despite

the antibiotic therapy, there was no decrease in inflammatory parameters, but an increase in C-reactive protein (82.4 mg/L), in addition, there were elevated prostate-specific antigen (PSA) values (51.40 ug/L) and was referred for further urological treatment, which proved metastatic prostate cancer.

**Discussion:** In prostate cancer with metastatic disease, one of the first signs can be fever of unknown origin due to a systemic inflammatory response. So far, only a few such cases have been described in the literature. PSA can be elevated in malignant disease as well as in acute prostatitis. In this case, a digital rectal examination of the prostate can be useful in casting doubt on a possible diagnosis. It is certainly necessary to do a detailed treatment in such patients.

**Conclusion:** In patients with symptoms of urinary tract inflammation along with fever and elevated PSA, the course of the disease should always be monitored in order to make a timely diagnosis and exclude the possibility that it is a malignant disease.

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## Rijetki oblici dijabetesa

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**Uvod s ciljem.** Dijabetes mladih s kasnijim početkom tip 5 (engl. Maturity-onset diabetes of the young tip 5 (MODY5)) rijedak je oblik dijabetesa koji često izmiče prepoznavanju zbog svojih nespecifičnih simptoma. Ova bolest se obično javlja zbog mutacija gena, no dijagnoza je često izazovna jer je poremećaj rijedak, a simptomati nisu uvijek očiti. Cilj ovog prikaza slučaja je prikazati dijagnostičke izazove i važnost pravovremenog prepoznavanja MODY5, posebno u kontekstu dijabetesa i povezanih komplikacija.

**Prikaz slučaja:** Muškarac, 28 godina, obratio se svom liječniku obiteljske medicine zbog ponavljanih epizoda mučnine, povraćanja, nadutosti i bolova u trbuhu koji su trajali šest mjeseci. Osim toga, imao je simptome poput žeđi, učestalog mokrenja i umora već šest godina, što je dovelo do dijagnoze dijabetesa tip 1 u drugoj bolnici. Bio je liječen inzulinom, međutim, često je hospitaliziran zbog dijabetičke ketoacidoze (DKA) za koju se ispostavilo da je posljedica nepravilnog uzimanja inzulina. K.L. je također imao komplikacije poput složenih cisti na bubrezima i prostati, kao i agenezu dorzalnog pankreasa. Nakon daljnjih testiranja, uključujući gensko testiranje, dijagnosticiran mu je sindrom 17q12 delecije, što je izazvalo promjene u njegovoj endokrinoj funkciji.

**Rasprava:** MODY5 rijetka je bolest koja se teško dijagnosticira jer često nalikuje drugim vrstama dijabetesa, a posebice dijabetesu tip 1. U ovom slučaju, K.L. je bio pogrešno dijagnosticiran zbog smanjenih funkcija otočića i čestih epizoda ketoacidoze. Međutim, dodatna ispitivanja otkrila su agenezu pankreasa i druge abnormalnosti koje su upućivale na genetski uzrok bolesti. Genetske analize su pokazale mutaciju koja uključuje 17q12 regiju, što ukazuje na sindrom 17q12 delecije. Ovaj slučaj ističe važnost razmatranja rijetkih genetskih uzroka dijabetesa u pacijenata s atipičnim prezentacijama simptoma. U ovome slučaju, upravo je manjak pankreatičnih enzima zbog ageneze dorzalnog pankreasa uzrokovao nestabilne razine glukoze u krvi, a time i otežano doziranje inzulinom zbog kojeg su epizode ketoacidoze bile učestale. Pacijentu K.L. nužno je bilo nadomjestiti enzime kako bi

inzulin bio pravilno doziran i kao takav u mogućnosti ostvariti svoj učinak. Iako MODY5 obično ne izaziva ozbiljne simptome u mladim osoba, dijagnoza i pravovremeno liječenje ključni su za sprječavanje komplikacija.

**Zaključak.** Pacijentu je dijagnosticiran MODY5 kao dio sindroma 17q12 delecije, što je proširilo spektar genetskih uzroka dijabetesa. Ovaj slučaj naglašava važnost sveobuhvatne dijagnostičke obrade u pacijenata s atipičnim ili neadekvatno kontroliranim dijabetesom. Pravovremena genetska analiza može pomoći u postavljanju točne dijagnoze, optimizaciji terapije i pružanju odgovarajuće podrške pacijentovoj obitelji.

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## ■ Rare forms of diabetes

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**Introduction with objective.** Maturity-onset diabetes of the young type 5 (MODY5) is a rare form of diabetes often overlooked due to its nonspecific symptoms. This condition typically results from genetic mutations, but diagnosis is often challenging because the disorder is rare and symptoms are not always apparent. The aim of this case report is to highlight the diagnostic challenges and the importance of timely recognition of MODY5, particularly in the context of diabetes and associated complications.

**Case report.** Male, 28-year-old consulted his family physician for recurrent episodes of nausea, vomiting, bloating, and abdominal pain lasting six months. Additionally, he had experienced symptoms such as thirst, frequent urination, and fatigue for six years, which led to a diagnosis of type 1 diabetes at another hospital. He was treated with insulin but was frequently hospitalized due to diabetic ketoacidosis (DKA), which was later found to be caused by irregular insulin administration. K.L. also had complications such as complex cysts in the kidneys and prostate, as well as dorsal pancreas agenesis. Further testing, including genetic analysis, led to a diagnosis of 17q12 deletion syndrome, which caused alterations in his endocrine function.

**Discussion.** MODY5 is a rare disease that is difficult to diagnose as it often mimics other types of diabetes, particularly type 1 diabetes. In this case, K.L. was misdiagnosed due to impaired islet cell function and frequent episodes of ketoacidosis. However, additional investigations revealed pancreatic agenesis and other abnormalities pointing to a genetic cause of the disease. Genetic analyses identified a mutation involving the 17q12 region, indicating 17q12 deletion syndrome. This case highlights the importance of considering rare genetic causes of diabetes in patients with atypical presentations of symptoms. In this instance, the lack of pancreatic enzymes due to dorsal pancreas agenesis caused unstable blood glucose levels, making insulin dosing challenging and leading to frequent episodes of ketoacidosis. Enzyme supplementation was crucial for proper insulin dosing and its effective action. While MODY5 usually does not cause severe symptoms in young

individuals, accurate diagnosis and timely treatment are essential to prevent complications.

**Conclusion.** Patient was diagnosed with MODY5 as part of 17q12 deletion syndrome, expanding the spectrum of genetic causes of diabetes. This case underscores the importance of comprehensive diagnostic workups in patients with atypical or inadequately controlled diabetes. Timely genetic analysis can aid in making an accurate diagnosis, optimizing therapy, and providing appropriate support for the patient's family.

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## ■ Ambulantni mikrobiološki testovi u svakodnevnoj praksi liječnika obiteljske medicine

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**Uvod s ciljem:** Jedan od najčešćih razloga dolaska na pregled liječniku opće/obiteljske medicine (LOM) jesu infektivne bolesti, među kojima s najvećom incidencijom respiratorne, probavne i urogenitalne infekcije. Od iznimne je važnosti za pacijenta, ali i cjelokupni javnozdravstveni sustav, ove široko rasprostranjene i česte bolesti adekvatno liječiti, vodeći računa istovremeno o zaštiti zdravlja pacijenta i implikacijama neadekvatnog ili prekomjernog liječenja antimikrobnim agensima na razvoj bakterijske rezistencije na antibiotike. LOM stoga mora biti izvrstan kliničar i detaljno upoznat sa simptomima i znacima bolesti kako bi pravodobno i empirijski procijenio uzročnika i primijenio adekvatne mjere liječenja, što nerijetko nije lako zbog preklapanja njihovih simptoma. U takvim dvojbenim situacijama, LOM će uputiti pacijenta na mikrobiološko ispitivanje kako bi potvrdio svoju empirijsku procjenu ili razlučio dilemu o kojem se uzročniku radi. Razvojem medicine i tehnologije, danas su sve dostupniji i ambulantni, povoljni, rutinski i brzi, tzv. point-of-care (POC) mikrobiološki testovi, koji uvelike mogu pomoći LOM u inicijalnom postavljanju dijagnoze. Cilj ovog prikaza slučaja jest naglasiti važnost ambulantnih mikrobioloških testova u svakodnevnoj praksi LOM u svrhu lakšeg i bržeg postavljanja točne dijagnoze i liječenja pacijenta uz smanjenje primjene prekomjernih i nepotrebnih mjera liječenja.

**Prikaz slučaja:** 31-godišnja pacijentica dolazi na pregled LOM radi grlobolje i febriliteta u drugom danu bolesti. Inače bez kroničnih i bez značajnijih ranijih oboljenja. Epidemiološka analiza bez osobitosti, radi kao učiteljica. Pri pregledu se uočava izrazito hiperemično ždrijelo uz hipertrofirane tonzile s mjestimičnim gnojnim eksudatom. Regionalni limfni čvorovi glave i vrata se ne palpiraju uvećani. Auskultatorni nalaz na srcu i plućima je uredan. Izmjerena je tjelesna temperatura 38.3 °C. Pacijentici se ordinira antibiotička terapija fenoksimetilpenicilina u dozi 3x800 mg dnevno kroz deset dana, uz opće

mjere simptomatskog liječenja. S obzirom na opće stanje pacijentica se nakon dva dana mirovanja vraća u radni kolektiv. Nakon deset dana pacijentica dolazi na kontrolni pregled, navodeći da se inicijalno krenula oporavljati uz povlačenje simptoma grlobolje i febriliteta nakon tri dana terapije, ali unazad dva dana se ponovno pogoršava, febrila do 38.5 °C, promukla je te osjeća slabost i iscrpljenost mišićne mase. Pacijentici se u ordinaciji naprave brzi mikrobiološki testovi na SARS-CoV-2 koji je negativan te influencu kojom se dokaže virus influence tip B. S obzirom na dokazanu influencu te anamnezu i kliničku sliku, pacijentici se ordinira oseltamivir u dozi 2x75mg dnevno kroz 5 dana uz nastavak općih mjera liječenja - polivitaminske terapije i mirovanja. Na kontroli za nekoliko dana navodi poboljšanje stanja i postupnu regresiju upalnih simptoma.

**Rasprava:** Uslijed sezone gripe, posebno kod osoba zaposlenih u većim kolektivima, te nakon pada imuniteta uzrokovanog gnojnim tonzilitisom, ovaj slučaj je česta pojava u ordinaciji LOM, koji diferencijalno dijagnostički može posumnjati na komplikaciju inicijalne bolesti (tonzilitisa), infektivnu mononukleozu, a najčešće, kao i u ovom prikazu slučaja, novonastalu infekciju virusnim uzročnikom. U svrhu lakšeg i bržeg postavljanja prave dijagnoze, POC mikrobiološki testovi, poput navedenih i široko dostupnih testova za bolesti gripe i COVID-19, mogu biti od velike pomoći LOM.

**Zaključak:** Ovaj prikaz slučaja ukazuje na važnost POC mikrobioloških testova u svakodnevnoj praksi LOM, s ciljem jednostavnog i preciznog postavljanja dijagnoze i adekvatnog liječenja.

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## ■ Point-of-care microbiological tests in the GP's daily practice

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**Introduction and aim:** Ones of the most common reasons of visiting general practitioners (GPs) are infectious diseases, among which in the highest incidence are respiratory, digestive and urogenital infections. It is vastly important for the patient and the entire public health, to adequately treat these widespread and frequent diseases, taking into account the implications of inadequate or excessive treatment with antimicrobial agents on the development of bacterial resistance to antibiotics. GPs therefore have to be an excellent clinician in order to timely and empirically assess the causative agent and apply adequate treatment measures, which is often not easy due to the symptoms overlap. In such doubtful situations, GPs will refer the patient to a microbiological examination. Outpatient, inexpensive, routine and rapid microbiological tests, known as a point-of-care (POC) tests, are increasingly available today, which can greatly help GPs in the initial setting of an accurate diagnosis. The aim of this case report is to emphasize the importance of POC microbiological tests in the GP's daily practice.

**Case report:** A 31-year-old female complains of a sore throat and fever in the second day of the illness. Generally, without chronic and significant previous diseases. Epidemiological analysis without particularities, works as a school teacher. A hyperemic pharynx with hypertrophied tonsils with localized purulent exudate is observed. Regional lymph nodes are not palpated enlarged. Auscultatory findings on the heart and lungs are normal. The measured body temperature was 38.3 °C. She was prescribed antibiotic therapy with phenoxymethylpenicillin in a dose of 3x800 mg a day for ten days. Considering her general condition, after two days of rest, she returned to work. After ten days, the patient comes for a follow-up examination, stating that she initially began to recover with the withdrawal of symptoms of sore throat and febrility after three days of therapy, but after few days she worsened again, with fever up

to 38.5 °C, she was hoarse and felt weakness and muscle exhaustion. The patient underwent rapid microbiological tests for SARS-CoV-2, which was negative, and for influenza, which proved influenza virus type B. Considering the anamnesis and proven influenza, the patient was prescribed oseltamivir at a dose of 2x75mg per day for 5 days with the continuation of general treatment measures - polyvitamin therapy and rest. At the follow-up in a few days, she reported an improvement and a gradual regression of inflammatory symptoms.

**Discussion:** Due to the flu season, especially among people working in larger collectives, and after a drop in immunity caused by purulent tonsillitis, cases like this have a frequent occurrence in the GP's practice, whose differential diagnosis may suspect a complication of the initial disease (tonsillitis), infectious mononucleosis, and a new onset viral infection. In order to make the right diagnosis easier and faster, POC microbiological tests, such as the listed and widely available tests for flu and COVID-19, can be of great importance to GPs.

**Conclusion:** This case report indicates the importance and help of POC microbiological tests in the GP's daily practice, for the purpose of easier and faster precise diagnosis and adequate treatment.

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## ■ Simulacijska edukacija na razini primarne zdravstvene zaštite

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**Uvod s ciljem:** U medicinski hitnim situacijama naročito je bitno ispravno i brzo reagirati radi sprječavanja trajnih posljedica za zdravlje, odnosno smrti. Timovi primarne zdravstvene zaštite (PZZ) dnevno se susreću s najviše pacijenta te uz sve veći administrativni pritisak može doći do ne optimalnog zbrinjavanja pacijenta u hitnom stanju. Erasmus+ projekt Transsimed pokrenut je 2022. godine s ciljem poboljšanja zdravstvenih ishoda pacijenata tijekom hitnih stanja putem simulacijske edukacije timova PZZ. Projekt je financiran sredstvima Europske Unije. Nositelj projekta je Zdravstveni dom Ljubljana, a parteri su Katedra za obiteljsku medicinu Medicinskog fakulteta Sveučilišta u Zagrebu, Dom zdravlja Zagreb – Centar (DZZC) te Katedra za obiteljsku medicinu Medicinskog fakulteta Sveučilišta svetog Ćirila i Metoda u Skoplju. Cilj ovog sažetka je prezentirati rad i preliminarne rezultate hrvatskog tima projekta Transsimed te približiti simulacijsku edukaciju timovima PZZ.

**Ispitanici i metode:** U prostorima DZZC opremljen je simulacijski centar hiper-realističnim simulatorom te je educirano 15 instruktora (liječnici i medicinske sestre) koji provode edukaciju osnovnog i naprednog održavanja života uz korištenje automatskog vanjskog defibrilatora namijenjenu timovima PZZ. U pripremi su moduli vještina i zbrinjavanja anafilakse. Edukacije su krojene prema resursima i specifičnostima timova PZZ. Da bi se osigurala maksimalna korisnost, polaznici prije pohađanja edukacije moraju riješiti pred-test s minimalnih uspjehom od 75%, a test se piše i nakon edukacije. Tada još polaznici anketiraju svoju spremnost na hitna stanja, zadovoljstvo edukacijom i instruktorima.

**Rezultati:** Projekt završava krajem kolovoza 2025. godine, no dosadašnji rezultati su vrlo obećavajući. U simulacijskom centru u Zagrebu educirano je 264 polaznika, a 740 ljudi prisustvovalo je na predavanjima i radionicama projekta. Svi polaznici koji su prošli edukaciju imaju

bolje napisan test nakon edukacije, osjećaju se spremniji za hitna stanja, navode da im takav tip edukacije treba te izražavaju želju za kontinuirano pohađanje takve vrste edukacije. Prosječna razlika u znanju prije i poslije edukacije bila je 19,75%.

**Zaključak:** Prema preliminarnim rezultatima, simulacijska edukacija dobro je prihvaćena i djelotvorna metoda obnavljanja znanja i vještina timova PZZ. Izostanak kontinuiteta drastično smanjuje učinkovitost edukacije, stoga uspostava simulacijskog centra koji vodi brigu o tome je ključna.

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## ■ Simulation-based education at the primary healthcare level

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**Introduction with aim:** In medical emergencies, it is especially important to respond correctly and quickly to prevent permanent health damage or even death. Primary healthcare (PHC) teams encounter the highest number of patients daily, and with increasing administrative pressure, sub-optimal management of emergencies can occur. The Erasmus+ project Transsimed was launched in 2022 with the goal of improving patient safety during emergencies through simulation-based education for PHC teams. The project is funded by the European Union. The project lead is the Health Center Ljubljana, and the partners include the Chair of family medicine –School of Medicine of University in Zagreb; Health center Zagreb - Center (HCZC); and the Chair of family medicine –School of Medicine of Ss. Cyril and Methodius University in Skopje. The aim of this summary is to present the work and preliminary results of the Croatian team in the Transsimed project, and to familiarize PCH teams with simulation education.

**Methods:** A simulation center equipped with a hyper-realistic simulator was established at the premises of the HCZC, and 15 instructors (physicians and nurses) were trained. These instructors conduct modules for PHC providers on basic and advanced life support using automated external defibrillator. Skills and anaphylaxis management modules are in preparation. The training sessions are tailored to the specifics of PHC. To maximize effectiveness, participants must complete a pre-test with a minimum score of 75% before attending the training. A post-training test is also conducted. Afterwards, participants complete surveys on their readiness for emergencies, satisfaction with the training, and their evaluation of the instructors.

**Results:** The project concludes in August 2025, but the results so far are very promising. 264 participants were trained in the simulation center in Zagreb, and 740 people attended the project's

lectures and workshops. All participants who have completed the training demonstrate better test results post-training, feel more prepared for emergencies, express that this type of education is necessary. Average relative intake/outtake knowledge difference was 19,75%.

**Conclusion:** According to preliminary results, simulation education is a well-accepted and effective method of renewing the knowledge and skills of PHC teams. The lack of continuity drastically reduces the effectiveness of education, therefore the establishment of a simulation center that keeps track of it is essential.

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## ■ Specifični pristup u liječenju varikoznih vena s ulkusom u specijalističkoj ambulanti obiteljske medicine

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**Uvod s ciljem:** Venski ulkusi nastaju zbog kronične venske insuficijencije koja započinje pokretanjem kaskade događaja koji dovode do patoloških promjena u venama i tkivima (destrukcije venskih zalistaka ili kronične opstrukcije vene). Posljedica je kronična venska hipertenzija, a završni stadij venske insuficijencije je venski ulkus. Cilj ovog rada je prikaz specifičnog pristupa u liječenju varikoznih vena s ulkusom u specijalističkoj ambulanti obiteljske medicine, uz evaluaciju konzervativnog i intervencijskog liječenja kako bi se poboljšala kvaliteta života bolesnice i smanjila učestalost recidiva rana.

**Prikaz slučaja:** Bolesnici (74) s recidivirajućim venskim ulkusima na potkoljenicama, kliničkim pregledom i ultrazvučnim nalazom obojenim doplerom nožnih vena potvrdila se kronična venska insuficijencija površinskog i perforantnog sustava. Prema CEAP klasifikaciji, bolesničina rana klasificirana je u skupinu C6r, Ep, As,p, Pr. Ambulantno se radio mehanički debridman, primjenjivala odgovarajuća pokrivala za rane, te postavljala fiksaciona i kompresivna terapija kratkog vlaka. Bolesnici i obitelji objašnjene su mogućnosti etiološkog liječenja endovenskom laserskom ablacijom i skleroterapijom.

**Rasprava:** Primjenom visokoupijajućih celuloznih pokrivala sa aktivnim ugljenom i impregniranim srebrom, uz fiksacioni zavoj i kompresivnu terapiju, nakon dvotjednog liječenja rane su pokazale znakove cijeljenja – na desnoj potkoljenici prisutno je granulacijsko tkivo uz smanjenje sekrecije, edema i odsutnost mirisa, dok je rana na lijevoj potkoljenici uska s dobro razvijenim granulacijskim tkivom. Gležanjski indeks je uredan, čime je potvrđena sigurnost primjene kompresivne terapije.

**Zaključak:** Multidisciplinarni pristup koji uključuje dijagnostiku, pravilnu lokalnu i kompresivnu

terapiju, edukaciju bolesnice i obitelji, ključan je za uspješno liječenje venskih ulkusa. Etiološko liječenje endovenskom laserskom ablacijom može dodatno smanjiti recidive i ubrzati cijeljenje. Kronične rane predstavljaju značajan zdravstveni i ekonomski problem, stoga njihovo liječenje zahtijeva sustavan i individualiziran pristup.

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## ■ Specific approach in the treatment of varicose veins with ulcer in a family specialist clinic

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**Introduction with the aim:** Venous ulcers result from chronic venous insufficiency, which begins with the activation of a cascade of events leading to pathological changes in veins and tissues (destruction of venous valves or chronic venous obstruction). The consequence is chronic venous hypertension, with the final stage of venous insufficiency manifesting as lower leg ulcers. The aim of this case is to present a specific approach to treating varicose veins with ulcers in a specialized family medicine clinic, evaluating both conservative and interventional treatment methods to improve the patient's quality of life and reduce the recurrence of wounds.

**Case report:** A 74-year-old patient with recurrent venous ulcers on the lower legs was diagnosed with chronic venous insufficiency of the superficial and perforating venous systems through clinical examination and color Doppler ultrasound of the leg veins. According to the CEAP classification, the patient's wound was classified as C6r, Ep, As,p, Pr. Outpatient treatment included mechanical debridement, the application of appropriate wound dressings, fixation, and short-stretch compression therapy. The patient and her family were informed about the possibility of etiological treatment using endovenous laser ablation and sclerotherapy.

**Discussion:** The application of highly absorbent cellulose dressings with activated charcoal and impregnated silver, along with fixation bandages and compression therapy, led to signs of wound healing after two weeks of treatment. On the right lower leg, granulation tissue was present, with reduced secretion, edema, and no odor, while the wound on the left lower leg was narrow with well-developed granulation tissue. The ankle-brachial index was normal, confirming the safety of compression therapy.

**Conclusion:** A multidisciplinary approach that includes diagnostics, appropriate local and compression therapy, patient and family education is crucial for the successful treatment of venous ulcers. Etiological treatment with endovenous laser ablation can further reduce recurrences and accelerate healing. Chronic wounds represent a significant health and economic issue, requiring a systematic and individualized approach to treatment.

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## ■ Tuberkuloza pluća – dugi put do dijagnoze

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**Uvod s ciljem:** Tuberkuloza je zarazna bolest uzrokovana bakterijom *Mycobacterium tuberculosis*, koja prvenstveno zahvaća pluća, ali može se pojaviti i u koži, mozgu, kostima, zglobovima, limfnim čvorovima, probavnom, genitalnom i mokraćnom sustavu. Prenosi se kapljično. Simptomi su aktivne plućne tuberkuloze dugotrajni suhi kašalj koji prelazi u kašalj s gnojnim iskašljajem, iskašljavanje krvi, otežano disanje, brzo zamaranje u naporu, bol u prsištu. Ostali simptomi uključuju opću slabost, umor, gubitak apetita, mršavljenje, noćno znojenje. Pravi dokaz aktivne tuberkuloze izolacija je *Mycobacterium tuberculosis* iz iskašljaja (sputuma) ili aspirata bronha – mikroskopski i kultivacijom. Cilj je ovog rada ukazati na to da je tuberkuloza i danas jedna od najozbiljnijih i najraširenijih zaraznih bolesti te podsjetiti da mislimo na nju kao jednu od diferencijalnih dijagnoza pri pojavi navedenih simptoma.

**Prikaz slučaja:** Pacijentica u dobi od 68 godina javila se u ordinaciju obiteljske medicine (OOM) zbog produktivnog kašlja uz povremeni osjećaj otežanog disanja. Boluje od arterijske hipertenzije, drugih kroničnih bolesti nema. Zbog bronhalnih zvižduka u auskultatornom nalazu liječena je pod dijagnozom bronhitisa. S obzirom da kašalj nije prolazio, već se karakter kroz 2 mjeseca promijenio u suhi, pacijentica je upućena na laboratorijske pretrage koje su pokazale CRP 52 i rentgen srca i pluća koji je pokazao ožiljne promjene. Pregled pulmologa odbila je jer se osjećala nešto bolje nakon uvedene antibiotske terapije. Za 3 tjedna dolazi do pogoršanja stanja u vidu porasta CRP-a na 70, boli pod lopaticama, zamaranja u naporu, slabijeg apetita, gubitka na tjelesnoj masi, zbog čega pacijentica ipak odlazi na pregled pulmologa koji pod dijagnozom pneumonije preporuča dvojni antibiotsku terapiju i inhalacije te CT toraksa ukoliko ne dođe do promjene na rentgenu. Pacijentica je poslana i dati iskašljaj na *Mycobacterium tuberculosis*. Nakon kratkotrajnog poboljšanja stanja ponovno pogoršanje dovodi do hospitalizacije na Klinici za pulmologiju radi obrade infiltrata otvorene etiologije i nodozne sjene, a zatim pacijentica završava i

kao COVID pozitivna. Uz odgovarajuću terapiju dolazi do poboljšanja stanja i otpusta, ali se kroz 2 mjeseca ponovno pokaže potreba za hospitalizacijom zbog progresivne dinamike infiltrata i brojnih inhomogenih zasjenjenja pluća na rtg snimci. Primljena je pod sumnjom na tumorski proces. Konačno se dolazi do prave, osnovne dijagnoze – tuberkuloze (TBC), potvrđene nalazom iskašljaja. Nakon 4 mjeseca liječenja u Bolnici za plućne bolesti i TBC i otpijene kombinirane terapije antituberkulotika pacijentica je znatno bolje, a daljnje povremene kontrole obavlja kod pulmologa.

**Zaključak:** Zlatni standard u dijagnostici tuberkuloze iskašljaj je pozitivan na mikobakteriju. Liječnik obiteljske medicine ima ključnu ulogu u prepoznavanju simptoma i znakova i pravodobnom upućivanju pacijenta na dijagnostičke pretrage, te u suradnji s drugim specijalistima. Također, dobro poznaje svoje pacijente pa mu je najčešće poznata socioekonomska i epidemiološka situacija pacijenta. Osim educiranosti liječnika, važna je i edukacija i suradljivost bolesnika kako bi se što prije postavila ispravna dijagnoza i provelo odgovarajuće liječenje bez kojeg je stopa smrtnosti od tuberkuloze visoka.

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## ■ Pulmonary Tuberculosis – A Long Road to Diagnosis

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**Introduction with aim:** Tuberculosis is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*, which primarily affects the lungs but can also occur in the skin, brain, bones, joints, lymph nodes, and the digestive, genital, and urinary systems. It is transmitted via droplets. Symptoms of active pulmonary tuberculosis include a prolonged dry cough that develops into a cough with purulent sputum, hemoptysis, shortness of breath, rapid fatigue on exertion, and chest pain. Other symptoms include general weakness, fatigue, loss of appetite, weight loss, and night sweats. Definitive evidence of active tuberculosis is the isolation of *Mycobacterium tuberculosis* from sputum or bronchial aspirate—detected both microscopically and by culture. The aim of this paper is to underscore that tuberculosis remains one of the most serious and widespread infectious diseases today, and to remind us to consider it as a differential diagnosis when the above-mentioned symptoms appear.

**Case Report:** A 68-year-old female patient presented to a family medicine office due to a productive cough and occasional shortness of breath. She has a history of arterial hypertension but no other chronic illnesses. Because of bronchial wheezes found on auscultation, she was treated under the diagnosis of bronchitis. Since the cough did not subside and changed from productive to dry over two months, the patient was referred for laboratory tests, which showed a CRP of 52, and for a chest X-ray, which revealed scarring changes. She declined a pulmonologist's examination because she felt somewhat better following antibiotic therapy. After three weeks, her condition worsened again with an elevated CRP of 70, pain under the shoulder blades, exertional fatigue, decreased appetite, and weight loss. Consequently, the patient finally went to see a pulmonologist, who diagnosed pneumonia and recommended dual antibiotic therapy, inhalations, and a CT scan of the thorax if there was no improvement on repeat chest X-ray. The patient was also instructed to submit sputum samples for *Mycobacterium tuberculosis* testing.

Following a brief improvement, her condition deteriorated once more, leading to hospitalization in the Pulmonology Clinic for further work-up of an infiltration of unknown etiology and nodular shadows. Subsequently, the patient also tested positive for COVID-19. With appropriate therapy, her condition improved, and she was discharged. However, within two months, she required readmission due to progressive infiltrative changes and numerous inhomogeneous opacities on the chest X-ray. She was admitted under the suspicion of a tumorous process. Ultimately, the correct underlying diagnosis—tuberculosis (TB)—was confirmed by sputum testing. After four months of treatment in the Hospital for Lung Diseases and TB, along with combined antitubercular therapy, the patient's condition improved significantly. She continues to attend occasional follow-up appointments with a pulmonologist.

**Conclusion:** The gold standard in diagnosing tuberculosis is a sputum sample positive for mycobacteria. The family physician plays a key role in recognizing symptoms and signs and promptly referring the patient for diagnostic testing, in collaboration with other specialists. The family doctor also knows patients well, including their socioeconomic and epidemiological circumstances. In addition to the physician's level of education, patient education and cooperation are crucial in arriving at a timely and correct diagnosis and administering appropriate treatment—without which the mortality rate from tuberculosis is high.

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## ■ “Hodanje i osjet uz studentski posjet”

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**Uvod:** U zimskim se mjesecima pregled stopala često zaobilazi u svakodnevnoj liječničkoj praksi. Dijabetička neuropatija (DN) kronična je komplikacija šećerne bolesti (ŠB) prisutna u polovice oboljelih, a cjeloživotni rizik za razvoj dijabetičkog ulkusa stopala u oboljelih od ŠB iznosi 25%. Pravovremena intervencija može reducirati nastanak ulkusa za čak 60%, a potrebu za amputacijom za 85% u onih s visokorizičnom DN. ŠB povećava rizik i za razvoj periferne arterijske bolesti (PAB) ubrzanjem aterosklerotskih procesa. PAB otežava cijeljenje ulkusa i povisuje rizik amputacije donjeg ekstremiteta. U pacijentima sa ŠB redovita fizička aktivnost smanjuje rizik nastanka DN poboljšanjem razine glikemije, ublažava bol pri već nastaloj DN te doprinosi smanjenju ulkusa uzrokovanih PAB. Stoga je cilj sažetka prikazati multidisciplinarni studentski projekt namijenjen korisnicima doma za starije osobe nad kojima se proveo probir na DN i PAB te ih se educiralo o posljedicama ŠB i adekvatnoj prevenciji istih.

**Rasprava:** “Hodanje i osjet uz studentski posjet” projekt je studenata Studentske sekcije za endokrinologiju i dijabetologiju Medicinskog fakulteta i studenata Kineziološkog fakulteta Sveučilišta u Zagrebu koji se od siječnja do ožujka 2024. održao u Domu za starije osobe Centar. Cilj projekta bio je primarna prevencija ŠB i sekundarna prevencija komplikacija iste. U projekt je uključeno 50 sudionika sa i bez dijagnoze ŠB. Projekt se temeljio na kliničkome probiru na DN i PAB, edukaciji, grupnome radu te organiziranoj tjelovježbi. Probir je uključivao provedbu Michigan testa za otkrivanje DN te Edinburški upitnik i četverominutni testa hoda za otkrivanje PAB, a provodili su ga studenti medicine pod nadzorom liječnika. Studenti medicine potom su u tri navrata proveli edukaciju o važnosti tjelovježbe za cjelokupno zdravlje, kroničnim komplikacijama ŠB s naglaskom na dijabetičko stopalo i

higijenu stopala te interaktivnu radionicu s bolesnicima oboljelim od ŠB, njihovim simptomima, liječenju i kvaliteti života. Studenti kineziologije osmislili su i proveli dvomjesečni program tjelovježbe u Domu koji je uključivao vježbe razgibavanja, mišićne snage i izdržljivosti prilagođen dobi i mogućnostima osoba starije životne dobi. Projektom su sudionici potaknuti na nastavak vježbanja nakon kraja projekta te stvaranje nove rutine. Kontinuiranom se tjelovježbom smanjuje rizik od razvoja krvožilnih i neuroloških komplikacija, razvoja kontrakture, a poboljšava se i ravnoteža što smanjuje rizik pada, iznimno opasnog u starijoj dobi. Važno je spomenuti i psihološku potporu koja je pružena korisnicima Doma; osim što su se povezali s volonterima, povezali su se i međusobno.

**Zaključak:** Ovim je sažetkom prikazan primjer uspješne multidisciplinarnе suradnje studenata medicine i kineziologije kojom je korisnicima Doma za starije osobe Centar modelom “učenja kroz rad” (engl. “learning by doing”) pružena edukacija o nastanku i tijeku ŠB, kroničnim komplikacijama ŠB i mogućem vlastitom utjecaju na ublažavanje istih; proveden je klinički probir na DN i PAB te dvomjesečni program tjelovježbe, a na kraju je projekta održana interaktivna radionica tijekom koje su štićenici Doma izmijenili vlastita iskustva te je principima grupnog rada ostvarena daljnja interakcija štićenika i voditelja projekta. Planira se proširenje projekta i uključivanje većeg broja liječnika u provođenje probira na DN i PAB.

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## ■ “Walking and Sensation Test on a Student Request”

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**Introduction with aim:** Foot examinations are often neglected in clinical practice during the winter. Diabetic neuropathy (DN) is a chronic complication of diabetes mellitus (DM) present in half of those affected with DM, while the lifetime risk of developing a diabetic foot ulcer in individuals with DM is 25%. Timely intervention can reduce the occurrence of ulcers by up to 60% and the need for amputation by 85% in those with high-risk DN. DM also increases the risk of developing peripheral arterial disease (PAD) by accelerating atherosclerotic processes. PAD complicates ulcer healing and increases the risk of lower limb amputation. In patients with DM, regular physical activity lowers the risk of developing DN by improving blood glucose levels, alleviates pain from existing DN and reduces ulcers caused by PAD. Therefore, the aim of this summary was to present a multidisciplinary student project designed for the residents of a nursing home, which involved screening for DN and PAD, as well as educating them on the consequences of DM and appropriate prevention methods.

**Discussion:** “Walking and Sensation Test on a Student Request” is a project organised by students from the Student Section for Endocrinology and Diabetology at the School of Medicine and students from the Faculty of Kinesiology, University of Zagreb. The project took place at the Senior Citizens' Home "Centar" from January to March 2024. The goal was primary prevention of DM and secondary prevention of its complications. Fifty residents, both with and without DM, participated in the project. The project focused on clinical screening for DN and PAD, education, group work and physical exercise. The screening included the Michigan Test for detecting DN and the Edinburgh questionnaire with a four-minute walking test for detecting PAD, all conducted by medical students under the supervision of a

physician. The medical students delivered three educational sessions on the importance of physical activity for overall health, chronic complications of DM with a focus on foot hygiene, and an interactive workshop about symptoms, treatment, and quality of life. Kinesiology students designed and implemented a two-month exercise program that included flexibility, muscle strength and endurance exercises adapted to the age and capabilities of the residents. The project encouraged participants to continue exercising after the project ended and to establish a new active routine. Residents did not only connect with volunteers, but they also strengthened connections among themselves.

**Conclusion:** This summary presents a successful multidisciplinary collaboration between medical and kinesiology students, through which the residents of the Senior Citizens' Home 'Centar' were provided with education on the potential personal impact on DM and its chronic complications using the 'learning by doing' model. A clinical screening for DN and PAD was conducted, along with a two-month exercise program and an interactive workshop during which the residents shared their personal experiences. Plans are in place to expand the project and involve a larger number of physicians in conducting screenings for DN and PAD.

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## ■ Gonoreja -prikaz slučaja

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**Uvod s ciljem:** Gonoreja (gonokokna infekcija) je spolno prenosiva infekcija (SPI) koju uzrokuje obligatni humani patogen, gram-negativna bakterija *Neisseria gonorrhoeae*. Gonoreja se prenosi spolnim putem, odnosno oralnim, analnim ili vaginalnim spolnim odnosom te prijenosom s majke na dijete tijekom poroda. Gonokokna infekcija druga je najčešća bakterijska spolno prenosiva bolest i ima asimptomatski tijek kod 10%-90% žena i 10%-40% muškaraca što odgađa dijagnozu te pogoduje stvaranju komplikacija i daljnjem širenju infekcije. Najčešće kliničke manifestacije gonokokne bolesti u muškaraca uključuju gnojni iscjedak iz penisa, disuriju i nelagodu u testisima. Kada su prisutni, simptomi kod žena često su blagi ili nespecifični i lako se mogu zamijeniti sa drugim vaginalnim ili mokraćnim infekcijama. Gonoreja se danas smatra velikim globalnim javnozdravstvenim problemom zbog rastućeg broja slučajeva kroz protekle desetljeće u cijelom svijetu, kao i rastućom antimikrobnom rezistencijom (AMR) *Neisserie gonorrhoeae*. Cilj ovog rada je istaknuti ulogu liječnika obiteljske medicine u smanjenju prijenosa i AMR-a kod gonoreje kroz pridržavanje aktualno preporučenih smjernica za liječenje i promicanje odgovornog spolnog ponašanja.

**Prikaz slučaja:** Muškarac u dobi od 34 godine javio se u ordinaciju obiteljske medicine žaleći se na učestalo mokrenje, bolove i iscjedak iz mokraćne cijevi koji traju dva dana. Heteroseksualno orijentiran, inženjer građevine u vezi s istom djevojkom posljednje dvije godine. Bolesnik nije čest posjetitelj ordinacije i nije imao kroničnih bolesti. Na pitanje o nezaštićenom spolnom odnosu odgovorio je potvrdno, navodeći da je imao nezaštićeni spolni odnos sa strankinjom prije 7 dana tijekom službenog puta u Austriji. Fizikalnim pregledom utvrđeni su vitalni znakovi: krvni tlak 110/70, puls 75, temperatura 36,2°C. Venerološki status pokazao je mukopurulentan iscjedak na vanjskom spolovilu i eritem vanjskog ušća uretre. Da potvrdimo sumnju na gonoreju bolesnika smo uputili da napravi PCR (lančanu reakciju polimerazom) na urogenitalne mikoplazme i ureaplazme, klamidiju

(CUM) i *Neisseria gonorrhoeae* te urinokulturu s antibiogramom. Savjetovali smo apstinenciju od spolnih odnosa do dobivanja nalaza. Na kontrolnom pregledu nalazi pacijenata pokazali su pozitivan PCR na *Neisseria gonorrhoeae*. Pacijent je upućen dermatologu zbog jednokratne aplikacije ceftriaksona od 500 mg i.m. Preporučili smo daljnju apstinenciju od nezaštićenih spolnih odnosa 7 dana nakon liječenja antibiotikom. Savjetovano je da treba obavijestiti i spolnog partnera, te da se djevojka treba javiti svom obiteljskom liječniku ili ginekologu radi terapije.

**Rasprava.** Rastući promiskuitet i sve raniji početak spolne aktivnosti dva su važna čimbenika koji pridonose širenju spolno prenosivih infekcija. Gledajući stanje u Europi, postoji trend povećanja broja slučajeva istih među svim ključnim populacijama, pri čemu je najznačajniji porast zabilježen među muškarcima koji imaju spolne odnose s muškarcima (MSM). Štoviše, primjećuje se da međunarodna putovanja kao i migracija stanovništva igraju ključnu ulogu u širenju multirezistentnih SPI.

**Zaključak.** Uloga liječnika obiteljske medicine je prepoznavanje kliničke slike gonokokne infekcije, te liječenje bolesnika i svih njegovih spolnih partnera kako bi se prekinuo prijenos infekcije i smanjio broj komplikacija. Anamneza, klinički pregled, a posebno seksualna anamneza ključni su u postavljanju dijagnoze. Liječnici bi trebali stvoriti atmosferu u kojoj će se pacijenti osjećati sigurno razmjeniti informacije, korištenjem otvorenih pitanja; izbjegavati pretpostavke o seksualnim preferencijama, praksama i rodu/spolu. Za dobivanje potpune seksualne anamneze može se koristiti model pet P (partneri, praksa, stavovi o trudnoći, prethodne SPI i zaštita od SPI). Savjetovanje pacijenata o odgovornom spolnom ponašanju, uključujući dosljednu i pravilnu upotrebu kondoma tijekom vaginalnog, analnog i oralnog seksa, ključni je način na koji obiteljski liječnik može pomoći u smanjenju prijenosa SPI.

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## ■ Gonorrhea-case report

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**Introduction with aim:** Gonorrhoea (gonococcal infection) is a sexually transmitted infection (STI) caused by the obligate human pathogenic, Gram-negative bacterium *Neisseria gonorrhoeae*. Gonorrhea is spread during sexual contact, including oral, anal or vaginal intercourse or from mother-to-child during childbirth. Gonococcal infection is the second most common bacterial STI and can cause asymptomatic course in 10%-90% of women and 10%-40% of men resulting in delayed diagnosis, complications and uninterrupted transmission. The most common clinical manifestations of gonococcal disease in men include purulent discharge from the penis, dysuria, and testicular discomfort. When present, symptoms in female are often mild or nonspecific and can easily be mistaken for another type of vaginal infection or a bladder infection. Gonorrhea today is considered a major public health concern globally due to highest number of cases worldwide over the past decade along with the increasing antimicrobial resistance (AMR) in *Neisseria gonorrhoeae*. The aim of this paper is to highlight the role of family physician in reducing transmission and AMR in Gonorrhea by adhering to recommended treatment guidelines and promoting safer sexual practices.

**Case presentation.** A 34-year-old male patient came to the family medicine office complaining of frequent urination, pain and discharge from the urethra for the past two days. He was heterosexually oriented, construction engineer in a relationship with the same girlfriend for the last two years. The patient was not a frequent visitor to the office and had no chronic diseases. When asked about unprotected sexual activity he answered affirmatively, stating that he had unprotected sexual intercourse with a foreign female 7 days ago during his business trip to Austria. On physical examination, vital signs showed: blood pressure 110/70, pulse 75, and temperature 36.2°C. Venereological status showed mucopurulent discharge on the external genitalia and erythema of the external urethral ostium. For confirmation of suspected gonorrhea we refer the patient to polymerase chain reaction

(PCR) for urogenital mycoplasmas and ureaplasmas, chlamydia (CUM) and *Neisseria gonorrhoeae* as well as urine culture with an antibiogram. We advised abstinence from sexual intercourse until the results were received. At the follow-up examination, the patients results showed positive PCR for *Neisseria gonorrhoeae*. In order to administer a single dose of Ceftriaxone 500 mg i.m. he was referred to a dermatologist. We also recommend further abstinence from unprotected sexual relations for 7 days after antibiotic treatment. We note that the sexual partner should also be informed, and the patient was told that the girlfriend should contact her family physician or gynecologist for therapy.

**Discussion.** Increased promiscuity and onset of sexual activity at an early age are two important contributing factors to the spread of sexually transmitted diseases. Focusing on Europe, an increasing trend in cases is observed among all key populations with the most significant rise observed among men who have sex with men (MSM). Moreover, international travels as well as population migration play a key role in the spread of multi-resistant STIs.

**Conclusion.** The role of family physicians is to recognize the the clinical presentation of the gonococcal infection, as to provide treatment to the patient and all their sexual partners to interrupt transmission chains and to reduce the overall disease burden. Anamnesis, clinical examination, and especially sexual history are key in diagnosing. Physicians should create supportive space where patient feel safe sharing information by using open-ended questions; avoiding assumptions regarding sexual preferences, practices, and gender/sex. To obtain a complete sexual history, the five P's (partners, practices, pregnancy attitudes, previous STIs, and protection from STIs) model can be used. Safer sex counseling their patients, including consistent and correct condom use during vaginal, anal and oral sex, is the crucial way family physician can help reduce transmission of STIs.

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## ■ Gonoreja -prikaz slučaja

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**Uvod s ciljem:** Gonoreja (gonokokna infekcija) je spolno prenosiva infekcija (SPI) koju uzrokuje obligatni humani patogen, gram-negativna bakterija *Neisseria gonorrhoeae*. Gonoreja se prenosi spolnim putem, odnosno oralnim, analnim ili vaginalnim spolnim odnosom te prijenosom s majke na dijete tijekom poroda. Gonokokna infekcija druga je najčešća bakterijska spolno prenosiva bolest i ima asimptomatski tijek kod 10%-90% žena i 10%-40% muškaraca što odgađa dijagnozu te pogoduje stvaranju komplikacija i daljnjem širenju infekcije. Najčešće kliničke manifestacije gonokokne bolesti u muškaraca uključuju gnojni iscjedak iz penisa, disuriju i nelagodu u testisima. Kada su prisutni, simptomi kod žena često su blagi ili nespecifični i lako se mogu zamijeniti sa drugim vaginalnim ili mokraćnim infekcijama. Gonoreja se danas smatra velikim globalnim javnozdravstvenim problemom zbog rastućeg broja slučajeva kroz protekle desetljeće u cijelom svijetu, kao i rastućom antimikrobnom rezistencijom (AMR) *Neisserie gonorrhoeae*. Cilj ovog rada je istaknuti ulogu liječnika obiteljske medicine u smanjenju prijenosa i AMR-a kod gonoreje kroz pridržavanje aktualno preporučenih smjernica za liječenje i promicanje odgovornog spolnog ponašanja.

**Prikaz slučaja:** Muškarac u dobi od 34 godine javio se u ordinaciju obiteljske medicine žaleći se na učestalo mokrenje, bolove i iscjedak iz mokraćne cijevi koji traju dva dana. Heteroseksualno orijentiran, inženjer građevine u vezi s istom djevojkom posljednje dvije godine. Bolesnik nije čest posjetitelj ordinacije i nije imao kroničnih bolesti. Na pitanje o nezaštićenom spolnom odnosu odgovorio je potvrdno, navodeći da je imao nezaštićeni spolni odnos sa strankinjom prije 7 dana tijekom službenog puta u Austriji. Fizikalnim pregledom utvrđeni su vitalni znakovi: krvni tlak 110/70, puls 75, temperatura 36,2°C. Venerološki status pokazao je mukopurulentan iscjedak na vanjskom spolovilu i eritem vanjskog ušća uretre. Da potvrdimo sumnju na gonoreju bolesnika smo uputili da napravi PCR (lančanu reakciju polimerazom) na urogenitalne mikoplazme i ureaplazme, klamidiju

(CUM) i *Neisseria gonorrhoeae* te urinokulturu s antibiogramom. Savjetovali smo apstinenciju od spolnih odnosa do dobivanja nalaza. Na kontrolnom pregledu nalazi pacijenata pokazali su pozitivan PCR na *Neisseria gonorrhoeae*. Pacijent je upućen dermatologu zbog jednokratne aplikacije ceftriaksona od 500 mg i.m. Preporučili smo daljnju apstinenciju od nezaštićenih spolnih odnosa 7 dana nakon liječenja antibiotikom. Savjetovano je da treba obavijestiti i spolnog partnera, te da se djevojka treba javiti svom obiteljskom liječniku ili ginekologu radi terapije.

**Rasprava.** Rastući promiskuitet i sve raniji početak spolne aktivnosti dva su važna čimbenika koji pridonose širenju spolno prenosivih infekcija. Gledajući stanje u Europi, postoji trend povećanja broja slučajeva istih među svim ključnim populacijama, pri čemu je najznačajniji porast zabilježen među muškarcima koji imaju spolne odnose s muškarcima (MSM). Štoviše, primjećuje se da međunarodna putovanja kao i migracija stanovništva igraju ključnu ulogu u širenju multirezistentnih SPI.

**Zaključak.** Uloga liječnika obiteljske medicine je prepoznavanje kliničke slike gonokokne infekcije, te liječenje bolesnika i svih njegovih spolnih partnera kako bi se prekinuo prijenos infekcije i smanjio broj komplikacija. Anamneza, klinički pregled, a posebno seksualna anamneza ključni su u postavljanju dijagnoze. Liječnici bi trebali stvoriti atmosferu u kojoj će se pacijenti osjećati sigurno razmjeniti informacije, korištenjem otvorenih pitanja; izbjegavati pretpostavke o seksualnim preferencijama, praksama i rodu/spolu. Za dobivanje potpune seksualne anamneze može se koristiti model pet P (partneri, praksa, stavovi o trudnoći, prethodne SPI i zaštita od SPI). Savjetovanje pacijenata o odgovornom spolnom ponašanju, uključujući dosljednu i pravilnu upotrebu kondoma tijekom vaginalnog, analnog i oralnog seksa, ključni je način na koji obiteljski liječnik može pomoći u smanjenju prijenosa SPI.

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## ■ Kortikosteroidima inducirana hiperglikemija kod pacijentice s dijabetesom melitusom tipa 1 – izazovi u sustavnom liječenju dermatološke bolesti

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**Uvod s ciljem:** Autoimune dermatološke bolesti koje se neuspješno liječe topikalnim pripravcima u kliničkoj praksi često zahtijevaju sustavnu primjenu kortikosteroida koji u visokim dozama mogu izazvati ozbiljne nuspojave. Poseban oprez potreban je kod pacijenata s dijabetesom melitusom tipa 1 (DM1), kod kojih kortikosteroidi ometaju djelovanje inzulina i destabiliziraju glikemiju. Stoga je u tih pacijenata potrebno pomno praćenje profila glukoze u krvi, primjenjivanih doza inzulina, nerijetko uz izbjegavanje sustavne terapije kortikosteroidima. Cilj ovog prikaza je naglasiti važnost konzultacije s obiteljskim liječnikom prije početka uzimanja terapije preporučene od strane specijalista specifično-konzilijarne zdravstvene zaštite, kao i ključnu ulogu primjereno uzete anamneze uz bilježenje svih postojećih komorbiditeta u ordiniranju lijeka, radi izbjegavanja teških nuspojava po primjeni istog.

**Prikaz slučaja:** 42-godišnja pacijentica s dijabetesom melitusom tipa 1 žena javlja se u ordinaciju svog obiteljskog liječnika zbog ekcematoznih promjena kože na obje potkoljenice u trajanju od nekoliko tjedana. Dermatološkom obradom isključila se reumatska i infektivna podloga bolesti, a promjene su tijekom godinu dana u više navrata liječene topikalnim pripravcima bez uspjeha, zbog čega joj dermatolog preporučio pulsnu terapiju metilprednizolonom per os (32-16-8-4-2-ex). Pacijentici se telefonskim putem bez fizičke konzultacije s obiteljskim liječnikom propiše preporučena terapija. Peti dan uzimanja metilprednizolona pacijentica se ponovno javlja svom obiteljskom liječniku, vrlo uznemirena zbog izmjerenih vrlo visokih koncentracija glukoze u krvi natašte i postprandijalno (patološki profil GUK-a) unatoč redovitoj primjeni inzulina te dolazi na pregled iduće jutro. Po uvidu u nalaz dermatologa, primijenjene doze prepisane kortikosteroidne terapije, zdravstveni karton pacijentice s DM1 koja četiri puta dnevno uzima inzulini te bilježeni dnevnik GUK-a tijekom uzimanja terapije, patološke se razine GUK-a

shvate kao nuspojava lijeka uzrokovana interferencijom s inzulinom. Zbog komorbiditeta DM1 u naše pacijentice, koji dermatološkom obradom nije uzet u obzir niti pismeno zabilježen prilikom uzimanja dermatološke anamneze prije uvođenja sustavne terapije kortikosteroidom u visokim dozama, kao i zbog izostanka fizičke konzultacije s obiteljskim liječnikom prije početka liječenja, uputnim se pismom stanje pacijentice šalje na ponovni uvid dermatologu sa zahtjevom o promjeni terapije s ciljem izlječenja aktualne dermatološke bolesti, a sukladno komorbiditetima i stalnoj terapiji, na osnovu čega će se planirati novi oblik liječenja.

**Rasprava:** Terapija sustavnim kortikosteroidima često je neprimjerena za bolesnike sa šećernom bolešću. Kako visoke doze primijenjenog lijeka nerijetko izazivaju hiperglikemiju kao rezultat oponirajućeg djelovanja kortikosteroida na inzulini, poželjno je u dijabetičara prilagoditi vrstu i dozu lijeka sukladno nalazu glikemije da bi se izbjegli njegovi neželjeni učinci. Osim toga, od iznimne je važnosti uloga obiteljskog liječnika i drugih specijalista kao članova specifično-konzilijarne zdravstvene zaštite (SKZZ) pri ordiniranju lijeka, pri čemu obje strane prije uvođenja terapije primjerenom intervencijom u obzir trebaju uzeti sve komorbiditete pacijenta, na osnovu čega se odabire novi oblik terapije s ciljem svođenja nuspojava na najmanju moguću razinu u korist zadovoljavajuće djelotvornosti lijeka.

**Zaključak:** Budući da uvođenje terapije visokim dozama sustavnih kortikosteroida može rezultirati ozbiljnim nuspojavama, ključno je pažljivo procijeniti komorbiditete pacijenta, napose dijabetičara, s ciljem izbjegavanja hiperglikemije. Osim toga uloga obiteljskog liječnika nezamjenjiva je u ordiniranju takve terapije, kao i razmatranju alternativnih metoda liječenja u slučaju teških nuspojava.

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## ■ Corticosteroid-induced hyperglycemia in a patient with type 1 diabetes mellitus – challenges in the systemic treatment of dermatological diseases

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**Introduction with aim:** Autoimmune dermatological diseases that are unsuccessfully treated with topical preparations in clinical practice often require systemic corticosteroid therapy, which at high doses can result in serious side effects. Careful consideration is needed in patients with type 1 diabetes mellitus, in whom corticosteroids interfere with insulin and destabilize glycemia. Therefore, close monitoring of blood glucose profile, insulin use, and often the avoidance of systemic corticosteroid therapy is necessary in these patients. The aim of this case is to emphasize the importance of consultation with the family doctor before starting therapy recommended by a specialist in specific-consultative healthcare, as well as the crucial role of a thorough medical history and documentation of all existing comorbidities when prescribing medication, in order to avoid severe side effects from its use.

**Case report:** A 42-year-old female patient with type 1 diabetes mellitus presents to her family doctor due to eczema-like skin changes on both lower legs, lasting for several weeks. Dermatological examination rules out rheumatic and infectious causes, and the affected skin area has been treated multiple times with topical preparations over the past year without improvement, leading the dermatologist to recommend pulse therapy with methylprednisolone orally (32-16-8-4-2-ex). The patient is prescribed the recommended therapy by phone without a physical consultation with the family doctor. On the fifth day of taking methylprednisolone, the patient returns to her family doctor, very distressed due to the measured very high blood glucose levels both fasting and postprandially, despite regular insulin use, and she comes for an examination the next morning. Upon reviewing the dermatologist's findings, the prescribed corticosteroid doses, the patient's medical history with T1DM (who takes insulin four times daily), and the daily noted blood glucose levels, high blood glucose levels are understood as a side effect of

the medication due to interference with insulin. Due to the comorbidity of T1DM in our patient, which was not considered or documented in the dermatological history before the initiation of systemic high-dose corticosteroid therapy, and the lack of a physical consultation with the family doctor before starting the treatment, the patient's condition is sent back to the dermatologist requesting a new therapy protocol with the aim of successful treatment of the current dermatological condition. The new treatment protocol based on the comorbidities and ongoing insulin therapy has to be started.

**Discussion:** Systemic corticosteroid therapy is often inappropriate for patients with diabetes. Since high doses of the administered medication can result in hyperglycemia due to its antagonistic effect on insulin, it's necessary to adjust the type and dose of the medication in diabetic patients according to glucose levels to avoid side effects. Furthermore, both the family doctor and any other specialist in specific-consultative healthcare team should consider the patients comorbidities before prescribing medication to minimize side effects while maximizing the effectiveness of the medication.

**Conclusion:** Since the administration of high doses of systemic corticosteroids can result in serious side effects, it is crucial to evaluate the patient's comorbidities, especially in diabetics, in order to avoid hyperglycemia. Furthermore, the role of the family doctor is crucial in prescribing such therapy, as well as considering alternative treatment methods in the case of severe side effects.

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## ■ Kognitivno testiranje u ordinaciji liječnika obiteljske medicine

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**Ključne riječi:** demencija, test minimalne mentalne procjene, memantin

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**Uvod s ciljem:** Demencija je naziv skupine bolesti koje se većinom pojavljuju u starijoj životnoj dobi, a uzrokovana je kognitivnim poremećajem rada mozga. Postoje različite vrste demencije od kojih je najčešća Alzheimerova demencija. Među brojnim testovima za rano otkrivanje, klasificiranje i praćenje kognitivnih promjena u demencijama, za liječnika obiteljske medicine kao najbolji pokazatelj koristi se test minimalne mentalne procjene (engl. Mini Mental State Examination – MMSE). On se sastoji od pet grupa pitanja koja obuhvaćaju orijentaciju, prepoznavanje, pozornost i računanje, pamćenje i govor, a koji se boduju. Maksimalan broj bodova je 30, a rezultat testa označava stupanj demencije: blaga (21-26), umjerena (15-20), srednje teška (10-14) i teška (< 10). Cilj rada je prikazati primjenu kognitivnog testiranja u ordinaciji liječnika obiteljske medicine.

**Prikaz slučaja:** Pacijentica u dobi od 75 godina dolazi na konzultaciju u ordinaciju liječnika obiteljske medicine u pratnji kćeri koja navodi kako je kod majke unazad godinu dana primjetila pogoršanje u pamćenju. Heteroanamnestički od kćeri doznajemo kako u obitelji nitko nije bolovao od demencije ili drugih neuroloških bolesti. Iz kartona pacijentice vidljivo je da do sada nije teže bolovala, nema kronične bolesti niti stalnu terapiju, povremeno pije diklofenak 75 mg zbog križobolje. U razgovoru kćer pobliže opisuje majčine tegobe i svakodnevicu. Pacijentica živi sama u stanu u istom naselju kao i kćer koja ju svakodnevno obilazi. Organiziran je dnevni nadzor pacijentice kao i topli obrok jer ona više ne zna kuhati. Pacijentica nove događaje ne pamti, primjetili su teškoće u oblačenju, a povremeno ne zna koje je doba dana, godina ili mjesec. Prepoznaje obitelj i susjede. Noć provodi sama, pacijentica navodi da dobro spava. Kćer navodi kako se majka jednom izgubila u trgovini zbog čega je intervenirala policija. Pacijentica smatra da ona nema problema te kako obitelj pretjeruje. Učinjen je fizikalni pregled koji je uredan. Neurološki status pokazuje blagu ideomotoričku apraksiju pri izvođenju naredbi za motoričke zadatke (poteškoće u shvaćanju pri izvođenju npr.

testa prst-nos-prst i test peta-koljeno), no nakon dodatnog pojašnjavanja ih izvodi. Hod je uredan, sfinktere uredno kontrolira. U psihološkom statusu orijentirana je prema sebi i drugima kao i u prostoru, a vremenski je dezorijentirana. Nije auto niti heterodestruktivna, negira obmane osjetila i suicidalne misli. Napravljen je MMSE dobivenih vrijednosti 14/30 bodova koji govori u prilog srednje teške demencije, a pacijentica pokazuje slabe vizuoprostorne i izvršne vještine te je u govoru vidljiv problem pronalaženja riječi. Pacijentici i kćeri objašnjeni su rezultati testa te kako su prisutni znakovi demencije, uz naglašen problem s kratkoročnim pamćenjem. Učinjena laboratorijska obrada, uključujući lipidogram, jetrene i bubrežne parametre, hormone štitnjače, vitamin B12 bila je uredna. Savjetovani su učiniti pregled neurologa i psihijatra, a po preporuci neurologa učinjen je CT mozga koji je pokazao kortikalnu atrofiju mozga te je neurolog postavio dijagnozu Alzheimerove demencije. Po preporuci psihijatra i neurologa u terapiju je uveden memantin 10mg uvečer uz oksazepam 10mg po potrebi. U ordinaciji liječnika obiteljske medicine izvršeno je savjetovanje pacijentice i kćeri, razgovor o bolesti i preporuka mogućnosti smještaja pacijentice u ustanovu za starije osobe radi cjelodnevnog nadzora.

**Zaključak:** Zbog starenja svjetske populacije i broja oboljelih od preko 35 milijuna ljudi samo od Alzheimerove demencije, demencija je postala velik javnozdravstveni problem. Liječnik obiteljske medicine kod pacijenata koje dugo ima u skrbi može prepoznati promjene u kogniciji i ponašanju, pravodobno provesti MMSE i dijagnostičku obradu, uputiti pacijenta neurologu i psihijatru te time poboljšati kvalitetu života oboljele osobe u obitelji i zajednici.

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## ■ Cognitive testing in a family medicine doctor's office

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**Introduction with aim:** Dementia is the name of a group of diseases that mostly appear in old age, and are caused by cognitive disorders of the brain. There are different types of dementia, the most common of which is Alzheimer's dementia. Among the numerous tests for early detection, classification and monitoring of cognitive changes in dementia, the Mini Mental State Examination (MMSE) is used as the best indicator for a family medicine doctor. It consists of five groups of questions covering orientation, recognition, attention and calculation, memory and speech, which are scored. The maximum number of points is 30, and the test result indicates the degree of dementia: mild (21-26), moderate (15-20), medium (10-14) and severe (< 10). The aim of the paper is to show the application of cognitive testing in the family medicine doctor's office.

**Case report:** A 75-year-old female patient comes for a consultation at the family medicine doctor's office, accompanied by her daughter, who states that she noticed a deterioration in her mother's memory during the last year. We learned from the daughter's heteroanamnesis that no one in the family suffered from dementia or other neurological diseases. It is evident from the patient's medical record that she has no chronic diseases or ongoing therapy, and she occasionally takes diclofenac 75 mg for low back pain. In the conversation, the daughter describes her mother's ailments and everyday life in more detail. The patient lives alone in an apartment in the same neighborhood as her daughter, who visits her every day. Daily monitoring of the patient was organized as well as a hot meal because she no longer knows how to cook. The patient does not remember new events, family noticed difficulties in dressing, and sometimes she does not know what time of day, year or month it is. The patient recognizes family members and neighbors. She spends the night alone, the patient states that she sleeps well. The daughter states that the mother once got lost in the store, which is why the police intervened. The patient believes that she has no problems and that the family is exaggerating. A physical examination was performed, which was in order. The neurological status shows mild ideomotor apraxia when performing commands for motor tasks (difficulties in understanding when

performing, for example, the finger-nose-toe test and the heel-knee test), but after additional clarification, she performs them. The gait is orderly, the sphincters are properly controlled. In psychological status, she is oriented towards herself and others as well as in space, and she is disoriented in time. She is not auto or heterodestructive, she denies deception of the senses and suicidal thoughts. An MMSE with values of 14/30 points was made, which speaks in favor of moderately severe dementia, and the patient shows weak visual and spatial executive skills, and a word-finding problem is visible in her speech. The results of the test were explained to the patient and her daughter and that there were signs of dementia, with a problem with short-term memory emphasized. Laboratory work-up, including lipids in the blood, liver and kidney parameters, thyroid hormones, vitamin B12 were normal. They were advised to undergo an examination by a neurologist and a psychiatrist, and according to the neurologist's recommendation, a CT scan of the brain was performed, which showed cortical brain atrophy, and the neurologist diagnosed Alzheimer's dementia. On the recommendation of the psychiatrist and neurologist, memantine 10 mg in the evening was introduced into the therapy along with oxazepam 10 mg as needed. In the family medicine doctor's office, the patient and her daughter were consulted, the illness was discussed and the possibility of the patient's placement in an institution for the elderly for all-day supervision was recommended.

**Conclusion:** Due to the aging of the world's population and the number of patients of over 35 million people suffering from Alzheimer's dementia, dementia has become a major public health problem. A family medicine doctor can recognize changes in cognition and behavior in patients he has in care for a long time, perform MMSE and diagnostic work-up in a timely manner, refer the patient to a neurologist and psychiatrist, and with that improve the quality of life of the patient.

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## ■ Imuna trombocitopenija vezana uz *Helicobacter pylori* infekciju

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**Uvod s ciljem:** Trombocitopenija je stanje koje se često prezentira nespecifičnim simptomima, što može dovesti do odgađanja dijagnoze ili pogrešnog tumačenja kliničke slike. Simptomi poput gingivalnog krvarenja, petehija, spontanih modrica, epistakse, produljenog menstrualnog krvarenja te opće slabosti i umora mogu upućivati na širok spektar poremećaja, uključujući infekcije, koagulacijske poremećaje ili ginekološke probleme. Upravo zbog nespecifične prirode ovih simptoma, trombocitopenija često ostaje neprepoznata sve do provođenja laboratorijskih testova. Cilj ovog rada je ilustrirati važnost kliničkih simptoma u prepoznavanju sekundarnih uzroka trombocitopenije, kao što je infekcija bakterijom *Helicobacter pylori*.

**Prikaz slučaja:** Bolesnica stara 46 godina javila se u ordinaciju liječnika obiteljske medicine zbog pojave spontanih modrica i osipa na nogama te pojačanog krvarenja desni prilikom pranja zuba. Inače je zdrava, ne uzima nikakvu kroničnu terapiju. Puši posljednjih dvadesetak godina 10 cigareta dnevno. Tijekom fizikalnog pregleda uočene su petehije na donjim ekstremitetima, kao i na jeziku i bukalnoj sluznici. Laboratorijskim nalazima utvrđena je teška trombocitopenija s brojem trombocita  $1 \times 10^9/L$ , zbog čega je upućena na žurni pregled hematologa. Tijekom hospitalizacije dijagnostičkim postupcima isključeni su sekundarni uzroci trombocitopenije, a detaljnijim testiranjem potvrđena je prisutnost infekcije *H. pylori*. Nakon provedene eradikacijske terapije i liječenja visokim dozama glukokortikoida, došlo je do postupne normalizacije broja trombocita, čime je potvrđena dijagnoza imunološki posredovane trombocitopenije izazvane infekcijom *H. pylori*. U bolesnice se protekle tri godine redovito prate laboratorijski nalazi te nije zabilježen recidiv trombocitopenije.

**Rasprava:** Imuna trombocitopenija (ITP) autoimuni je poremećaj karakteriziran izoliranim smanjenjem broja trombocita u perifernoj krvi zbog njihove povećane destrukcije i smanjene proizvodnje. Iako je etiologija ITP-a često idiopatska, sve je više dokaza koji ukazuju na povezanost s

infekcijom *H. pylori*. Pretpostavlja se da infekcija ovom bakterijom može potaknuti imunološke mehanizme koji vode do stvaranja protutijela protiv trombocita, što rezultira njihovom perifernom destrukcijom. U većine bolesnika s ITP-om nakon provođenja eradikacijske terapije dolazi do normalizacije broja trombocita. Važno je napomenuti značaj pravovremenog prepoznavanja infekcije kao uzroka trombocitopenije, čime se izbjegava nepotrebno liječenje drugih hematoloških stanja.

**Zaključak:** Trombocitopenija izazvana *H. pylori* infekcijom rijetko se prepoznaje, ali pravovremeno postavljanje dijagnoze i adekvatno liječenje mogu značajno poboljšati ishod. Liječnici obiteljske medicine trebaju imati na umu povezanost ove infekcije s trombocitopenijom i koristiti sveobuhvatan pristup u dijagnostici kako bi se pravovremeno započelo liječenje.

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## ■ Helicobacter pylori-associated immune thrombocytopenia

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**Introduction with aim:** Thrombocytopenia is a condition that often presents with non-specific symptoms, which can lead to delayed diagnosis or misinterpretation of the clinical picture. Symptoms such as gingival bleeding, petechiae, spontaneous bruising, epistaxis, prolonged menstrual bleeding, and general weakness and fatigue may indicate a wide range of disorders, including infections, coagulation disorders, or gynecological problems. Precisely because of the non-specific nature of these symptoms, thrombocytopenia often remains unrecognized until laboratory tests are performed. The aim of this paper is to illustrate the importance of clinical symptoms in the recognition of secondary causes of thrombocytopenia, such as *Helicobacter pylori* infection.

**Case Report:** A 46-year-old female presented to her family medicine physician with bleeding gums and petechiae on her lower extremities. Laboratory tests revealed severe thrombocytopenia, with a platelet count of  $1 \times 10^7/L$ , prompting urgent referral to a hematologist. During hospitalization, diagnostic workup excluded secondary causes of thrombocytopenia, while further testing confirmed infection with *H. pylori*. The patient underwent eradication therapy combined with high-dose glucocorticoids. Following treatment, her platelet count gradually normalized, confirming the diagnosis of immune thrombocytopenia caused by *H. pylori* infection. Over the subsequent three years of regular follow-up, her platelet counts remained stable, with no evidence of thrombocytopenia relapse, indicating sustained remission.

**Discussion:** Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by an isolated decrease in the number of platelets in the peripheral blood due to their increased destruction and reduced production. Although the etiology of ITP is often idiopathic, there is increasing evidence suggesting an association with *H. pylori* infection. It is assumed that infection with this bacterium can stimulate immune mechanisms that lead to the formation of antibodies against platelets, resulting in their peripheral destruction.

In most patients with ITP, the number of platelets normalizes after the eradication therapy. It is important to note the importance of timely recognition of infection as a cause of thrombocytopenia, thus avoiding unnecessary treatment of other hematological conditions.

**Conclusion:** Thrombocytopenia caused by *H. pylori* infection is rarely recognized, but timely diagnosis and adequate treatment can significantly improve the outcome. Family medicine doctors should keep in mind the association of this infection with thrombocytopenia and use a comprehensive approach in diagnosis in order to start treatment in a timely manner.

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## Amoksicilin i Mycoplasma pneumoniae - ima li učinka?

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**Uvod s ciljem** Mycoplasma pneumoniae (M.pneumoniae) jedna je od najvažnijih uzročnika atipične pneumonije. Najčešće se javlja u kasno ljeto i jesen s epidemijским razmjerima svakih godinu do 3 godine dana. Europski centar za prevenciju i kontrolu bolesti je za sezonu 2023./2024. bilježio povećanu incidenciju pneumonija uzrokovanih M.pneumoniae. Zbog često blažeg tijeka bolesti sa simptomima vrućice, slabosti, glavobolje te suhog, nadražajnog kašlja koji s vremenom postaje produktivan, često se naziva i „hodajuća pneumonija“. Specifičnost M.pneumoniae leži u njenoj građi, nedostatak stanične stijenke prirodno ju svrstava u skupinu bakterija rezistentnih na beta-laktame te ograničava njeno liječenje na makrolide. Azitromicin svojim antibakterijskim, imunomodulatornim i antiinflamatornim djelovanjem pokazuje brzu regresiju simptoma i uspješno izlječenje. Druga linija liječenja uključuje fluorokinolone i tetracikline. Globalna rezistencija makrolida na M.pneumoniae iznosi 28% sa značajnim geografskim varijacijama. U Europi ona iznosi prosječno 5%. Cilj ovog prikaza slučaja je ukazati na sličnosti kliničke slike i laboratorijskih nalaza M.pneumoniae i respiratornih virusa te važnost prepoznavanja i ordiniranja adekvatne terapije za infekciju M.pneumoniae.

**Prikaz slučaja** U ordinaciju liječnika obiteljske medicine (LOM) javlja se 58-godišnji pacijent sa simptomima slabosti, globalbolje i subjektivnog osjećaja vrućice koji traju dva dana. Na upit prijavljuje povremeni suhi kašalj. U fizikalnom nalazu nalazimo povišenu tjelesnu temperaturu 37.2°C, orofaringoskopski hiperemičnu sluznicu, blago edematozne lukove i uvulu s tonzilama unutar ždrijelnih lukova. Auskultacijski uredan šum disanja. Obzirom na trajanje i tijek bolesti postavi se dijagnoza akutnog virusnog faringitisa te preporuka simptomatske terapije ibuprofen a 600mg/2x/dan s kontrolom po potrebi. Pacijent se 6 dana nakon pregleda javlja u ordinaciju

LOM. Uvidom u medicinsku dokumentaciju saznaje se da je pacijent dva dana nakon našeg pregleda razvio suhi, nadražajni kašalj koji ga noću budi s febrilitetom do 38.2°C radi čega se javio u ordinaciju dežurnog LOM. Fizikalnim pregledom uočena je nadražena sluznica ždrijela te se auskultacijski desno, bazalno čuju krepitacije. Laboratorijski nalaz pokaže CRP 10,7mg/L; L 9,9x10<sup>9</sup>/L; seg.L 6,97x10<sup>9</sup>/L nakon čega se ordinira amoksicilin a 500mg 3 x dnevno 10 dana. Pacijent nam se javlja 4.dan uzimanja amoksicilina te se žali na iste simptome i ima jednak fizikalni status kao i kod dežurnog LOM. Na osnovu kliničke slike i tijeka bolesti, laboratorijskih nalaza te trenutne epidemiološke situacije postavi se sumnja na infekciju M.pneumoniae te se, bez dokaza patogena, ordinira azitromicin a 500mg/3 dana. Kontrolnim pregledom za 4 dana bilježi se potpuna regresija simptoma uz zadovoljavajući oporavak pacijenta.

**Rasprava** Infekciju M. pneumonia vrlo je važno prepoznati na vrijeme jer može dovesti do teške pneumonije. U kliničkoj se praksi, nerijetko, na osnovi kliničke slike i laboratorijskih nalaza sličnih infekciji M.pneumoniae susreće izdavanje amoksicilina, ili čak koamoksiklava. Povećana incidencija respiratornih infekcija izazvanih M.pneumoniae u jeseni 2024.godine dovodi do poželjnog ordiniranja azitromicina bez dokazanog patogena za sve respiratorne infekcije koje nalikuju na onu izazvanu M.pneumoniae kako bi se postigao imunitet krda.

**Zaključak** Prikaz slučaja naglašava važnost pravovremenog identificiranja uzročnika i propisivanja adekvatne terapije. Prije izdavanja antibiotske terapije potrebno je razmisliti o diferencijalnoj dijagnozi te trenutnoj epidemiološkoj situaciji određenog područja.

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## ■ Amoxicillin and *Mycoplasma pneumoniae* – Is it effective?

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**Introduction with Aim** *Mycoplasma pneumoniae* (*M. pneumoniae*) is a significant cause of atypical pneumonia, typically occurring in late summer and autumn, with epidemic outbreaks every 1-3 years. The European Centre for Disease Prevention and Control reported an increased incidence of *M. pneumoniae* pneumonia cases in the 2023/2024 season. Often called “walking pneumonia,” it presents with mild symptoms such as fever, fatigue, headache, and a dry cough that may later become productive. A key characteristic of *M. pneumoniae* is its lack of a cell wall making it resistant to beta-lactam antibiotics, which limits treatment options to macrolides. Azithromycin, known for its antibacterial, immunomodulatory, and anti-inflammatory effects, leads to rapid symptom regression and recovery. Second-line treatments include fluoroquinolones and tetracyclines. Global macrolide resistance in *M. pneumoniae* is estimated at 28%, with significant geographical variations. In Europe, the average resistance rate is around 5%. This case report highlights the similarities between clinical and laboratory findings of *M. pneumoniae* and respiratory viruses, as well as the importance of early recognition and adequate treatment of *M. pneumoniae* infections.

**Case Report** A 58-year-old patient presented to a general practitioner (GP) with fatigue, sore throat, and a subjective feeling of fever lasting two days. Upon questioning, he reported an occasional dry cough. Physical examination revealed a slightly elevated body temperature of 37.2°C, hyperemic oropharyngeal mucosa, mildly edematous arches and uvula, while tonsils appeared normal. Lung auscultation was unremarkable. A diagnosis of acute viral pharyngitis was made, and symptomatic therapy with ibuprofen 600 mg twice daily was recommended, with follow-up as needed. Six days later, the patient returned to the GP's office. His medical records revealed that two days after the initial visit, he developed a dry, irritating

cough that disrupted his sleep and fever reaching up to 38.2°C, prompting him to seek care from an on-call GP. Physical examination showed irritated pharyngeal mucosa, and crackles upon auscultation at the right lung base. Laboratory tests indicated CRP 10.7 mg/L, leukocytes  $9.9 \times 10^9/L$ , segmented neutrophils  $6.97 \times 10^9/L$ . Amoxicillin 500 mg three times daily for 7 days was prescribed. Four days into amoxicillin therapy, the patient revisited the GP with persistent symptoms and unchanged physical findings. Based on the clinical presentation, course of illness, laboratory results, and current epidemiological situation, *M. pneumoniae* infection was suspected. Without confirmatory pathogen testing, azithromycin 500 mg daily for 3 days was prescribed. A follow-up examination four days later showed complete symptom resolution and satisfactory patient recovery.

**Discussion** Early recognition of *M. pneumoniae* infection is crucial, as it can lead to severe pneumonia. In clinical practice, amoxicillin or co-amoxiclav is often prescribed for symptoms and laboratory findings similar to *M. pneumoniae* infection. The increased incidence of respiratory infections caused by *M. pneumoniae* in autumn 2024 suggests that empirical azithromycin treatment may be appropriate for respiratory infections resembling *M. pneumoniae* pneumonia, even without pathogen confirmation, to promote herd immunity.

**Conclusion** This case report highlights the importance of early pathogen identification and appropriate antibiotic therapy. Before prescribing antibiotics, it is essential to consider differential diagnoses and the current epidemiological situation in the region.

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## ■ Diabetes melitus tip 1

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**Uvod s ciljem:** Kvaliteta života igra važnu ulogu u bolesnikovom doživljaju bolesti i utječe na koji će se način pacijent suočiti s problemima i komplikacijama koje određena bolest donosi.

Tijek šećerne bolesti obilježen je razvojem kroničnih komplikacija koje, osim na zdravlje, utječu i na kvalitetu života bolesnika. Dok je najveća incidencija dijabetes melitusa tip 1 još uvijek u ranoj adolescenciji sve se češće dijagnosticira u odrasloj dobi. Početak je obično manje akutan nego u djetinjstvu i donosi niži, iako još uvijek značajan, rizik od komplikacija i rane smrtnosti. U ovom prikazu slučaja cilj je pokazati kako pravovremena sumnja i točna dijagnostika mogu uvelike ubrzati proces točne dijagnoze i početka liječenja. Ovakvim pristupom liječenja smanjit ćemo komplikacije, produžiti životni vijek i poboljšati kvalitetu života.

**Prikaz slučaja:** Pacijent, star 62 godine, nepušač, do sada zdrav. U obiteljskoj anamnezi negira dijabetes. Dolazi u ambulantu obiteljskog liječnika zbog eritema i ranice na palcu desne noge. Prilikom ulaska u ambulantu primjećuje se kako je bolesnik vidno smršavio. U zadnjih 8 mjeseci navodi gubitak od oko desetak kilograma, ali to pripisuje zdravom načinu ishrane kojeg se pridržava. Prilikom pregleda fizikalni status bio je potpuno uredan, osim eritema uz manju bulu na dorzumu palca. Tokom uzimanja anamneze, pokušava se saznati ima li još neke od simptoma kao što su poliurija i polidipsija, jer se sumnja kako je moguće da se radi o dijabetes melitusu. Bolesnik navodi kako u zadnje vrijeme ide češće mokriti, ali je to pridavao tome što je počeo piti više tekućine. Kako je pacijent došao krajem radnog vremena i nije bio na tašte, glukometrija se nije provela. Naručen je na vađenje krvi sutradan, previjena ranica na palcu, te uveden amoksicilin s klavulanskom kiselinom i metronidazol. Sljedeći dan stigli su laboratorijski nalazi iz kojih se izdvaja GUK 20,4 mmol/L, kolesterol 7,6, LDL 4,7, trigliceridi 12,8, HbA1c 14,0%. Zbog ozbiljnosti situacije te dugačkih listi čekanja dijabetologa, pacijentu je izdana C2 uputnica. Pregledan je kroz hitni prijem, te je istog dana zbog visokih vrijednosti HbA1c i potrebe za uvođenjem

bazalnog inzulina pregledan i od strane dijabetologa. U terapiju je uveden metformin 1x500 mg s povećanjem u optimalnim intervalima do 2x2000 mg, sitagliptin 1x100mg, inzulin degludek 8j u 22h s povećanjem za po 2j do postizanja ciljnih vrijednosti glikemije i atorvastatin 20 mg. Nakon 3 tjedna dolazi na kontrolu, te sada laboratorijske vrijednosti pokazuju GUK 7,8 mmol/L, HbA1c 12,4 %.

**Rasprava:** U ovom prikazu slučaja razvidno je kako pacijent primarno dolazi zbog rane na palcu koja mu predstavlja najveći problem zbog boli prilikom hoda. Prilikom uzimanja anamneze sve ostale simptome zanemaruje i pripisuje novom načinu života. Kao obiteljski liječnik bitno je poznavati svoje pacijente i primijetiti kako fizičke tako i psihičke promijene. Važno je birati dijagnostičke pretrage koje će brzo potvrditi naše sumnje kako bi što prije započeli s terapijom.

**Zaključak:** Zbog posljedica kroničnih komplikacija nužno je da se do točne dijagnoze dođe što prije. Ciljane dijagnostičke pretrage i detaljna anamneza uvelike nam mogu pomoći u donošenju brze i točne dijagnoze. Pravovremeno liječenje dovodi do poboljšanja kvalitete života, a time i bolesnikove želje da aktivno sudjeluje u planu liječenja.

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## ■ Diabetes mellitus type 1

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**Introduction with a goal:** Quality of life plays an important role in the patient's experience of the disease and influences the way the patient will face the problems and complications that a certain disease brings. The course of diabetes is marked by the development of chronic complications that, in addition to health, also affect the patient's quality of life. While the highest incidence of type 1 diabetes mellitus is still in early adolescence, it is increasingly diagnosed in adulthood. The onset is usually less acute than in childhood and brings a lower, although still significant, risk of complications and early mortality. In this case report, the goal is to show how suspicion at right time and accurate diagnostics can greatly accelerate the process of accurate diagnosis and the start of treatment. With this approach to treatment, we will reduce complications, extend life expectancy and improve quality of life.

**Case report:** Patient D.Š., 62 years old, non-smoker, previously healthy. He denies diabetes in his family history. He comes to the family doctor's office because of erythema and a wound on his right big toe. When entering the office, I notice that the patient has visibly lost weight. He reported losing about 10 kilograms in the last 8 months, but attributed this to the healthy diet he follows. During the physical examination, he was completely normal, except for erythema with a small bump on the dorsum of the thumb. During the conversation, I tried to find out if he had any other symptoms, such as polyuria and polydipsia, because I suspected that it was possible that he had diabetes mellitus. He said that he had been urinating more frequently lately, but he attributed this to the fact that he had started drinking more fluids. Since the patient came at the end of working hours and was not fasting, I decided not to perform a glucometer, so I ordered a blood test the next day, bandaged the wound on his thumb, and administered amoxicillin with clavulanic acid and metronidazole. The next day, the laboratory results came back, which showed GUK 20.4 mmol/L, cholesterol 7.6, LDL 4.7, triglycerides 12.8, HbA1c 14.0%. Aware of the seriousness of the situation and the long waiting

list for a diabetologist, I decided that the patient would receive the fastest treatment through the emergency room, so I issued a C2 referral. On the same day, due to high HbA1c values and the need to introduce basal insulin, he was examined by a diabetologist. The therapy included metformin 1x500 mg with an increase in optimal intervals to 2x2000 mg, sitagliptin 1x100 mg, insulin degludec 8 days at 10 pm with an increase of 2 days until the target glycemia values were achieved, and atorvastatin 20 mg. After 3 weeks, he comes for a check-up, and now the laboratory values show GUK 7.8 mmol/L, HbA1c 12.4%.

**Discussion:** In this case report, we can see that the patient primarily comes because of a wound on his thumb, which is his biggest problem due to pain when walking. When taking the history, he ignores all other symptoms and attributes them to a new lifestyle. As a family doctor, it is important to know your patient and notice both physical and psychological changes. It is important to choose diagnostic tests that will quickly confirm our suspicions so that we can start therapy as soon as possible.

**Conclusion:** Due to the consequences of chronic complications, it is essential to reach an accurate diagnosis as soon as possible. Targeted diagnostic tests and a detailed history can greatly help us make a faster and more accurate diagnosis. Timely treatment leads to an improvement in the quality of life, and thus the patient's desire to actively participate in the treatment plan.

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## ■ Svrbež kože kod starih

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**Uvod s ciljem:** Svrbež (pruritus) je neugodna senzacija na koži koji izaziva neodoljivu potrebu za češanjem. Suha koža praćena svrbežom jedna je od najčešćih tegoba među osobama starije životne dobi. Kronični svrbež može veoma negativno uticati na kvalitetu života, uzrokujući iritaciju, poremećaje spavanja i depresiju. Cilj rada je da pregledom literature ukaže na ovaj vrlo čest problem starije populacije i značaj njegovog rešavanja.

**Rasprava:** Svrbež je čest simptom koji se može javiti kod svih, ali je najčešći kod osoba starijih od 65 godina. Može se pojaviti čak i nakon blagog dodira, što se naziva aloknesis. Najčešći uzrok je suha koža, koja se može prevenirati korištenjem blagih higijenskih preparata, uljnih kupki i emolijentnih krema s ureom nakon kupanja, te izbjegavanjem vrućih kupki. Ako svrbež ne prestaje unatoč ovim mjerama, potrebno je razmotriti druge uzroke poput parazitarne infekcije, nuspojava lijekova, neuroloških i psihogenih poremećaja, sistemskih bolesti (dijabetes, anemija, bolesti jetre i bubrega, bolesti štitnjače) ili paraneoplastičnih sindroma. Svrbež se javlja na koži sa ili bez lezija. Za postavljanje konačne dijagnoze često je potrebna detaljna dijagnostička obrada, a ponekad i biopsija kože. Senilni pruritus je pojam koji se odnosi na kronični svrbež kod osoba starijih od 65 godina, često bez jasnog uzroka (idiopatski). Pregledom literature se uočava da polovina starije populacije ima kronični svrbež (prevalencija varira od 11% do 78%). Kronični svrbež značajno narušava kvalitetu života, uzrokujući iritaciju, sekundarne infekcije kože zbog češanja, poremećaje spavanja i depresiju. Pogoršanje kvalitete života ekvivalentno je uticaju hroničnog bola. Neki pacijenti s kroničnim svrbežom imaju toliko izraženu depresiju, da pre imaju želju za kraćim životom bez svrbeža, nego duljim s prisutnim simptomima. Termin senilni pruritus je uveden

da se opiše hronični svrbež pacijenata starijih od 65 godina, koji i pored velike učestalosti u ovoj populaciji nije dovoljno proučavan. I dalje nije poznato da li je senilni pruritus poseban entitet ili se odnosi na hronični pruritus. Terapija se sastoji od općih mjera i medikamentoznog liječenja. Opće mjere uključuju adekvatnu higijenu i zaštitu kože, izbjegavanje sintetičke odjeće i odjeće od vune, alkohola i toplih kupki. Neovisno o uzroku svrbeža, suhoća kože pogoršava sve vrste svrbeža, a učinkovito se rješava emolijensima s 5-15% uree. Medikamentozna terapija ovisi o uzroku svrbeža; najčešće se koriste H1-antihistaminici, kortikosteroidi, imunomodulatori, dok su biološki lijekovi još u fazi ispitivanja.

**Zaključak:** Za liječnike je izazov utvrditi točan uzrok svrbeža zbog heterogenosti patogeneze. Pristup svakom pacijentu mora biti individualiziran, jer je svrbež simptom mnogih bolesti s različitim prognozom. S globalnim produljenjem životnog vijeka i starenjem stanovništva, ovaj problem postaje sve veći, stoga su potrebna daljnja istraživanja kako bi se poboljšala kvaliteta života ove sve brojnije populacije.

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## ■ Pruritus in the Elderly

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**Introduction with aim:** Pruritus is an unpleasant skin sensation that elicits an irresistible urge to scratch. Xerosis accompanied by pruritus is among the most common complaints in the elderly. Chronic pruritus significantly diminishes quality of life. This paper aims to highlight this prevalent issue in the elderly population and the importance of its management through a literature review.

**Discussion:** Pruritus is a frequent symptom that can occur in anyone but is most prevalent in individuals over 65 years old. In the elderly, pruritus can be triggered even by a light touch, known as alloknosis, and may represent a serious medical issue involving skin dryness. Xerosis is the most common cause of pruritus in the elderly. Preventive measures include using mild, non-aggressive hygiene products, oil-based baths, emollient creams containing urea post-bathing, and avoiding hot baths. If pruritus persists despite addressing skin dryness, other causes should be considered. Pruritus can present with or without visible skin changes and may be associated with parasitic infections, medication use, neurological and psychogenic disorders, systemic diseases such as diabetes, anemia, liver and kidney diseases, thyroid disorders, paraneoplastic causes, among others. A definitive diagnosis requires thorough diagnostic evaluation, and in some cases, skin biopsy of lesions. Senile pruritus is predominantly idiopathic chronic pruritus. Literature indicates that half of the elderly population experiences chronic pruritus, with prevalence rates ranging from 11% to 78%. Chronic pruritus markedly impairs quality of life, leading to skin irritation, secondary infections from scratching, sleep disturbances, and depression. The impact on quality of life is comparable to chronic pain. Many patients with chronic pruritus report depression so severe that they would prefer a shorter life without

pruritus over a longer life with symptoms. The term "senile pruritus" describes chronic pruritus in patients over 65 years old. Despite its high prevalence, it remains under-researched. It is still unclear whether senile pruritus is a distinct entity or a subset of chronic pruritus. Treatment involves general measures and appropriate pharmacotherapy. General measures include proper skin hygiene and protection, avoiding synthetic and wool clothing, alcohol, and hot baths. Regardless of the pruritus cause, skin dryness exacerbates all types and is effectively managed with emollients containing 5–15% urea. Pharmacotherapy depends on the underlying cause and commonly includes H1-antihistamines, corticosteroids, immunomodulators, with biological agents still under investigation.

**Conclusion:** Determining the exact cause of pruritus is challenging for physicians due to its heterogeneous pathogenesis. An individualized approach is essential, as pruritus is a symptom of various diseases with differing prognoses. With global increases in life expectancy and an aging population, this issue has become more prominent, necessitating further research to enhance the quality of life in this growing demographic.

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## ■ Psihosuport obitelji kod pacijenata oboljelih od demencije

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**Uvod s ciljem:** Demencija je sporo progresivna bolest propadanja intelektualnih i kognitivnih sposobnosti uključujući pamćenje, razmišljanje i sposobnost učenja. Kod sumnje na demenciju u ordinaciji obiteljske medicine ispituje se kognitivni status MiniCog, Minimental i Montreal cognitive assesment testovima. Cilj ovog rada prikazati je kako pomoći obitelji oboljelih pri lakšem nošenju s nastalom situacijom i pružanju oboljelom najbolje skrbi.

**Prikaz slučaja:** Kćer pacijenta dolazi na konzultaciju u ordinaciju očevo liječnika obiteljske medicine, radi dogovora o daljnjim terapijskim mogućnostima. Naime 80-o godišnjem ocu unazad nekoliko mjeseci dijagnosticirana je vaskularna demencija. Pregledom u ordinaciji liječnika obiteljske medicine, učinjenim Minimental testom, postavljena je sumnja na demenciju, te je upućen na daljnju obradu neurologu i psihijatru, čime je dijagnoza potvrđena. Od postavljanja dijagnoze i uvođenja terapije, kći navodi pogoršanje stanja demencije. Navodi kako je u dva navrata otac hitnom medicinskom pomoći upućen psihijatru u hitnu psihijatrijsku ambulantu u dementnoj epizodi. Kći je prilikom konzultacije izrazito zabrinuta radi očevo stanja. Naime otac i majka žive sami i nije sigurna može li se majka samostalno brinuti o očevim sadašnjim potrebama. Prilikom konzultacije pojašnjena je mogućnost kućne njege kao pomoći prilikom obavljanja svakodnevne higijene, te edukacija obitelji o progresiji i tijeku bolesti, te potencijalnim opasnostima i potrebi o stalnom nadzoru bolesnika. Također kćeri je pojašnjeno kako će s vremenom doći do pogoršanja bolesti, te vjerojatno obitelj neće više biti u mogućnosti skrbiti se o ocu i da je dobro razmisliti o adekvatnom smještaju, jer se obitelj u ovoj bolesti i psihički i fizički iscrpljuje. Kućna skrb u početku može biti bolja opcija, a u kasnijem stadiju bolesti bolja opcija postaje dom za starije i nemoćne. Kućna njega i obiteljska skrb su manje stresni za dementnu osobu, ujedno su manji

financijski teret, ali veći psihički i fizički teret za obitelj. Isto tako neadekvatna kućna skrb su potencijalno opasni i za oboljelog i obitelj. U nastavak liječenja uključena je kućna njega radi pomoći prilikom obavljanja svakodnevne higijene, te Centar za socijalnu skrb radi postupka oduzimanja poslovne sposobnosti kako bi se spriječile moguće manipulacije dementne osobe od strane nepoznatih osoba. Obitelji je pojašnjeno kako postupiti prilikom pacijentove uznemirenosti koja je sve češća, koje su fizičke, farmakološke i psihičke metode relaksacije. Pojašnjeno je kako se uznemirenost najčešće javlja prilikom promjene poznate okoline, osjećaja nemoći, nemogućnosti prisjećanja situacija, osoba ili predmeta, uslijed halucinacija i dezorijentiranosti. Iznimno je bitno prilikom takvih situacija ostati smiren, imati razumijevanja i strpljenja. Daljnjom progresijom bolesti obitelj pristaje na smještaj oca u dom za starije i nemoćne radi pružanja adekvatne brige i nadzora.

**Zaključak:** Osim za oboljelog demencija predstavlja veliko opterećenje i za obitelj oboljelog te ih emocionalno i fizički iscrpljuje. Potrebno je osigurati oboljelom i obitelji adekvatnu pomoć prilikom skrbi za oboljelog. Uloga liječnika obiteljske medicine je da kao nositelj skrbi koordinira kućnu njegu, patronažnu službu, palijativnu skrb, Centar za socijalnu skrb i u konačnici Dom za starije i nemoćne.

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## ■ Psychosupport to families in patients with dementia

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**Introduction and aim:** Dementia is a slowly progressive disease of deterioration of intellectual and cognitive abilities including memory, thinking and learning ability. When dementia is suspected in the general practitioners office, the cognitive status is tested with the MiniCog, Minimental and Montreal cognitive assessment tests. The aim of this paper is to show how to help the families of patients to cope with the situation and provide the patients with the best care.

**Case report:** The patient's daughter comes for a consultation at her father's general practitioners doctor's office, in order to consult on further therapeutic options. The 80-year-old father was diagnosed with vascular dementia a few months ago. After an examination at the general practitioners doctor's office, a minimental test was performed, dementia was suspected, and he was referred to a neurologist and psychiatrist for further treatment, which confirmed the diagnosis. Since the diagnosis and the introduction of therapy, the daughter reports a worsening of father's dementia. He states that on two occasions the father was referred to a psychiatrist in an emergency psychiatric outpatient clinic by emergency medical aid in a demented episode. During the consultation, the daughter is extremely worried about her father's condition. Namely, the father and mother live alone and she is not sure if the mother can independently take care of the father's current needs. During the consultation, it was explained the possibility of home care as an aid in performing daily hygiene, as well as educating the family about the progression and course of the disease, as well as potential dangers and the need for constant monitoring of the patient. It was also explained to the daughter that the disease will worsen over time, and the family will probably no longer be able to take care of her father, and that it is good to think about adequate accommodation, because the family is both mentally and physically exhausted by this disease. In the beginning, home care may

be a better option, and in the later stages of the disease, a nursing home becomes a better option. Home care and family care are less stressful for a demented person, they are also less of a financial burden, but a greater mental and physical burden for the family. Likewise, inadequate home care is potentially dangerous for both the patient and the family. In the continuation of the treatment, home care is included to help with daily hygiene, and the Social Welfare Center for the procedure of revocation of business capacity in order to prevent possible manipulations of a demented person by unknown persons. It was explained to the family how to act in the event of the patient's agitation, which is becoming more frequent, what are the physical, pharmacological and psychological methods of relaxation. It was explained that anxiety most often occurs when familiar surroundings change, feelings of helplessness, inability to recall situations, persons or objects, due to hallucinations and disorientation. It is extremely important to remain calm, understanding and patient in such situations. With further progression of the disease, the family agrees to place the father in a nursing home in order to provide adequate care and supervision.

**Conclusion:** In addition to the diseased, dementia is a great burden for the diseased family and exhausts them emotionally and physically. It is necessary to provide the patient and the family with adequate help when caring for the patient. The role of the general practitioner doctor is to coordinate home care, outpatient care, palliative care, the Center for Social Care and, ultimately, the nursing home.

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## ■ ACNES sindrom

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**Uvod s ciljem:** ACNES sindrom (anterior cutaneous nerve entrapment syndrome – hrv. sindrom uklještenja prednjeg kožnog živca) karakteriziran je lokaliziranim kroničnim tupom boli većinom na jednoj strani trbušne stijenke. Nastaje uklještenjem kutanih ogranaka donjih torakoabdominalnih interkostalnih živaca u predjelu lateralnog ruba m. rectus abdominis. Čest je uzrok boli u području abdomena, ali se nerijetko pogrešno dijagnosticira i ostaje neprepoznat.

**Prikaz slučaja:** Pacijentica u dobi 14 godina javila se na pregled u ordinaciju obiteljskog liječnika zbog supraumbilikalnih bolova u abdomenu, grčevita karaktera, u trajanju od 7 dana. Bol je ocijenila s 8-10 na VAS (vizualno-analogni skali) boli (1-10). Bol je bila jača prilikom pokreta. Nije imala mučninu niti je povraćala. Pacijentica je imala stolicu svaka dva dana, uredne konzistencije i bez patoloških primjesa. Pacijentica je bila afebrilna, slabog apetita i uredno je mokrila. Jednake tegobe su se javljale unazad pet godina, dva puta godišnje, zbog čega je u više navrata obrađivana kod specijalista kirurga i gastroenterologa, bez postavljene dijagnoze. Prilikom javljanja boli, od lijekova je uzimala pantoprazol, trospijev klorid i ibuprofen, pri čemu ne dolazi do poboljšanja, a bol kroz nekoliko dana spontano regresira. Dva dana ranije na hitnom prijemu je isključena akutna kirurška bolest. U ordinaciji obiteljske medicine prilikom pregleda abdomen je bio u razini prsnog koša, čujne peristaltike, mekan, bolan na palpaciju u području desnog m. rectus abdominis supraumbilikalno, bezbolan na palpaciju u donjem desnom kvadrantu. Jetra i slezena se nisu palpirale uvećanima. Lumbalna sukusija je obostrano bila negativna. Carnettov znak je bio pozitivan. Postavljena je sumnja na ACNES sindrom te je pacijentica zajedno s uputnim pismom upućena na pregled u hitnu službu. Bolnički učinjen UZV abdomena je bio uredan. Upućena je specijalistu anesteziologu koji je lokalno u područje boli primijenio

injekciju anestetika 2% lidokaina i 4 mg deksametazona nakon čega odmah dolazi do nestanka boli. Anesteziolog se složio da je klinička slika odgovarala ACNES sindromu.

**Rasprava:** ACNES sindrom često ostaje neprepoznat. Uglavnom se javlja kod mladih osoba, češće u žena, ali može se javiti u bilo kojoj dobi i kod oba spola. Bol se većinski javlja jednostrano, češće na desnoj strani abdomena nego na lijevoj (4:1) i 3-4x češće ispod razine pupka nego iznad. Područje najjače boli je obično lokalizirano u području lateralnog dijela m. rectus abdominis u promjeru od par centimetara i pojačava se na dodir. Carnettov test koji se ispituje podizanjem glave i ramena iz ležećeg položaja čime se napinju trbušni mišići te upućuje na bol koja ima ishodište u trbušnoj stijenci je većinski pozitivan. Dijagnoza se postavlja temeljem anamneze i fizikalnog pregleda, dok se ostala dijagnostika radi zbog isključivanja drugih uzroka. Liječi se injekcijama lokalnog anestetika i kortikosteroida pri čemu dolazi do trenutnog popuštanja boli i u oko 20% pacijenata neće doći do ponovne pojave boli. U refraktornim slučajevima liječenje je kirurški.

**Zaključak:** Uzimajući u obzir visoku incidenciju ACNES sindroma te česte pogreške u postavljanju dijagnoze i liječenju, ključno je razmotriti ovaj sindrom kao mogući uzrok abdominalnih bolova, kako bi se izbjegle nepotrebne dijagnostičke pretrage uz pravovremeno i adekvatno liječenje pacijenata.

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## Hereditarna hemokromatoza

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**Uvod s ciljem:** Aminotransferaze, alanin aminotransferaza (ALT) i aspartat aminotransferaza (AST) vrlo su osjetljivi pokazatelji akutnog jetrenog oštećenja. Povišene vrijednosti aminotransferaza pronalazimo kod nealkoholne masne bolesti jetre, alkoholne bolesti jetre, infekcija, toksičnih oštećenja uzrokovanih lijekovima te u nešto rjeđim slučajevima poput autoimunih bolesti jetre, Wilsonove bolesti, manjka  $\alpha$ 1-antitripsina te hereditarne hemokromatoze. Cilj ovog prikaza slučaja je prikazati važnost uloge liječnika obiteljske medicine u prepoznavanju uzroka povišenih aminotransferaza te upućivanja na žurniju daljnju obradu.

**Prikaz slučaja:** Pacijentica u dobi od 52 godine javila se u ambulantu liječnika obiteljske medicine zbog kroničnog umora unazad 2 mjeseca, druge tegobe je negirala. Upućena je na vađenje krvi. U laboratorijskom nalazu bili su vidljivi povišeni jetreni enzimi, ALT 689 U/L, AST 311 U/L, GGT 223 U/L, ALP 92 U/L (uredna vrijednost), te povišen ukupni bilirubin 22  $\mu$ mol/L, Fe 43,6  $\mu$ mol/L i UIBC 11  $\mu$ mol/L. Pacijentica puši unazad 30 godina, negira konzumaciju alkohola, operirala žučni mjehur prije 6 godina, nema kroničnu terapiju. Pregledom abdomena utvrđeno je da je mekan, bezbolan na palpaciju te bez organomegalije. Koža i vidljive sluznice bile su urednog izgleda. Pacijentica je upućena na hitnu gastroenterološku obradu gdje su joj učinjene još dodatne laboratorijske pretrage. Serologija na autoimuni hepatitis, OGTT, bakar u 24h urinu i lipidogram došli su urednih vrijednosti. Izdvajala se povišena vrijednost feritina 1382  $\mu$ g/L. Učinjen je MR jetre koji je uputio na znakove blaže primarne hemokromatoze. Dodatno, pacijentica je upućena na genotipizaciju HFE gena čime je potvrđena dijagnoza hereditarne hemokromatoze. Indicirane su venepunkcije nakon kojih se pacijentica odmah osjećala bolje, a laboratorijske vrijednosti polako su se počele vraćati u normalu.

**Rasprava:** Postoje 4 tipa nasljedne hemokromatoze od kojih svi uključuju mutacije koje ometaju sposobnost tijela da inhibira apsorpciju željeza. Zbog preopterećenja željezom dolazi do bolesti jetre koja vodi do ciroze, pigmentacije kože, dijabetesa, artropatije, erektilne disfunkcije te zatajenja srca. Genetsko testiranje indicirano je kod povišenih vrijednosti feritina i saturacije transferrina kako bi se dokazala dijagnoza. Genetsko testiranje i probir treba razmotriti kod članova uže rodbine. Liječenje se provodi venepunkcijom. Kada se postignu vrijednosti željeza u serumu unutar referentnih vrijednosti, venepunkcije se mogu raditi povremeno kako bi se razine feritina održavale između 50 i 100 ng/ml.

**Zaključak:** Postoje brojni uzroci povišenih jetrenih aminotransferaza. Važno je prepoznati vrijednosti aminotransferaza koje zahtijevaju žurniju obradu te pronaći njihov uzrok kako bi se liječenje započelo što ranije te spriječio razvoj komplikacija.

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## ■ Hereditary hemochromatosis

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**Introduction with aim:** Aminotransferases, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are very sensitive indicators of acute liver damage. Elevated aminotransferase values are found in nonalcoholic fatty liver disease, alcoholic liver disease, infections, toxic damage caused by drugs, and in somewhat rarer cases such as autoimmune liver diseases, Wilson's disease,  $\alpha$ 1-antitrypsin deficiency and hereditary hemochromatosis. The aim of this case report is to show the importance of the role of family physicians in identifying the cause of elevated aminotransferases and referring patients for more urgent further treatment.

**Case report:** A 52-year-old patient came to the family physician's office because of chronic fatigue for the past 2 months, she denied any other complaints. She was referred for blood sampling. The laboratory results showed elevated liver enzymes, ALT 689 U/L, AST 311 U/L, GGT 223 U/L, ALP 92 U/L (normal value), and elevated total bilirubin 22  $\mu$ mol/L, Fe 43, 6  $\mu$ mol/L and UIBC 11  $\mu$ mol/L. The patient has been smoking for 30 years, denies alcohol consumption, had gall bladder surgery 6 years ago, has no chronic therapy. Examination of the abdomen reveals that it is soft, painless on palpation and without organomegaly. The skin and visible mucous membranes had a neat appearance. The patient was sent to emergency gastroenterological treatment, where additional laboratory tests were performed. Serology for autoimmune hepatitis, OGTT, copper in 24-hour urine and lipidogram came with normal values. The elevated ferritin value of 1382  $\mu$ g/L stood out. An MRI of the liver was performed, which indicated signs of milder primary hemochromatosis. In addition, the patient was referred for genotyping of the HFE gene, which confirmed the diagnosis of hereditary hemochromatosis. Venipuncture was indicated, after which the patient immediately felt

better, and the laboratory values slowly began to return to normal.

**Discussion:** There are 4 types of hereditary hemochromatosis, all of which involve mutations that interfere with the body's ability to inhibit iron absorption. Due to iron overload, liver disease occurs, which leads to cirrhosis, skin pigmentation, diabetes, arthropathy, erectile dysfunction and heart failure. Genetic testing is indicated, when ferritin values and transferrin saturation are elevated, to confirm the diagnosis. Genetic testing and screening should be considered in close relatives. Treatment is carried out by venipuncture. When serum iron values within the reference range are achieved, venipuncture can be performed periodically to maintain ferritin levels between 50 and 100 ng/ml.

**Conclusion:** There are numerous causes of elevated liver aminotransferases. It is important to recognize aminotransferase values that require more urgent treatment and to find their cause in order to start treatment as early as possible and prevent the development of complications.

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## ■ Kronični suhi kašalj u podlozi alergijske astme - prikaz slučaja

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**Uvod s ciljem:** Kronični suhi kašalj vrlo je čest razlog dolaska u ambulantu obiteljske medicine. Uzroci istog mogu biti mnogobrojni: od alergijskih tegoba gornjeg ili donjeg dijela respiratornog sustava, posljedica ranije preboljelih respiratornih infekcija (npr. post-COVID), nuspojava na ACE inhibitore, malignoma respiratornog trakta ili drugih sijela do kronične astme, koja u blažim oblicima često ostaje neprepoznata i samim time neadekvatno liječena. Astma se definira kao kronična upala donjih dišnih puteva različite etiologije koja se klinički očituje nekim od sljedećih simptoma: zaduhe, sipnje ("zviždanja"), kratkog daha, kroničnog kašlja i stezanja u prsima, a patofiziološki određenim ograničenjem protoka zraka u dišnim putovima (1). Među brojnim podtipovima najčešća je alergijska astma, u kojoj je kronična upala potaknuta alergijskom preosjetljivošću, a postoji još i tzv. tusigeni ekvivalent astme koji se klinički manifestira samo kroničnim kašljem, bez osjećaja dispneje.

**Prikaz slučaja:** 28-godišnja bolesnica javlja se početkom proljeća u ambulantu obiteljske medicine zbog suhog kašlja koji traje unazad 3 tjedna te blažeg subjektivnog osjećaja kratkog daha, bez tipične zaduhe ili tahipneje. Tegobe su započele kratkotrajnom respiratornom virozom koja je trajala prvih nekoliko dana, ali se kašalj poslije progresivno pojačavao. Navodi da je slične simptome imala i ranije i to uglavnom sezonski, u jesen i proljeće, a ponekad i u drugim dijelovima godine. Najizraženija "egzacerbacija", bila je nakon preboljenja covid 2021. Tada je učinjena i spirometrija koja je bila uredna. Također je ranije ordiniran desloratadin i montelukast koji su pokazali povoljan učinak. U kliničkom statusu pri dolasku imala je uredno ždrijelo, bez limfadenopatije, prohodan nos i blago pooštren šum disanja. Laboratorijski nalazi bili su uredni te je zbog sumnje na alergijsku etiologiju tegoba uveden flutikazon u inhalaciji 2x1 udah tijekom mjesec dana te montelukast. Terapija je dovela do regresije simptoma, no iste godine u jesen, pacijentica se javlja u ambulantu zbog osjećaja otežanog disanja u posljednje vrijeme, koji je povremeno praćen osjećajem stezanja i probadanja u prsima (neovisno o naporu). U statusu obostrano bazalno pooštreno disanje, ali bez wheezinga te je ponovo

ordiniran flutikazon, montelukast i salbutamol do 4x1 udah p.p. U međuvremenu je učinjena i spirometrija (FVC 103%, FEV1 97%, TI 79, PEF 92%, FEF 50%) s bronhodilatacijskim testom: FEV1 + 430 ml (+ 11%). Premda je spirometrija bila uredna, test je bio pozitivan, čime je dokazana astma, a daljnjom pulmološkom obradom dokazana je i alergijska preosjetljivost na grinje kućne prašine. U terapiju je tada uveden ciklezonid 2x1 udah uz salutamol, no zbog alergijske reakcije koja se dovela u vezu s ciklezonidom (urtikarija kože lica, crvenilo i svrbež), isti je zamijenjen s fiksnom kombinacijom beklometazona i formoterola, nakon čega je pacijentica osjećala subjektivno znatno poboljšanje.

**Rasprava:** Dugotrajni suhi kašalj patologija je koja se često susreće u obiteljskoj medicini. Ponekad je teško otkriti točan uzrok i postići za pacijenta zadovoljavajuć terapijski učinak, no potrebno je, na temelju anamnestičkih podataka i kliničke slike, razmišljati diferencijalno-dijagnostički te doći do pravog uzroka kašlja kako bi se moglo započeti s prikladnom terapijom. Alergijska astma jedan je od češće zastupljenih uzroka navedene problematike, no često ostaje neprepoznata i sukladno tome, neadekvatno liječena, pogotovo ako se radi o blažem kliničkom obliku. Ipak, pravovremeno postavljanje dijagnoze i započinjanje s kortikosteroidnom terapijom pacijentu može značajno olakšati simptome i postići dobar terapijski učinak. Stoga je pacijentice sa sumnjom na astmu potrebno pravovremeno uputiti na dijagnostičku obradu kako bi se sumnja potvrdila te započelo s ciljanom terapijom.

**Zaključak:** Inhalacijski kortikosteroidi, sami ili u kombinaciji s bronhodilatatorom, ovisno o tipu i težini, osnova su za liječenje astme, a za dijagnozu ponekad nije dovoljan samo nalaz spirometrije, već je potrebno učiniti i bronhodilatacijski test. LOM imaju ključnu ulogu u prepoznavanju pacijenata s astmom i upućivanju na specijalističku obradu kako bi se započela ciljana terapija te prevenirao razvoj simptoma i pogoršanje kliničke slike. Postavljanje ispravne dijagnoze i adekvatna terapija mogu značajno reducirati simptome astme, poboljšati kvalitetu života pacijenata te smanjiti mogućnost komplikacija.

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## ■ Chronic dry cough due to allergic asthma - case report

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**Introduction with aim:** Chronic dry cough is very common reason for visiting a family medicine clinic. There can be numerous causes of this type of cough: from allergic hypersensitivity of the upper or lower part of the respiratory system, previous respiratory infections (e.g. post-COVID syndrome), side effects of ACE inhibitors, malignancies in the respiratory tract or in the other areas, or chronic asthma, which in mild forms often remains unrecognized and thus inadequately treated. Asthma is defined as chronic inflammation in lower respiratory tract due to various etiology, which is clinically manifested by some of the following symptoms: dyspnea, wheezing, shortness of breath, chronic cough or tightness in the chest and pathophysiologically followed by obstructed air flow in the lower respiratory tract. Among the many subtypes, the most common one is allergic asthma, in which chronic inflammation is triggered by allergic hypersensitivity. Furthermore, there also exists so-called tussogenic equivalent of asthma, which is clinically manifested only by a chronic cough, without a feeling of dyspnea.

**Case Presentation:** A 28-year-old patient presents to the family medicine doctor in the beginning of spring complaining about dry cough that has been lasting for the past 3 weeks, followed by subjective feeling of shortness of breath, without typical dyspnea or tachypnea. These symptoms had started with a short-term respiratory virus that lasted for the first few days, but the cough progressively intensified afterwards. She states that she had similar symptoms earlier before, mostly seasonally, in autumn and spring, but sometimes in the other parts of the year, also. The worst "exacerbation" was after recovering from covid in 2021. Spirometry was done, which was unremarkable. Both desloratadine and montelukast had also been prescribed earlier, which showed a beneficial effect. In terms of clinical status upon arrival, she had a normal pharynx, no lymphadenopathy, a clear nose and slightly increased breath sounds. The laboratory findings were normal, so due to the suspicion of an allergic etiology of the complaints, fluticasone 2 x 1 inhalation for a month and montelukast were introduced. The therapy led to a regression of the symptoms, but in the autumn of the same year, the patient came to the clinic because of feeling difficulty breathing, which was occasionally accompanied by a feeling of tightness and stabbing

in the chest (regardless of effort). In the clinical status, bilateral basal breathing sounds were increased, but without wheezing. Fluticasone, montelukast and salbutamol were again prescribed to reduce the symptoms. In the meantime, spirometry (FVC 103%, FEV1 97%, TI 79, PEF 92%, FEF 50%) with a bronchodilation test was also performed: FEV1 + 430 ml (+ 11%). The test was positive, which proved asthma diagnosis, and further pulmonology treatment proved allergic hypersensitivity to house dust mites. Ciclesonide 2x1 inhalation with salbutamol was then introduced in therapy, but due to allergic reaction associated with ciclesonide (facial skin urticaria, redness and itching), it was replaced by fixed combination of beclomethasone with formoterol, after which the patient subjectively felt much better.

**Discussion:** Long-term dry cough is a symptom often encountered in family medicine. Sometimes it is difficult to find the exact cause and achieve adequate therapeutic effect, but it is necessary - based on anamnestic data and the clinical presentation - to think between different possible diagnosis to find the real cause of cough in order to start appropriate therapy in time. Allergic asthma is one of the most common causes of chronic cough, but it often remains unrecognized and, accordingly, inadequately treated, especially if it appears in mild clinical form. However, timely diagnosis and initiation of corticosteroid therapy can significantly relieve symptoms and achieve appropriate therapeutic effect. Therefore, patients with suspected asthma should be promptly referred to pulmonological diagnostic procedures in order to confirm the diagnosis and start targeted therapy.

**Conclusion:** Inhaled corticosteroids, alone or combined with bronchodilator (depending on the type and severity), are crucial for asthma treatment. Family physicians play a key role in identifying patients with asthma and referring them to specialist treatment in order to initiate targeted therapy and prevent worsening of the symptoms or deterioration in the clinical status. For diagnosis sometimes not only the spirometry findings are sufficient, but a bronchodilation test is also necessary. Correct diagnosis and adequate therapy can significantly reduce asthma symptoms, improve patients' quality of life and reduce the possibility of complications.

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## ■ Od prvog simptoma do dijagnoze: priče pacijenata o dijagnosticiranju raka u primarnoj zdravstvenoj zaštiti

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**Uvod s ciljem:** Kašnjenja u dijagnosticiranju raka značajno utječu na preživljavanje i kvalitetu života. Ta kašnjenja često proizlaze iz čimbenika povezanih s pacijentima, zdravstvenim radnicima, zdravstvenim sustavima i širim društvenim utjecajima. Naše istraživanje koristi narativni pristup kako bi istražilo iskustva pacijenata tijekom njihova dijagnostičkog procesa. Ova metoda pripovijedanja pruža jedinstveni uvid u osobna iskustva, otkrivajući prepreke i prilike za unapređenje zdravstvene zaštite.

**Ispitanici i metode:** Ova kvalitativna studija uključuje odrasle pacijente ( $\geq 18$  godina) kojima je dijagnosticiran rak u europskim zemljama, trenutno fokusirana na pilot-podatke iz Grčke, Italije, Makedonije i Švedske. Sudionici se pozivaju putem pacijentskih udruga, društvenih mreža i timova za skrb o pacijentima s rakom. Priče o dijagnostičkom procesu prikupljaju se na dobrovoljnoj osnovi fleksibilnim metodama, uključujući pisane narative, audio ili videozapise, intervjue ili strukturirane mape iskustva. Podaci će se analizirati klasičnom metodom utemeljene teorije, koja uključuje iterativno kodiranje za identificiranje kategorija i koncepata. Priče će se uspoređivati kako bi se razvila glavna kategorija, a nakon postizanja saturacije, rezultati će se kontekstualizirati postojećom literaturom za predstavljanje konačne utemeljene teorije.

**Rezultati:** Do trenutka pisanja prikupljen je mali broj priča iz pilot-zemalja, ali one još nisu analizirane.

**Zaključak:** Ovo istraživanje ima za cilj pružiti uvid u perspektive pacijenata o dijagnostičkom procesu raka i generirati ideje za poboljšanje pravovremene dijagnoze raka. Korištenjem pripovijedanja želimo identificirati prepreke i olakšavatelje tijekom dijagnostičkog procesa, postavljajući temelje za daljnja istraživanja o perspektivama pacijenata u medicinskim studijama.

Osim toga, ovaj rad će doprinijeti vrijednim uvidima o kašnjenjima povezanim s pacijentima u dijagnostici raka, potencijalno informirajući šira istraživanja i napore za poboljšanje pravovremene dijagnoze.

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## ■ From First Symptom to Diagnosis: Patient Stories about Cancer Diagnosis in Primary Care

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**Introduction:** Delays in cancer diagnosis significantly impact survival and quality of life. These delays often result from factors linked to patients, healthcare providers, healthcare systems, and broader community and societal influences. Our research uses a storytelling approach to explore patients' experiences during their cancer diagnostic journey. This narrative method provides unique insights into personal experiences, uncovering barriers and opportunities to improve care delivery.

**Sample and methods:** This qualitative study recruits adult patients ( $\geq 18$  years) diagnosed with cancer across European countries, currently focusing on pilot data from Greece, Italy, Macedonia, and Sweden. Participants are invited through patient associations, social media, and cancer care teams. Stories of the cancer diagnosis journey are collected on a voluntary basis using flexible methods, including written narratives, audio or video recordings, interviews, or a structured journey mapping tool. The data will be analyzed using classic grounded theory, involving iterative coding to identify emerging categories and concepts. Stories will be compared to develop a main category, and once saturation is achieved, the findings will be contextualized with existing literature to present a final grounded theory.

**Results:** At the time of writing, a small number of stories have been collected from the pilot countries, but these have not yet been analyzed.

**Conclusion:** This research aims to provide insights into patients' perspectives on the cancer diagnostic process and to generate ideas for improving timely cancer diagnosis. By using storytelling, we aim to identify barriers and facilitators in the diagnostic journey, laying the foundation for further research on patient perspectives in medical studies. Additionally, this work will contribute valuable insights into patient-related

delays in cancer diagnostics, potentially informing broader research and efforts to improve timely diagnosis.

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## ■ Slabost noge kao prvi simptom amitrofične lateralne skleroze

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**Uvod** Amiotrofična lateralna skleroza (ALS) je progresivna neurodegenerativna bolest gornjeg i donjeg motornog neurona, karakterizirana progresivnom mišićnom slabosti koja postepeno zahvaća sve mišiće. Prvi znak bolesti može biti asimetrična slabost i atrofija mišića ekstremiteta ili bulbarni simptomi. Incidencija ALS-a u Europi je 1.5 – 4.7/100.000, najčešće se pojavljuje u dobi od 60 do 75 godina. Zbog porasta incidencije ALS-a i brze progresije bolesti, neophodna je žurna dijagnostika i terapija ovih bolesnika. Cilj rada je bio prikazati izazov dijagnosticiranja i liječenja mlađe odrasle bolesnice s ALS-om od strane liječnika obiteljske medicine (LOM-a).

**Prikaz slučaja** 26-godišnja bolesnica se javila na pregled LOM-u kada je 4 mjeseca od prometne nezgode primijetila slabost desne noge uz miaglju. U statusu je bila bez neuroloških ispada i urednih laboratorijskih parametara. Nakon 2 mjeseca javlja se na pregled zbog slabosti desne ruke, disfagije i otežanog govora. Pregledom se utvrdio povišen tonus desne noge, u pozicijsko-supinacijskom položaju desna je ruka tonula kao i desna noga u Mingazzinijevom položaju. Žurno je upućena neurologu na daljnju obradu. EMNG ekstremiteta pokazao je vrlo tešku aksonalnu motornu neuropatiju u više spinalnih regija koji su upućivali na bolest motornih neurona. Nakon kompletne neurološke obrade isključene su druge bolesti, nalaz genetskog testiranja na bolest motornog neurona je bio negativan te je postavljena dijagnoza ALS-a. Bolesnica je liječena riluzolom, vitaminskim, visokoenergetskim i proteinskim pripravcima uz fizikalnu terapiju koja se nakon pogoršanja stanja bolesnice provodila u kući. Bolesnica je cijelo vrijeme bila pod kontrolom neurologa i LOM-a (ambulantno i kroz kućne posjete). Osim skrbi za samu bolesnicu, LOM je savjetovao obitelj i pružao im psihološku podršku. Unatoč multidisciplinarnom pristupu, bolesnica je preminula uslijed respiratorne insuficijencije 12 mjeseci od pojave prvog simptoma.

**Rasprava** ALS je brzoprogresivna, fatalna neurološka bolest motornih neurona mozga, moždanog debla i kralježnične moždine. S napretkom bolesti bolesnici razvijaju kliničku sliku kombinacije znakova oštećenja gornjeg (gubitak fine motorike) i donjeg motornog neurona (mišićna slabost) te bulbarnih simptoma (dizartrija, disfagija). Na ALS možemo posumnjati u bolesnika s brzim razvojem spastičke i atrofične slabosti bez ispada osjeta. Ne postoji specifični dijagnostički biomarker pa se dijagnoza ALS-a postavi u prosjeku gotovo 12 mjeseci od pojave simptoma na temelju anamneze, neurološkog pregleda, elektrofizioloških ispitivanja (elektromioneurografije), slikovnih pretraga (MR mozga) i laboratorijskih testova s ciljem isključivanja stanja koja mogu imitirati ALS. Etiopatogeneza ALS-a je nepoznata te specifično liječenje nije moguće. Provode se simptomatski i suportivni postupci, a jedini lijek koji se koristi u liječenju je riluzol. Svrha terapije je ublažiti komplikacije i unaprijediti kvalitetu života oboljelog. Multidisciplinarni pristup je važan za bolesnika - o njemu brinu liječnici obiteljske medicine, neurolozi, farmakolozi, specijalisti palijativne medicine, fizioterapeuti, radni i govorni terapeuti, psiholozi, psihijatri, nutricionisti, socijalni radnici i medicinske sestre s iskustvom palijativne skrbi.

**Zaključak** ALS je neizlječiva bolest kratkog tijeka, gdje LOM može ublažiti neke od simptoma i time pomoći oboljelom i njegovoj obitelji. Skrb o pacijentu tijekom posljednjeg stadija bolesti važni su aspekti rada LOM-a, kao i cijelog multidisciplinarnog tima koji sudjeluje u liječenju oboljelih od ALS-a.

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## ■ Leg weakness as the first symptom of amyotrophic lateral sclerosis

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**Introduction** Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease of the upper and lower motor neurons, characterized by progressive muscle weakness that gradually affects all muscles. The first sign of the disease may be asymmetric weakness and atrophy of the muscles of the extremities or bulbar symptoms. The incidence of ALS in Europe is 1.5 – 4.7/100,000, it most often appears between the ages of 60 and 75. Due to the increase in the incidence of ALS and the rapid progression of the disease, urgent diagnosis and therapy of these patients is necessary.

**The aim** The aim of the paper was to present the challenge of diagnosing and treating a young adult patient with ALS by a family medicine doctor (physician).

**Case report** A 26-year-old patient came for an examination at the physician when, 4 months after the traffic accident, she noticed weakness in her right leg along with myalgia. Her status was without neurological symptoms and normal laboratory parameters. After 2 months, weakness of the right hand, dysphagia and difficulty speaking appeared, and she was urgently referred to a neurologist for further treatment. It has a negative heredity for neuromuscular diseases. The examination revealed an increased tone of the right leg, in the positional-supination position the right arm sank, as did the right leg in the Mingazzini position. EMNG of the extremities showed very severe axonal motor neuropathy in multiple spinal regions suggestive of motor neuron disease. Furthermore, the patient was hospitalized at the Clinic for Neurology of KBC Rijeka, after a complete neurological examination, other diseases were excluded, the result of genetic testing for motor neuron disease was negative, and a diagnosis of ALS was made. The patient was treated with riluzole, vitamin, high-energy and protein preparations, and she stayed at the Department of Physical and Rehabilitation Medicine for physical therapy. Later, physical therapy was carried out at home, and the patient was under the control

of a neurologist and physician, on an outpatient basis and through home visits. Physician advised the families and provided them with psychological support. The patient died due to respiratory failure 12 months after the onset of the first symptom.

**Discussion** ALS is a rapidly progressive, fatal neurological disease of the motor neurons of the brain, brainstem and spinal cord. As the disease progresses, the patient develops a clinical picture of a combination of signs of upper (loss of fine motor) and lower motor neurons (muscle weakness) and bulbar symptoms (dysarthria, dysphagia). ALS can be suspected in a patient with rapid development of spastic and atrophic weakness without loss of sensation. There is no specific diagnostic biomarker, so the diagnosis of ALS is made on average almost 12 months after the onset of symptoms based on history, neurological examination, electrophysiological tests (electromyoneurography), imaging tests (MR of the brain) and laboratory tests - excluding conditions that can mimic ALS. The etiopathogenesis of ALS is unknown and specific treatment is not possible. Symptomatic and supportive procedures are carried out, and the only drug used in the treatment is riluzole. The purpose of therapy is to alleviate complications and improve the patient's quality of life. A multidisciplinary approach is important for the patient - he is cared for by family medicine doctors, neurologists, pharmacologists, palliative medicine specialists, physiotherapists, occupational and speech therapists, psychologists, psychiatrists, nutritionists, social workers and nurses with palliative care experience.

**Conclusion** ALS is an incurable disease of a short course, where physician can alleviate some of the symptoms and thereby partly help the patient and his family. Patient care during the last stage of the disease is an important aspect of the work of physician, as well as of the entire multidisciplinary team involved in the treatment of ALS patients.

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