

Zašto neki političari, novinari i zdravstveni djelatnici zagovaraju cijepljenje djece protiv covid-19?

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Sažetak

U hrvatskim je medijima sve više govora o cijepljenju djece protiv covid-19, unatoč maloj ulozi djece u prijenosu novog koronavirusa i njihovom malom riziku od teških simptoma, postojanju drugih oblika prevencije, činjenici da klinička ispitivanja nisu dovršena, raznih problema u provedenim ispitivanjima i rastućoj zabrinutosti oko sigurnosti cjepiva i mogućih štetnih učinaka. Cilj je ovog kratkog pregleda odabrane znanstvene literature potaknuti kvalitetnu javnu raspravu prije donošenja potencijalno ishitrenih odluka.

Ključne riječi: medicinska etika; zaraza; nuspojava; medicinska metodologija; pedijatrija; bioetika

1. Uvod

Nalazimo se u 22. mjesecu otkako je Svjetska zdravstvena organizacija proglasila pandemiju bolesti covid-19 [1]. Podaci trenutno sugeriraju da pacijenti dijagnosticirani s covid-19 imaju relativno nizak rizik od razvijanja srednjeg ili teškog oblika bolesti te da je dijagnoza covid-19 povezana s niskom stopom smrtnosti [2–6]. Ipak, rizik od razvijanja teškog oblika bolesti i stopa smrtnosti povećani su u određenim dijelovima populacije kao što su starije osobe i osobe s komorbiditetima kod kojih covid-19 može dovesti do pogoršanja postojećih kardiovaskularnih, metaboličkih, dišnih i drugih poremećaja [7–17], a istraživanja pokazuju da covid-19 može biti povezan s pojavom raznih patoloških procesa [18–31]. Unatoč covid-19, razne druge medicinske pojave imaju dalekosežne posljedice za javno zdravstvo kao što su srčane bolesti, moždani udar, rak, kronične opstruktivne plućne bolesti, prometne i druge nesreće, dijabetes, depresija, alkoholizam, pretilost, kratkovidnost, lošiji socio-ekonomski status itd. [32–47]. Podaci trenutno pokazuju i da je smrtnost od covid-19 oko sto puta manja od smrtnosti od španjolske gripe [48].

2. Cijepljenje djece protiv COVID-19

2.1. Cjepiva bez presedana

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Trenutno se u Hrvatskoj provodi velika i naizgled žurna kampanja četirima cjepivima proizvođača Pfizer-BioNTech, Moderna, Janssen (Johnson & Johnson) i AstraZeneca. Proizvodi Pfizera i Moderne tzv. su mRNA-cjepiva. Ukratko, ta cjepiva koriste lipidne nanočestice u kojima je smješten onaj isječak ribonukleinske kiseline (RNK) koji kodira tzv. šiljasti protein (eng. *spike protein*) virusa SARS-CoV-2. Laičkim riječima, ljudski organizam virusnu RNK iz mRNA-cjepiva pri dolasku u stanicu prepoznaje kao ljudsku RNK, omogućujući joj tako da prenese uputu ljudskoj stanici da proizvodi šiljaste proteine virusa SARS-CoV-2, čemu slijedi imunosni odgovor organizma na navedene šiljaste proteine i, u očekivanom raspletu, stvaranje antitijela protiv tog specifičnog šiljastog proteina. Cjepiva proizvođača Janssen i AstraZeneca koriste drugačiju tehnologiju temeljenu na tehnologiji vektora virusne DNK u kojoj se koristi oslabljeni adenovirus (virus koji je jedan od uzročnika prehlade) pri čemu je genom adenovirusa genetski modificiran uvećanjem za isječak DNK-a koji kodira već spomenuti šiljasti protein virusa SARS-CoV-2. Dakle, u obama tipovima kandidata za cjepivo radi se o injekciji genetskog materijala virusa SARS-CoV-2 koji kodira spomenuti šiljasti protein i cilj je da ljudske stanice počnu proizvoditi te šiljaste proteine [49–53].

Niz je pojava vezano uz navedena cjepiva bez presedana. Ovo je:

- (1) prvi pokušaj da se koristi tehnologija mRNA-cjepiva za borbu protiv nekog uzročnika zaraze,
- (2) prvi put da se neki pripravak koristi kao cjepivo samo na temelju preliminarnih analiza o učinkovitosti,
- (3) prvo cijepljenje za koje ne postoje jasni pokazatelji o smanjenju zaraza, prenosivosti i smrtnosti,
- (4) prvi put da zdravstveni djelatnici javnosti govore da su nuspojave očekivane i/ili dobre,
- (5) prva uporaba polietilenskog glikola u injekciji,
- (6) prvo cijepljenje protiv nekog koronavirusa,
- (7) prva injekcija genetski modificiranih polinukleotida u općoj populaciji
- (8) i prvi put da je Moderna na tržište uspjela izbaciti bilo koji proizvod [49].

U nekim dijelovima svijeta već se naveliko krenulo i s cijepljenjem djece (< 17 god.) [54–59], a najavljuje se i cijepljenje novorođenčadi i djece mlađe od pet godina [60, 61]. Negdje se već najavljuje obavezno cijepljenje djece protiv covid-19 [62, 63]; u Austriji trenutni prijedlog zakona s kojim se slažu i vladajuće i oporbene političke stranke predviđa obvezu cijepljenja starijih od 13 godina od veljače 2022. [64], a raspravlja se i o uvođenju obaveze cijepljenja i za mlađe [65]; u Njemačkoj se raspravlja o uvođenju trajnih potkožnih “čipova” kako bi se “uopće znalo tko se nije cijepio” [66–68]. Neke institucije predviđaju da će proglašena pandemija trajati još 5–10 godina te da će biti potrebno kontinuirano cijepljenje, možda i svaka tri do četiri mjeseca [69–72]. Nedavno su i neki hrvatski političari, novinari i zdravstveni djelatnici počeli govoriti o cijepljenju djece, pri čemu se većinom susrećemo s pozivima na cijepljenje djece ili pozitivnim stavovima o cijepljenju djece. Primjerice, pedijatričar Iva Mihajlović Štefanović je u informativnoj emisiji HRT-a već u listopadu 2021. dala svoju preporuku o cijepljenju djece, bez jasnih argumenata, i izjavila “Ja ću i svoje dijete cijepiti.” [73] dok je trenutni predsjednik Zoran Milanović, također bez jasnih argumenata, izjavio “Djeca moraju biti u školi i djeca bi se trebala cijepiti.”, također u listopadu 2021. [74]. U naizgled sudbonosnom se listopadu i novinarka portala *Index.hr* Martina Pauček Šljivak pozabavila temom cijepljenja djece pitajući se u naslovu članka “Može li nas spasiti cijepljenje djece?” [75]. Ne nedostaju listopadni blagoslovi Krunoslava Capka i Alemke Markotić, dviju trenutno prominentnih ličnosti u hrvatskoj javnosti [75]. Ovakav način raspravljanja u javnosti o osjetljivom pitanju kao što je inokulacija

djece kandidatima za cjepiva za koje postoji niz ozbiljnih, a neodgovorenih pitanja začuđujući te je bio poticaj za istraživanje (odabrane) literature i pisanje teksta koji čitate.

Unatoč postojanju ozbiljnih pitanja u vezi učinkovitosti i sigurnosti trenutnih kandidata za cjepivo protiv covid-19, hrvatski mediji u svojem izvještavanju gotovo uvijek ističu pozitivne učinke trenutnih kandidata, zanemarujući ključna pitanja i zanemarujući mnoštvo istraživanja i rasprava objavljenih u znanstvenoj literaturi. To sugerira da mnogi hrvatski građani također nisu upoznati s informacijama iz navedenih znanstvenih publikacija budući da novinarstvo djeluje kao posrednik između znanstvenika i ostalih koji ne mogu samostalno čitati i razumjeti često zamršene i komplicirane znanstvene tekstove. Razlog jednostranosti medijskog izvještavanja i raspravljavanja zdravstvenih djelatnika i političara nije jasan. I od novinara i zdravstvenih djelatnika očekivalo bi se da će u raspravama o zdravstvenim temama nastojati obuhvatiti sve postojeće informacije na temelju kojih će donijeti sintetski zaključak. Vrijeme je u trenutno proglašenoj pandemiji da se rasprave počnu temeljiti na jasnim i detaljnim informacijama, informacijama iz različitih i brojnih izvora, provjerljivim informacijama te informacijama koje na ovaj ili onaj način zadovoljavaju visoke znanstvene kriterije.

U nastavku teksta osvrnut ću se na neka ključna i ozbiljna pitanja u vezi s učinkovitosti i sigurnosti trenutnih kandidata za cjepivo. U kratkim riječima, pitanja se svode na:

- (1) činjenicu da djeca ograničeno sudjeluju u prijenosu novog koronavirusa i nemaju izražen rizik od teškog oblika bolesti i smrti,
- (2) činjenicu da postoje i drugi oblici prevencije od zaraze novim koronavirusom,
- (3) činjenicu da klinička ispitivanja nisu dovršena,
- (4) nepostojanje adekvatnih kliničkih ispitivanja učinkovitosti i sigurnosti trenutnih kandidata za cjepivo te postojanje raznih metodoloških nejasnoća u provedenim preliminarnim ispitivanjima,
- (5) postojanje pokazatelja o pogreškama i prikrivanju pogrešaka tijekom preliminarnih kliničkih ispitivanja
- (6) i velik broj preliminarnih opservacijskih istraživanja koja pokazuju da inokulacija nekim od kandidata za cjepivo može biti povezana s raznolikim i ozbiljnim štetnim učincima na zdravlje koji nisu bili očekivani na temelju preliminarnih kliničkih ispitivanja koja su proveli proizvođači.

2.2. Djeca ograničeno sudjeluju u prijenosu novog koronavirusa i nemaju izražen rizik od teškog oblika bolesti i smrti

Dosadašnje su analize postigle sporazum da djeca imaju minimalan rizik od razvijanja srednjeg ili teškog oblika bolesti i smrti [37, 50, 1042–1064], čak i u slučaju postojanja ozbiljnih komorbiditeta [1048, 1064], te pokazuju da djeca imaju veću vjerojatnost da ih zarazi roditelj ili nastavnik nego da djeca zaraze roditelja ili nastavnika [37, 50, 1043, 1048, 1065–1067]. Primjerice, u jednom je istraživanju na oko 17 000 njemačke djece iz više od sto škola u razdoblju od šest tjedana utvrđeno tek devetnaest pozitivnih PCR-testova od ukupno 100 000 provedenih testova (0.00019 %) [1051].

2.3. Postoje i drugi oblici prevencije

Budući da je pretpostavljeni cilj cijepljenja djece protiv covid-19 smanjenje njihovog rizika od razvijanja teškog oblika bolesti i/ili smrti, očekivano bi bilo da će se prije takve odluke provesti široka stručna rasprava

o načinima prevencije covid-19 kod djece. Takva se rasprava u javnosti prema mojim saznanjima nije dogodila. Nejasno je zašto ako istraživanja pokazuju da postoji niz drugih mogućih intervencija koje mogu smanjiti rizik od zaraze i težinu simptoma covid-19 [76–85], uključujući izlaganje sunčevoj svjetlosti i povećanje unosa vitamina D [15, 79, 86–115], vitamina A [79, 92, 95, 116, 117], vitamina B [79, 92], vitamina C [7, 79, 92, 94, 118, 119], vitamina E [79, 92, 95], vitamina K [90, 95, 120], nekih minerala poput cinka, bakra, željeza, magnezija, mangana, natrija i selenija [79, 83–85, 92, 94, 108], konzumiranje organske hrane umjesto procesuirane hrane bogate kemikalijama [92, 121–123], konzumiranje organskog češnjaka, sjemenki crnjike, đumbira, brusnice, naranče, kurkume, ehinaceje, propolisa, soje, zelenog čaja i maslačka [83, 84, 92, 94, 124–126], unošenje probiotika [120, 125, 127] te omega-3 i -6 masnih kiselina [92]. Primjerice, jedno je istraživanje pretpostavilo da je razina vitamina D3 u krvi od 50 ng/mL povezana sa stopom smrtnosti od 0 % [87]. Povećanje fizičke aktivnosti i tjelovježbe također može doprinijeti prevenciji, primjerice u kontekstu prekomjerne težine i pretilosti kao rizičnih faktora od zaraze i razvijanja težih simptoma i raznih drugih medicinskih pojava vezanih uz manjak fizičke aktivnosti [100, 128–131]. Gradovi bi naprimjer mogli nastojati smanjiti toksično onečišćenje zraka i izlaganje ljudi elektromagnetskom zračenju koji mogu povećati rizik od zaraze i pogoršati simptome [123, 132–139].

Nejasno je zašto ne postoje kampanje za navedene preventivne mjere i nejasno je zašto javne zdravstvene ličnosti ignoriraju cijelu povijest znanja o borbi protiv zaraznih bolesti. Na *Službenoj stranici Vlade za pravodobne i točne informacije o koronavirusu* se kao jedina alternativa cjepivu navodi “lijek” koji, prema Vladi, “za sad ne postoji [...] i teško da će biti dostupan u skorije vrijeme” [140].

2.4. Klinička ispitivanja nisu dovršena

Činjenica jest da klinička ispitivanja trenutnih kandidata nisu dovršena. Primjerice, Pfizer trenutno predviđa da će ispitivanja njihovog kandidata biti završena 2. svibnja 2023. (nakon prvotno 31. siječnja 2023.) dok Moderna predviđa završetak ispitivanja 27. listopada 2022. Stoga nije jasno čemu žurba s cijepljenjem djece [141, 142].

Navedena dvo- do trogodišnja trajanja kliničkih ispitivanja već su ionako drastično ubrzana radi pretpostavljene izvanredne zdravstvene situacije [49, 50]. U publikaciji iz 2018. koju je sponzorirala Fundacija Billa i Melinde Gates navodi se razlika između triju tipova cjepiva: *jednostavna cjepiva*, *složena cjepiva* i *cjepiva bez presedana*. Cjepiva bez presedana odnose se na cjepiva protiv bolesti ili tipa bolesti za koji dosad nisu postojala adekvatna cjepiva i cjepiva razvijena na novim tehnologijama. Navedena publikacija procjenjuje da je za razvoj uspješnog cjepiva bez presedana potrebno 12.5 godina te da kandidati imaju 5 % šansi da prođu fazu 2 testiranja (procjena učinkovitosti) te 2 % da prođu i fazu 2 i fazu 3 (procjena koristi za populaciju) [143]. Ti su podaci zabrinjavajući ako uzmemo u obzir činjenicu da su neka od trenutnih cjepiva započela s distribucijom nakon svega šest mjeseci od registracije kliničkog ispitivanja [154].

2.5. Manjak ispitivanja i metodološke nejasnoće u provedenim kliničkim ispitivanjima

Primarni povod za poticanje ljudi na cijepljenje protiv covid-19 bile su objave primarnih analiza učinkovitosti koje su proveli proizvođači, a koje su iznjedrile rezultate o učinkovitosti kandidata oko i iznad 90 % injekcije dviju doza (tj. u prvih nekoliko tjedana nakon druge doze). Primjerice, Pfizerovo je ispitivanje provedeno na 37 706 ispitanika, 18 860 u skupini koja je primila kandidata za cjepivo te 18 846

u skupini koja je primila placebo. U skupini s cjepivom zabilježeno je 8 slučajeva covid-19, a u skupini s placebo 162. Rezultat od 95 % dobiven je na temelju jednostavne jednadžbe $E = 100 \times (1 - IRR)$, pri čemu E označava *učinkovitost* (eng. *efficacy*), a IRR omjer stopa prisutnosti covid-19 u skupini s cjepivom u usporedbi sa skupinom s placebo [144]. Osim izračunatih 95 % učinkovitosti, ne postoji ni jedan drugi pokazatelj o učinkovitosti kandidata u tom istraživanju. Ova je računica problematična iz nekoliko razloga.

- (1) Za medicinska je i druga istraživanja neobično da se u analizi velikog uzorka ne provode tzv. inferencijske statističke analize kojima bi se ispitala vjerojatnost istinitosti neke hipoteze (npr. hipoteze da je Pfizerov kandidat u usporedbi s placebo učinkovit u sprečavanju zaraze itd.). To priznaju i sami autori istraživanja: “Rezultati su deskriptivni i nisu temeljeni na testiranju formalnih statističkih hipoteza.” [144].
- (2) Iz kratkog opisa ispitanika gore je jasno da je istraživanje provedeno u populaciji u kojoj je novi koronavirus kolao u tek vrlo ograničenim količinama (0.009 % u placebo-skupini). Analizom takvog uzorka teško se može kvalitetno zaključivati u učinkovitosti kandidata. Ako i pretpostavimo da ta stopa covid-19 odražava stvarnu sliku te da je proizvođač s time računao, uzorak je trebao biti puno veći da bi se mogli uočiti nekakvi učinci kao što je to i inače slučaj kada se istražuju rijetke pojave [145–148].
- (3) Dizajn Pfizerovog kliničkog ispitivanja bio je iz nekog razloga takav da se niti ne može zaključivati o učinkovitosti kandidata na sprečavanje zaraze, smanjenje prijenosa te smanjenje broja hospitalizacija i smrti. To je zato što je jedina varijabla korištena za mjerenje učinkovitosti bila *prisutnost simptomatskog covid-19* (potvrđenog PCR-testom). Uopće nije jasno zašto Pfizer nije izvjestio i o zaraznosti ispitanika te broju ispitanika koji su bili hospitalizirani zbog covid-19 ili su od njega preminuli. Jedino što se iz tog istraživanja, dakle, da zaključiti, i to samo ako pretpostavimo da je učinkovitost kandidata adekvatno proučena, jest da Pfizerov kandidat smanjuje broj simptomatskih slučajeva (uključujući blage slučajeve, npr. samo kašalj). Pfizer nije niti izvjestio o težini simptoma koju su imali pojedini ispitanici s covid-19 pa ne možemo zaključivati ni koje to simptome točno i u kojoj mjeri Pfizerov kandidat može potisnuti [145]. S obzirom na navedeno, i ako ponovno pretpostavimo da je učinkovitost adekvatno analizirana, možemo jedino zaključiti da Pfizerov kandidat ima određeni terapijski učinak, a ne možemo zaključivati ima li preventivan učinak. Pobuđuje znatiželju da su neki javni zdravstveni djelatnici u medijima pogrešno tvrdili da se varijabla *prisutnost simptomatskog covid-19* odnosi samo na slučajeve s teškom (najvišom) razinom simptoma [149–151].
- (4) Barem je dvoje autora kritiziralo odabir načina računanja učinkovitosti kandidata koji predstavlja računicu relativnog smanjenja rizika (tj. ne uzima se u obzir koliko ispitanika nije imalo simptomatski covid-19). Računanjem apsolutnog smanjenja rizika na temelju objavljenih podataka dobivaju se mnogo niže vrijednosti učinkovitosti kandidata, primjerice za Pfizer 0.7 %, a za Modernu 1.1 % [152, 153].
- (5) Distribucija dobnih skupina u Pfizerovom uzorku također je problematična. Za ispitivanje kandidata za cjepivo za očekivati bi bilo da će uzorak biti najvećim dijelom sačinjen od ljudi u onoj skupini koja je najviše pogođena bolešću protiv koje se razvija cjepivo – u slučaju covid-19 ciljne skupine su starije osobe i osobe s komorbiditetima. Čudi stoga da je, na temelju dostupnih podataka, tek oko 22 % ispitanika bilo u dobi iznad 65 godina. Nadalje, za ispitivanja su primljene samo zdrave osobe i osobe “sa stabilnim kroničnim zdravstvenim stanjima” (uz nedostatno pojašnjenje kriterija za potonju skupinu). Budući da cjepiva mogu imati manju učinkovitost kod starijih osoba

i osoba s određenim bolestima, što je potvrđeno drugim istraživanjima i za trenutne kandidate, ovaj uzorak ne može dati odgovore na pitanja o učinkovitosti (i sigurnosti) kandidata u tim posebnim populacijama [50].

- (6) Nažalost, buduća randomizirana klinička ispitivanja koja bi ispitivala učinkovitost i sigurnost kandidata na dulja razdoblja i/ili ispravila prethodne pogreške praktički više nisu moguća jer su svi proizvođači ispitanicima u placebo-skupini već ponudili inokulaciju svojim kandidatom. Dosad je samo Moderna objavila koliki je broj ispitanika u placebo-skupini primio barem jednu dozu cjepiva: 98 % [154].
- (7) Znači, pobuđuju i neka druga pitanja. Primjerice, zašto je Pfizer iz analiza isključio 3 410 slučajeva kod kojih je postojala “sumnja u covid-19” te zašto ni Pfizer ni Moderna o tome nisu izvijestili u publikacijama i dokumentima prosljeđenima zdravstvenim institucijama koje njihove kandidate odobravaju za uporabu [147, 148]? Slično nisu izvijestili da je kod 477 ispitanika (nepoznato koliko u kojoj skupini) postojala “sumnja u covid-19”, a da ti ispitanici iz nepoznatog razloga nisu bili podvrgnuti PCR-testiranju [155]. Što se dogodilo s 371 ispitanikom koji je isključen iz analiza zbog “važnih devijacija u protokolu u prvih sedam dana od primanja druge doze”? Zašto je ih bilo disproporcionalno više u skupini s cjepivom (311) u usporedbi s placebo-skupinom (60) [147]? Nije jasno o kakvim se “devijacijama” radi, a uobičajeno je za znanstvena istraživanja da se isključenja ispitanika brojačano i detaljno opišu. S obzirom na malen broj slučajeva u studiji (170), isključenja i uključivanja malog broja ispitanika iz analiza ili u analize mogu dramatično promijeniti rezultate računanja učinkovitosti. Kako je Pfizer tijekom svojeg ispitivanja uspio zabilježiti devet slučajeva ponovne zaraze novim koronavirusom, u trenutku kada je u svijetu bio poznat, u najboljem slučaju, 31 slučaj ponovne zaraze [147]? Zašto je Pfizerov protokol predvidio mogućnost neizravnog izlaganja cjepivu (izravno je inokulacijom)? Specifično, u protokolu je bilo naznačeno da se izlaganje cjepivu u trudnoći moralo javiti odgovornoj osobi u roku od 24 sata te se među načinima izlaganja navodi i “izlaganje iz okoliša” koje uključuje izlaganje “udisanjem ili kožnim kontaktom”, a predviđena je mogućnost i dviju razina neizravnog izlaganja: “Muški član obitelji ili pružatelj zdravstvenih usluga koji je izložen studijskoj intervenciji [cjepivu] udisanjem ili kožnim kontaktom izloži svoju partnericu prije ili oko vremena začeća.” (67.–68. str.) [156]. Nejasno je i zašto su se proizvođači odlučili u svojim pripravicima koristiti samo genetski materijal koji kodira šiljasti protein kad se u prethodnim istraživanjima na miševima pokazalo da se adekvatni imunosni odgovor događa samo s cjepivima protiv covid-19 koja sadrže genetski materijal koji uz šiljasti protein kodira i tzv. proteine M i E novog koronavirusa, a da cjepivo temeljeno samo na šiljastom proteinu ne donosi gotovo nikakav imunosni odgovor (jedno od istraživanja provela je Moderna) [157, 158]. Brojna pitanja trenutno odjekuju u prazno i ostaju bez adekvatnih odgovora proizvođača.
- (8) Nažalost, proizvođači su objavili tek vrlo malo podataka o trenutnim ispitivanjima i nije jasno kada će i hoće li podaci u potpunosti biti dostupni javnosti. Razlog tajnovitosti nije jasan. S obzirom da su ti podaci nužni za provjeru dosad objavljenih podataka o učinkovitosti i sigurnosti te proširenje našeg znanja o samim cjepivima, skupina znanstvenika skupljenih pod nazivom Javno zdravstvo i medicinari za transparentnost (eng. *Public Health and Medical Professionals for Transparency*) tužila je američku Upravu za hranu i lijekove (eng. FDA prema *Food and Drug Administration*) koja je pak od suda zatražila vremensko razdoblje od 55 godina za objavu potpunih podataka što bi značilo da bi podaci javnosti mogli biti dostupni tek 2076. godine. Kao razlog tako dugačkog razdoblja Uprava je navela manjak radne snage za obradu zahtjeva [159, 160].

Navedeni argumenti nisu zaustavili Nenada Jarića Dauenhauera, novinara portala *Index.hr*, da izjavi: “[Pfizerovo cjepivo] je postalo jedno od *najprovjerenijih*² koja su ikada dobila potpuno odobrenje.” [161].

Važno je imati na umu da navedene metodološke nejasnoće i propusti otvaraju pitanja i o sigurnosti cjepiva. Mnogo je znanstvenika izrazilo zabrinutost zbog slabe kvalitete provedenih istraživanja i nedostupnosti velikog broja podataka o ispitanicima, mnogi i u kontekstu sigurnosti cjepiva [49, 50, 52, 145–148, 152–154, 162–212, 824–833].

Iz navedenih je točaka jasno da je na temelju postojećih podataka teško raspravljati o učinkovitosti trenutnih kandidata za cjepivo, bili oni u stvarnosti učinkoviti ili ne. Nakon distribucije trenutnih kandidata za cjepivo razna su istraživanja na razne načine pokušala provjeriti njihovu učinkovitost. Sve više preliminarnih istraživanja pokazuje da cijepljene osobe značajnim dijelom sudjeluju u prijenosu novog koronavirusa. Osobe cijepljene dvjema dozama mogu se zaraziti, prenositi uzročnika te razviti težak oblik bolesti i umrijeti [162, 213–216]. Virus se od zaraženih cijepljenih može i izolirati u staničnim kulturama [217]. Neka su istraživanja pokazala da i cijepljeni i necijepljeni mogu u sličnom kapacitetu prenositi novi koronavirus [218–224]. U jednom je još neregistriranom istraživanju među zatvorenicima jednog zatvora utvrđeno 95 osoba s pozitivnim PCR-testom od čega je 78 zatvorenika (82 %) bilo cijepljeno [223]. U srpnju je u američkoj saveznoj državi Massachusetts tijekom raznih događaja zabilježeno 469 slučajeva covid-19, 346 (74 %) od njih je bilo cijepljeno, a 274 (79 %) od tih 346 razvilo je simptome [219]. Od 1. siječnja do 30. travnja 2021. u SAD-u je službeno zabilježeno 10 262 slučaja covid-19 kod cijepljenih, od čega je 995 (10 %) bilo hospitalizirano, a 160 (2 %) je preminulo [225]. U jednom je istraživanju u staračkom domu u kojem su svi štićenici bili cijepljeni, a osoblje barem testirano, zabilježeno 119 slučajeva covid-19 među štićenicima, uključujući s teškim simptomima. Autori su zaključili da je cijepljenje u njihovom uzorku bilo povezano s “nedostatnom imunosti i manjkom zaštite protiv kolonizacije ili zaraze” [226]. Slični su slučajevi objavljeni i drugdje [227]. Jedno je epidemiološko istraživanje podataka iz 68 država i 2 947 američkih okruga zaključilo da ne postoji statistički značajna povezanost između stope slučajeva covid-19 i stope procijepljenosti, ali da postoji pozitivan trend između dviju varijabli (odnosno, trend prema većim stopama covid-19 u populacijama s višom stopom procijepljenosti) [228], a slični rezultati dolaze i od jedne analize francuskih podataka [229]. Slična, zasad neregistrirana analiza podataka iz 145 država došla je do zaključka da je stopa procijepljenosti statistički značajno povezana s brojem slučajeva covid-19 i smrti povezanih s covid-19 u velikom dijelu država (87 %). Konkretno, cijepljenje je prema analizi bilo povezano s rastom od 261 % u broju slučajeva covid-19 te 463 % u broju smrti [230]. Međutim, nije jasno u kojoj su mjeri službeni podaci o procijepljenosti, slučajevima covid-19, hospitalizacijama i smrtnim slučajevima pouzdani i valjani za znanstvena istraživanja [7, 8, 50, 231–252]. Jedno je istraživanje došlo do zaključka da cijepljeni imaju statistički značajno veći rizik zaraziti se onim sojevima koji su povezani sa smanjenom neutralizacijom antitijela u usporedbi s necijepljenima [224]. Istraživanja također pokazuju da imunost hitro opada s vremenom; Pfizerovo pokazuje (relativnu) učinkovitost od 47 % nakon četiri mjeseca, Modernino 59 %, a AstraZenecino -19 % (minus implicira da se u uzorku zarazilo više cijepljenih nego necijepljenih). Nakon četiri mjeseca, učinkovitost nastavlja padati prema neučinkovitosti [253–257]. Također je poznato da neke populacije već ionako imaju slabiju mogućnost stvaranja imunosti s pomoću trenutnih kandidata, uključujući starije, osobe s višim indeksom tjelesne mase ili povišenim krvnim tlakom, pušače, muškarce itd. [258–262].

² Istaknuo Petar Gabrić.

Imajući na umu dosadašnje informacije iz teksta, nije primjerice jasno što je Marija Bubaš, pomoćnica ravnatelja Hrvatskog zavoda za javno zdravstvo, htjela reći kad je izjavila: “Sva [cjepiva] koja dolaze i dolaziti će u Hrvatsku, za koja se Hrvatska predbilježila i za koja je zainteresirana, a osobito ova tri cjepiva koja jesu tu, *sto posto*³ štite od umiranja u slučaju zaraze bolešću COVID-19”, dodajući: “Nadam se da svi žele život i da im je život dragocjen toliko da će se odlučiti za cjepivo koje im prvo dođe pod ruku” [263]. Na kojim je informacijama temeljena ova izjava? Zasigurno nije temeljena na podacima dostupnima od proizvođača, a nije temeljena ni na rezultatima drugih znanstvenih istraživanja.

Kandidati za cjepiva protiv covid-19 za djecu od pet do 15 godina nedavno su počeli objavljivati pozitivne rezultate s kliničkih ispitivanja. Primjerice, Pfizerov uzorak za djecu od 12 do 15 godina imao je 2 228 ispitanika. Teško je raspravljati o tako malom uzorku, a nema naznaka da problemi navedeni gore ne vrijede jednako i za ispitivanja na djeci [264, 265].

2.6. Pokazatelji o pogreškama i prikrivanju pogrešaka tijekom preliminarnih kliničkih ispitivanja

U studenom 2021. prestižni je medicinski znanstveni časopis *BMJ* (prema eng. *British Medical Journal*) objavio svjedočanstvo zviždačice Brook Jackson, regionalne direktorice u organizaciji Ventavia s kojom je Pfizer sklopio ugovor o provođenju dijela kliničkih ispitivanja Pfizerovog kandidata za cjepivo. Jackson je tajno prikupila interne tvrtkine dokumente, fotografirala, snimala razgovore s izvršnim direktorima i napravila kopije povjerljivih e-mailova. Jackson je razotkrila krivotvorenje istraživačkih podataka (čija priroda zasad još nije jasna), omogućavanje i osoblju i pacijentima da znaju jesu li u skupini za cjepivo ili placebo (što narušava cijeli dizajn istraživanja), zapošljavanje neadekvatno educiranih cjepitelja, nedostatak osoblja za provođenje PCR-testiranja i manjak praćenja onih pacijenata koji su imali nuspojave, uključujući teške nuspojave. Snimke komunikacija s izvršnim direktorima pokazuju da su bili svjesni krivotvorenja podataka i ostalih propusta te, prema izjavi jednog od izvršnih direktora, da je propusta bilo toliko da “tvrtka nije mogla kvantificirati tipove i broj pogrešaka koje su pronalazili pregledavajući dokumentaciju za kvalitetu kontrole”. Jackson je od Ventavie dobila otkaz isti dan kada je pogreške prijavila američkoj Upravi za hranu i lijekove (FDA), a Uprava nikad nije provela inspekciju. Uprava je inače u kolovožu 2021. objavila da se inspekcija provodila na svega devet od 153 lokacije na kojima su bila organizirana klinička ispitivanja. Manjak inspekcija Uprava je objasnila činjenicom “da je istraživanje bilo u tijeku pa podaci o istraživačkom novom lijeku potrebni za ovjeru i usporedbu nisu bili dostupni”. Zanimljivo je da je Pfizer i nakon Jacksonine prijave sklopio četiri daljnja ugovora s Ventaviom za provođenje kliničkih ispitivanja, uključujući klinička ispitivanja Pfizerovog kandidata kod djece i trudnica te ispitivanje treće doze (eng. *booster*) [155, 266].

S obzirom da, nažalost, detalji navedenog skandala nisu poznati, nije jasno u kojoj su mjeri navedene pogreške utjecale na ishod istraživanja, no on sigurno ne može značiti ništa dobro za već ionako upitnu kvalitetu provedenih istraživanja.

2.7. Moguće štetne posljedice za zdravlje

U prethodnim dvama razdjelima navedeno je više problematičnih aspekata u vezi s trenutnim cjepivima protiv covid-19 zbog kojih je objavljena učinkovitost tih cjepiva upitna. Postojanje tih problema i nejasnoća

³ Istaknuo Petar Gabrić.

također otvara pitanja o sigurnosti cjepiva. Proizvođači su nakon provedenih preliminarnih analiza objavili da su njihovi kandidati sigurni. Međutim, teško je raspravljati o sigurnosti cjepiva na temelju tih preliminarnih analiza. Primjerice, Pfizerova studija pratila je ispitanike do oko dva mjeseca nakon druge doze te je fokus bio na “lokalnim [bol na mjestu injekcije, crvenilo, oticanje] i sistemskim [povišena tjelesna temperatura, umor, glavobolja] štetnim” učincima. Što se drugo pratilo, a da nije bilo u fokusu, nije pretjerano jasno, no njihova se analiza u svakome slučaju temeljila na simptomima, tj. štetni učinak zabilježen je samo onda kada ga je ispitanik samostalno javio ispitivačima [144]. Pfizerovo ograničavanje na navedene medicinske pojave problematično je iz nekoliko razloga i ne ulijeva povjerenje u proizvođačeve objave o sigurnosti cjepiva.

- (1) Ovakav način praćenja mogućih štetnih učinaka kandidata za cjepivo ne može se ni u kojem slučaju smatrati kvalitetnim neovisno o bilo kojim drugim čimbenicima. Je li to razina kvalitete znanstvenih istraživanja s kojom se možemo zadovoljiti [49, 50]?
- (2) Šiljasti protein novog koronavirusa koji bi tijelo trebalo proizvoditi nakon cijepljenja protiv covid-19 izrazito je toksičan i već je u kontekstu zaraze novim koronavirusom bio povezan s raznim patološkim stanjima povezanim s hiperinflamacijom, hiperkoagulacijom, hipoksijom itd. kao što su primjerice oštećenje krvnih žila i povećanje propusnosti krvno-moždane barijere, ali i oštećenje testisa [169, 267–280]. Istraživanja sugeriraju da šiljasti protein često može samostalno izazvati navedene štete, neovisno o drugim proteinima novog koronavirusa [281–285]. To je potencijalno zabrinjavaćuje budući da cjepiva protiv covid-19 potiču sintezu šiljastog proteina što znači da bi taj šiljasti protein mogao kod cijepljenih izazvati jednaku takvu ili veću štetu. Mnogi autori su izrazili zabrinutost zbog uporabe šiljastog proteina u cjepivima protiv covid-19 i implikacija koje to može imati za sigurnost cjepiva [49, 50, 53, 171, 177, 183, 187, 190, 208, 286]. Nadalje, neki predviđaju da je šiljasti protein iz cjepiva čak štetniji od šiljastog proteina zarazom zbog zaobilazanja urođenog imunskog sustava cijepljenjem, veće količine šiljastih proteina koji ulaze u krvotok i dodatnim toksičnim učincima sastojaka lipidne nanočestice [49, 50, 53, 187].
- (3) Zato su neki očekivali da će istraživanje sigurnosti kandidata za cjepivo uključiti i primjerice mjerenja razine d-dimera za dokazivanje povećane koagulacije (zgrušavanje krvi) i stvaranja krvnih ugrušaka, c-reaktivnih proteina za dokazivanje povećanih upalnih procesa, troponina za dokazivanje oštećenja srca, okludina i kladina za dokazivanje povećane propusnosti krvno-moždane barijere, kisika u krvi za dokazivanje hipoksije, amiloida beta i fosforiliranog tau-proteina za dokazivanje povećane predispozicije za Alzheimerovu bolest, seruma HMGB1, CXCL13 i Dickkopf-1 za dokazivanje povećane predispozicije na autoimune bolesti itd. [50, 53].
- (4) Zbog manjka takvih mjerenja razina biomarkera ne mogu se uočiti patološke i/ili abnormalne promjene u tijelu primatelja cjepiva koje nakon dva mjeseca nisu dosegle razinu simptoma. Primjerice, poremećaj povećanog zgrušavanja krvi ne mora odmah biti prepoznat kao slučaj ozbiljne tromboze ili sl., ali svejedno može povećati predispoziciju za ozbiljne krvne ugruške u budućnosti zbog postojanja većeg broja mikrougrušaka nakon cijepljenja [50, 290, 291], naročito kod osoba životnih stilova koji promoviraju stvaranje krvnih ugrušaka [287–289].
- (5) Brojčanost, raznolikost i ozbiljnost štetnih događaja prijavljenih u službenim bazama podataka spontano prijavljenih štetnih događaja povezanih s cijepljenjem protiv covid-19 te štetnih učinaka povezanih s cijepljenjem covid-19 iz preliminarnih opservacijskih istraživanja primjene cjepiva u stvarnome svijetu nisu bile predviđene na temelju podataka koje su dosad objavili proizvođači [50].

- (6) Skandal s Ventaviom sugerira da barem neki slučajevi teških nuspojava nisu bili zabilježeni ili su neadekvatno zabilježeni [155]. Motivacija za takvo postupanje nije jasna.
- (7) Proizvođači načelno nisu objavili biodistribucijska istraživanja svojih kandidata kojima bi se ustanovilo u koje dijelove tijela i u kojoj količini odlazi cjepivo. Neki navode da prisutnost šiljastih proteina u plazmi cijepljenih implicira da oni mogu dospjeti do svakog dijela tijela [50, 292]. Istraživanja mRNK-cjepiva protiv gripe iz 2017. i mRNK-cjepiva protiv bjesnoće iz 2020. pokazala su da RNK odlazi u jetra i slezenu preko limfnog sustava da bi konačno završilo u krvotoku, i mozgu [293, 294]. I Modernino i AstraZenecino cjepivo dopijeva u mozak [295, 296]. Preliminarne analize sugeriraju i da Pfizerovo cjepivo dopijeva u razne organe, uključujući jajnike i koštanu srž [50, 297]. Potencijalna biodistribucija RNK-a u mozgu mogla bi biti vrlo problematična jer bi mogla navesti moždane stanice da proizvode šiljaste proteine što bi posljedično moglo dovesti do imunosnog napada tijela na vlastite moždane stanice ili moždane tromboze. Potonje možda objašnjava slučajeve cerebralne venske tromboze nakon cijepljenja protiv covid-19 (v. dolje). Štetni učinci šiljastog proteina na jajnike mogli bi imati katastrofične posljedice za plodnost i razmnožavanje [49, 50, 53].

Budući da su proizvođači nekvalitetno istražili sigurnost svojih kandidata za cjepivo, trenutno nam, da bismo spoznali o sigurnosti kandidata, preostaje jedino promatrati što se događa tijekom distribucije cjepiva u općoj populaciji. To je krajnje neobična i neočekivana situacija ako uzmemo u obzir da se radi o cjepivima koja su iz raznih aspekata bez presedana te da posljedično ne postoji povijest korištenja na temelju koje bi se mogla adekvatno procijeniti sigurnost i da se namjerava cijepiti najveći dio svjetske populacije.

Brojni su autori izrazili zabrinutost u vezi sa sigurnosti cijepljenja djece protiv covid-19, neki su izrazili mišljenje da se trenutna cjepiva ne bi trebala davati djeci [49, 50, 53, 172, 190, 286, 299–310]. Neka iskustva iz prošlosti pozivaju nas na oprez [302, 311–321].

U nastavku teksta slijedi kratki pregled dosadašnje (odabrane) znanstvene literature o štetnim događajima povezanim s cijepljenjem protiv covid-19. Iako pregled sadrži relativno mnogo bibliografskih jedinica, on predstavlja samo dio dosadašnje znanstvene literature, a novi radovi objavljuju se svaki dan te je za očekivati da će njihova dnevna stopa samo rasti povećanjem osviještenosti o štetnim učincima cijepljenja protiv covid-19 i njihovom detabuizacijom, rastućem broju distribuiranih doza cjepiva i rastućoj količini vremena proteklog od svake pojedine distribucije doze cjepiva. U dosadašnjoj znanstvenoj literaturi uglavnom se pronalaze studije slučaja (klinički prikaz pojedinog pacijenta) i serije slučajeva, a nedostaju istraživanja s većim brojem podataka i/ili ispitanika. Zbog toga je malo poznato o tipovima, učestalosti i težini pojedinih štetnih učinaka povezanih s cijepljenjem. Cjelovita slika potencijalno je ozbiljna. Pretpostavlja se da će se neki štetni učinci simptomatski prikazati tek za nekoliko godina ili desetljeća. Nadalje, rizik od štetnih učinaka i više težine simptoma moguće su povećani sa svakom novom dozom, naročito ako bi neki štetni učinci bili kumulativni i nepovratni [49, 50].

Važno je napomenuti da baze podataka spontano prijavljenih štetnih događaja povezanih s cijepljenjem pokazano znatno podcjenjuju razinu učestalosti pojedinih štetnih učinaka. Razni autori procjenjuju da takve baze podataka predstavljaju od primjerice 1 % do 20 % stvarnih slučajeva [50, 312, 322, 323]. Također, vjerojatnost da će neki štetni slučaj povezan s cijepljenjem naletiti na znanstveno vješte liječnike ili druge znanstvenike te da će oni napisati znanstveni članak i objaviti ga u relevantnom znanstvenom časopisu vjerojatno je vrlo malena.

Treba napomenuti da vremenska povezanost cijepljenja i štetnog događaja ne implicira nužno da je cijepljenje uzročno dovelo do štetnog događaja. Međutim, za neke poremećaje već postoji (rani) sporazum da su uzrokovani cijepljenje protiv covid-19, a nekoliko je analiza baza podataka spontanijh prijava štetnih događaja povezanih s cijepljenjem sugeriralo na temelju relativno čvrstih grupacija slučajeva oko vremena cijepljenja da veze između raznih poremećaja i cijepljenja nisu slučajne [50, 204, 322, 324–326].

Uznemiruju neki podaci iz baza spontano prijavljenih štetnih događaja. Primjerice, od 1. siječnja do 3. prosinca 2021. u američkoj je takvoj bazi podataka VAERS (prema eng. *Vaccine Adverse Event Reporting System*, ‘Sustav za prijavljivanje štetnih događaja povezanih s cijepljenjem’) prijavljeno 898 661 štetnih slučajeva za sva cjepiva (i cjepiva osim onih protiv covid-19). Od tih 898 661 štetnih slučajeva 858 913 odnosi se na cjepiva protiv covid-19. Od 18 563 smrti povezanih s cijepljenjem u tom razdoblju 17 998 se odnosilo na cjepiva protiv covid-19. Nažalost, ne znamo koliko je kojeg cjepiva podijeljeno u tom razdoblju i koliko na prijave utječe trenutna svjetska pozornost na covid-19, no usporedbe brojki i dalje su vrlo dramatične [1249].

Gotovo sve dolje navedene medicinske pojave zabilježene su i kod djece u bazama podataka spontano prijavljenih štetnih događaja [50].

Alergijske reakcije i anafilaksa – mRNK-cjepiva koriste lipidnu nanočesticu koja obaviju virusnu mRNK i sigurno je dovodi do stanice. U mRNK-cjepivima protiv covid-19 te su nanočestice sačinjene od ionizirajućih lipida, fosfolipida, kolesterola i polietilenskog glikola. Istraživanje na miševima pokazalo je da sastojci tih lipidnih nanočestica imaju izraziti upalni potencijal što može biti povezano s raznim abnormalnim pojavama [327]. Polietilenski glikol (PEG; koji se prvi put upotrebljava u injekciji) među njima je posebno problematičan te postoji znatan broj istraživanja koja PEG dovode u vezu s alergijskim reakcijama i anafilaksom [327–331]. Istraživanja na životinjama potvrđuju da izlaganje PEG-u može dovesti do anafilakse i kardiovaskularnog kolapsa [332, 333]. Problematično je što veliki udio ljudi ima razvijena antitijela protiv PEG-a jer su mu izloženi korištenjem svakodnevnih predmeta ili uzimanjem terapija koje sadrže PEG. Neka istraživanja pokazuju da od 42 do 72 % ljudi u danoj populaciji ima razvijena antitijela protiv PEG-a te su zabilježeni brojni slučajevi anafilakse nakon ponovnog izlaganju PEG-u [331, 334–341]. Iako je anafilaksa relativno rijetka pojava, može biti smrtonosna. Rizik od anafilakse zbog izlaganja PEG-u povećan je kod ljudi s razvijenim antitijelima protiv PEG-a pa je njihova uporaba u mRNK-cjepivima koja zahtijevaju više injekcija potencijalno zabrinjavajuća [342]. Sve je veći broj zabilježenih slučajeva anafilakse nakon primanja cjepiva protiv covid-19 [153, 170, 172, 343–353]. Jedno je preliminarno istraživanje kod zdravstvenih djelatnika ustanovilo stopu od 2.1 % alergijskih reakcija nakon jedne doze cjepiva, a 247 djelatnika na milijun doživjelo je anafilaksu što je oko 130 puta veća stopa anafilakse nego što se procjenjuje za druga cjepiva [49, 343, 351, 354, 355]. S obzirom da cijepljenje protiv covid-19 trenutno zahtijeva dvije doze te da se najavljuje još doza nakon druge doze, ti će brojevi rasti budući da je rizik od anafilakse uzrokovane PEG-om povećan sa svakom novom dozom terapije, jednim dijelom i jer se očekuje da će osobe bez razvijenih PEG-antitijela razviti ih nakon prve doze [50, 179, 332].

Autoimune i autoupalne bolesti – Više je autora izrazilo zabrinutost da bi trenutna cjepiva protiv covid-19 mogla dovesti do razvoja raznih autoimunih i autoupalnih bolesti [170, 286, 356–360, 809, 810]. Predložena su dva opća mehanizma: tzv. autoimuni/autoupalni sindrom uzrokovan adjuvansima (sindrom ASIA, prema eng. *autoimmune/inflammatory syndrome induced by adjuvants*) te autoimunost uzrokovana unakrsnom

reaktivnošću antitijela protiv SARS-CoV-2 i ljudskih tkivnih antigena. Prvotne teorije o mogućoj povezanosti cjepiva protiv covid-19 i sindroma ASIA nažalost se potvrđuju rastućim brojem opservacijskih istraživanja i podataka u bazama spontano prijavljenih štetnih učinaka povezanih s cjepivima. Specifično, zabilježeni su već brojni slučajevi poremećenog rada štitnjače, najčešće u obliku hipertireoze (pojačana aktivnost štitnjače) te inače rijetkih subakutnog tireoiditisa (upala štitnjače) i Gravesove bolesti [361–385]. Pacijenti sa subakutnim tireoiditisom nakon cijepljenja protiv covid-19 žale se na bolove u ramenima i vratu (čija razina može biti teška), psihomotoričku agitaciju (nenamjerno i besmisleno kretanje udova), poteškoće u gutanju, nagao gubitak tjelesne mase, psihički nemir, povećano znojenje, nesanicu, palpitacije (doživljen pojačani rad srca), osjetljivost na toplinu itd. Problematično je što postoje i slučajevi tihog (tj. bezbolnog) subakutnog tireoiditisa što može dovesti do nedijagnoze tireoiditisa ili pogrešne dijagnoze što pak može dovesti do pogoršanja i produljenja simptoma zbog neličenja. Posljedično je moguće da postoji mnogo pacijenata s tireoiditisom nakon cijepljenja protiv covid-19 koji zasad nisu identificirani [361]. Pacijenti s Gravesovom bolesti uz navedene simptome mogu razviti i Gravesovu oftalmopatiju koju karakteriziraju izbuljene oči. Razne su druge autoimune/autoupalne bolesti zabilježene koje su vjerojatno povezano sa spomenutom unakrsnom reaktivnošću antitijela protiv SARS-CoV-2 i ljudskih tkivnih antigena. Zabrinjavajuće je da antitijela protiv SARS-CoV-2 imaju mogućnost za reaktivnost s 28 od 55 ljudskih tkivnih antigena [358]. Primjerice, zabilježeni su slučajevi stečene hemofilije (jedan od poremećaja zgrušavanja s primjetno povećanim krvarenjem) [386, 387], mijastenije gravis (bolest koju obilježuje progresivna slabost mišića tijekom napora zbog poremećaja na neuromuskularnome spojištu) [388, 389], anemije (smanjena koncentracija hemoglobina i/ili eritrocita u krvi) [390–392] itd. Zabilježene su razne reumatske bolesti [393, 394], uključujući artritis (upala zglobova) [389, 395, 396], miozitis (upala mišića) [397], Stillovu bolest (povišena tjelesna temperatura, bolovi u zglobovima, kvrgavi osip, moguća oštećenja organa) [398–401], sustavni eritematozni lupus (prouzročuje oštećenje brojnih organa) [389, 402–405], Behçetovu bolest (zahvaća male i srednje krvne žile i popraćena je ponavljajućim vrijedovima na sluznici spolnih organa i oka te oštećenjem većega broja organskih sustava, a najčešće na usnoj sluznici) [389, 406], razne oblike vaskulitisa (upalne promjene krvnih žila pri kojima dolazi do infiltracije limfocita s trombozom, vaskularnom okluzijom, hemoragijom i ishemijom) [389, 407–423], reumatsku polimijalgiju (izraženi i rašireni bolovi i ukočenost) [389, 424–426], sinovitis (upala sinovijalnih tkiva unutrašnjosti zglobova) [389, 427] i druge [428]. Zabilježeni su i slučajevi autoimunog hepatitisa uzrokovanog cijepljenjem protiv covid-19 [429–445]. Rizik od autoimunog hepatitisa nakon cijepljenja protiv covid-19 povećan je nakon druge doze i vjerojatno sljedećih doza [444]. Iniče je rizik od autoimunih i autoupalnih poremećaja moguće povećan sa svakom novom imunizacijom namijenjenom stvaranju istog antitijela [446].

Važno je napomenuti i da mnoga druga stanja nakon cijepljenja koja ću navesti mogu predstavljati imunosno posredovane bolesti, no radi preglednosti ću ostale poremećaje navesti prema tjelesnim sustavima koje zahvaćaju.

Poremećaji s očima i vidom – Zabilježene su brojne poteškoće s očima koje mogu dovesti do poteškoća u vidu te se one isto često povezuju s autoimunim i autoupalnim procesima. Poteškoće uključuju eritemne edeme (nakupljanje tekućine u tkivnim prostorima zbog nedostatnoga uklanjanja tekućine iz tkiva uz upalno crvenilo) i osip s purpurama (promjena boje tkiva zbog krvarenja) na gornjim kapcima, odbijanje presatka rožnice (i 25 godina nakon transplantacije), episkleritis (upala episklernalnoga tkiva povezana s nelagodom i boli), odignuće mrežnice (odvajanje neurosenzorne mrežnice od mrežničnog pigmentnog epitela uz nakupljanje tekućine u subretinalnome prostoru), uveitis (upala srednje očne ovojnice), koroiditis (stražnji

uveitis kod kojega je upalom zahvaćena žilnica), različite oblike retinopatije, vaskularne okluzije mrežnice, nekrozu mrežnice (konačno nepovratno stanje smrti stanica mrežnice), optički neuritis (upala vidnoga živca) i druge. Pacijenti se žale na smanjenje ili gubitak vida, crvenilo, bol, fotofobiju (netolerancija ili intenzivna osjetljivost na svjetlost), krvarenje, glavobolju, bljeskove, percipirane strukture u vidnom polju koje ometaju vid itd. [447–458].

Miokarditis i perikarditis – Više nema sumnje da miokarditis (upala srčanog mišića) i perikarditis (upala srčane ovojnice) nisu tek “ekstremno rijetke” [459, 460] pojave nakon cijepljenja protiv covid-19, naročito kod djece i mladih. Postoji već vrlo velik broj preliminarnih opservacijskih istraživanja koja miokarditis i perikarditis dovode u uzročno-posljedičnu vezu s cijepljenjem protiv covid-19 [170, 172, 461–559]. Čini se da su najizloženiji dječaci i mladi muškarci. Jedno zasad još neregizirano (slabokvalitetno) istraživanje pokazalo je da zdravi dječaci od 12 do 15 godina starosti imaju između tri i šest puta veći rizik od razvijanja kardiovaskularnih poremećaja nakon cijepljenja protiv covid-19 nego što im je rizik od hospitalizacije zbog covid-19 [463]. Jedna je analiza javno dostupnih podataka o spontanom javljanju štetnih događaja povezanih s cjepivima pokazala da je već u prvih nekoliko tjedana nakon početka distribucije cjepiva među adolescentima između 12 i 15 godina rizik od miokarditisa bio povećan 19 puta u usporedbi s onime što bi se očekivalo s ostalim cjepivima [461]. Ta recenzirana studija objavljena u prestižnom časopisu misteriozno je i bez ikakvog objašnjenja izbrisana sa stranice časopisa. To je vrlo neobično za znanstvene časopise koji u pravilu objavljene radove mogu povući (eng. *retract*) u slučaju postojanja pogrešaka u radu, no i u tom slučaju sadržaj ostaje dostupan (uz napomenu o povlačenju, eng. *retraction*). U ovome slučaju uredništvo nije izrazilo nikakvu zabrinutost u vezi pogrešaka, već je ostavilo samo napomenu da je “članak povučen [eng. *withdrawn*] na zahtjev autora i/ili urednika”. Još se očekuje rasplet ove mini-drame te će, pretpostavljam, rad biti objavljen u nekom drugom časopisu. Bilo kako bilo, potrebna su daljnja istraživanja, no rastući broj opservacijskih istraživanja i spontanijih prijava miokarditisa i perikarditisa nakon cijepljenja protiv covid-19 zabrinjava, naročito ako uzmemo u obzir da su najviše pogođena djeca koja imaju još cijeli život pred sobom.

Tromboze i trombocitopenija – Uz miokarditis i perikarditis, najbrojnije su opservacije povećanog zgrušavanja krvi koje je povezano s raznim oblicima tromboza i trombocitopenije te je njihov rastući broj također zabrinjavajuć [170, 172, 560–650]. U medijima se ove pojave također nerijetko opisuju kao “ekstremno rijetke” [459, 651]. Iako se navedeni poremećaji u najvećem dijelu događaju nakon vektorskih cjepiva, mnogo je slučajeva i nakon mRNK-cjepiva. Trombocitopenija je potencijalno smrtonosna bolest obilježena smanjenjem broja trombocita, a očituje se pojavom hemoragičnih lezija, spontanijih gingivnih krvarenja te petehijama i ekhimoza na usnoj sluznici [652]. Posebno su zabrinjavajući slučajevi poremećaja zgrušavanja krvi u mozgu i specifično cerebralne venske tromboze koja je povezana s infarktom i moždanim krvarenjem te mogu u oko 50 % slučajeva povezanih s cijepljenjem protiv covid-19 dovesti do smrti [560]. Jasno je da posljedice smrti moždanih stanica i moždanog krvarenja kod osoba koje prežive mogu biti dramatične te konačno uključivati nemogućnost samostalnog svakodnevnog funkcioniranja. Zbog manjka kvalitetnijih istraživanja još uvijek nije jasno u kojoj su mjeri poremećaji zgrušavanja krvi zastupljeni kod cijepljenih osoba, a izgledno je da mnogi slučajevi još uvijek nisu identificirani jer se, pretpostavlja se, radi o mikrougrušcima koji nisu doveli do simptomatskog izražaja [50, 618]. Vjerojatnost od razvijanja poremećaja zgrušavanja krvi moguće je povećana sa svakom novom dozom cjepiva [50].

Neurološki poremećaji – Cijepljenje protiv covid-19 povezano je s raznim neurološkim poremećajima, uključujući već spomenute cerebralne venske tromboze, Guillain-Barréov sindrom (slabost mišića zbog autoimunog oštećenja perifernog živčanog sustava), mijelitis (upala kralježnične moždine s potencijalnom oštećenjem mijelinske ovojnice i aksona koji mogu dovesti do paralize), paraliza facijalnog živca, demijelinizaciju optičkog živca, mozga i kralježnične moždine (oštećenje mijelinske ovojnice koje može dovesti do gubitka vida, slabosti u udovima i paralize, parastezija itd.), moždano krvarenje, ishemijski moždani udar, aseptički meningoencefalitis, afaziju (gubitak govora), neuralgičnu amiotrofiju (slabost i atrofija mišića kojima prethodi teška bol), tinitus [49, 170, 207, 481, 653–679], reaktivaciju latentnog herpesa zoster (reaktivacija virusa *varicella zoster* pri padu imunosti koja se očituje osjetljivošću i bolnošću pojedinih dermatoma, nakon čega slijedi makulopapularni osip koji prelazi u mjehuriće i kraste) [680–710] itd. Brojne pojave reaktivacije latentnog herpesa zoster sugeriraju da ta cjepiva dovode do supresije urođenog imunskog sustava [49] što sugerira i jedno drugo neregulirano istraživanje [711]. Posebno su uznemirujuće nove dijagnoze multiple skleroze [389, 712] te slučaj demencije s hitrim propadanjem moždanog tkiva kod inače zdrave starije žene, jedan dan nakon druge doze cjepiva, praćeno delirijem, smanjenim pamćenjem i halucinacijama nakon pet dana. Nakon dva tjedna neurodegeneracija je dovela do respiratornog distresa i šoka te je pacijentica preminula mjesec dana nakon primanja druge doze [661]. U kontekstu neurodegeneracije, neki su pretpostavili da bi cjepiva protiv covid-19 mogla dovesti do prionskih bolesti i posljedično neurodegeneracije [49, 713, 714]. Prioni su pogrešno savijeni i/ili fragmentirani proteini koji obilježavaju izrazito progresivne i uvijek smrtonosne neurodegenerativne bolesti. U tom kontekstu zabrinjava da je Pfizer u svojoj dokumentaciji poslanoj Europskoj agenciji za lijekove (EMA-i) za odobrenje cjepiva naveo da u njegovim injekcijama postoje “fragmentirani specijesi” virusne RNK te da je u injekcijama korištenima za klinička ispitivanja bilo znatno manje tih “fragmentiranih specijesa” u injekcijama. Pfizer je bez previše argumenata tvrdio da navedeni fragmenti “vjerojatno [...] neće rezultirati ekspresijom proteina”. EMA je izrazila zabrinutost ostavivši komentar: “Te strukture [fragmentirani specijesi] slabo su opisane, a ograničeni dostupni podaci o ekspresiji proteina ne razrješuju u potpunosti nesigurnosti povezane s rizikom od sinteze proteina/peptida osim namijenjenog šiljastog proteina” [295, 808]. Pfizer dosad prema mojim saznanjima nije dao na raspolaganje nikakve nove relevantne informacije.

Ostalo – Nažalost, cijepljenje protiv covid-19 povezano je s raznim drugim poremećajima koje ću radi kratkoće i preglednosti samo navesti, uključujući limfadenopatiju (povećanje limfnih čvorova) [715–736], rabdomiolizu (naglo oštećenje i raspadanje skeletnih mišića) [737–743], ozljedu slezene i pankreatitis (upala slezene) [744, 745], ozljedu i upalu pluća [481, 746–750], oštećenje i upalu bubrega (uključujući glomerulonefritis) [751–760], razne i brojne kožne bolesti [761–800], dijabetes [385] itd. Neki pretpostavljaju da će trenutno masovno cijepljenje moguće dovesti do novih sojeva novog koronavirusa koji bi mogli biti otporni na cjepiva [49, 172, 183, 190, 801–803]. Više je autora pretpostavilo da bi cijepljenje protiv covid-19 moglo dovesti do tzv. poboljšanja ovisnog o antitijelima (ADE, prema eng. *antibody-dependent enhancement*), pojave u kojoj opetovana imunizacija (tj. stvaranje specifičnih antitijela) određenim procesima dovodi do veće zaraznosti uzročnika olakšavajući uzročniku ulazak u stanicu. Drugim riječima, osobe koje su provele više imunizacija protiv novog koronavirusa mogle bi biti suočene s ADE-om pri zarazi novim koronavirusom ili novim imunizacijama (npr. treća doza, četvrta doza itd.). ADE u najgorem slučaju može dovesti do citokinske oluje koja uzrokuje široko oštećenje lokalnog tkiva i može biti smrtonosna [49, 153, 172, 173, 177, 190, 804–807]. Jedno je istraživanje pokazalo da se RNK novog koronavirusa može obrnutom transkripcijom uklopiti u ljudsku DNK kod zaraženih [823] čime se otvara pitanje može li se to postići i cijepljenjem [49, 822].

Malo je podataka o cijepljenju u trudnoći. Trenutne preporuke institucija trudnicama za cijepljenje uglavnom se temelje na jednoj skromnoj analizi koja je zaključila da cijepljenje protiv covid-19 nije povezano s povećanim rizikom od spontanog pobačaja i smrti novorođenčeta [817]. Međutim, to je istraživanje kritizirano [811, 818] te je naknadno objavljen ispravak prvotnog članka u kojem autori konačno zaključuju da s njihovim podacima “nije mogla izračunati procjena rizika spontanog pobačaja” [819]. U baza podataka spontano prijavljenih štetnih događaja povezanim s cijepljenjem raste broj prijavljenih spontanih pobačaja nakon cijepljenja protiv covid-19, uključujući slučajeve svega nekoliko sati nakon injekcije [50, 170, 298, 1249]. Zabilježeni su i slučajevi prijenosa cjepiva s majke na dojenče preko majčinog mlijeka [298]. Brojne su prijave promjena u menstruaciji [50, 170, 1249]. Neki su autori izrazili zabrinutost oko mogućih štetnih učinaka cjepiva na plodnost i razmnožavanje, između ostalog distribucijom šiljastog proteina u jajnicima i testisima [49, 50, 170, 172, 275, 306, 811–821].

Nije jasno zašto se informacije iz ovog razdjela načelno ne mogu naći u hrvatskim medijima i izjavama hrvatskih zdravstvenih djelatnika. Nažalost, izvještavanje u medijima obilježeno je velikim dijelom pogrešnih informacija, provociranjem, pretjeravanjem te poticanjem straha i ostalih negativnih emocija [834–854].

3. Nefarmakološke mjere suzbijanja covid-19

3.1. Zatvaranje (eng. *lockdown*)

Hrvatska vlada je kao odgovor na covid-19 uvela niz tzv. mjera za suzbijanje pandemije koje su donijele ograničenja ljudskog ponašanja i prestanak funkcioniranja raznih postojećih sustava, a Vlada se nije libila uključiti i djecu u navedene mjere. Neke od istaknutijih mjera koje je Vlada uvela i primijenila na djeci su tzv. zatvaranje (eng. *lockdown*), zatvaranje škola i nošenje maski. Problematično je što za navedene mjere postoje tek slabi ili nikakvi pokazatelji u znanstvenoj literaturi da doprinose suzbijanju covid-19, a postoje pokazatelji da navedene mjere mogu dovesti do raznih štetnih učinaka na zdravlje i kvalitetu života i kod odraslih i kod djece. Iako su neka slabokvalitetna istraživanja pokazala da zatvaranje jest barem vremenski povezano s određenim smanjenjem prijenosa novog koronavirusa u populaciji [13, 855–858], neka druga slabokvalitetna istraživanja i rasprave nisu došli do takvih zaključaka i/ili su ustanovili da zatvaranje nije povezano sa smanjenjem težine simptoma i smrtnosti [859–884], naročito kod zdravih mladih osoba [870].

Istovremeno, brojna su istraživanja i rasprave pokazale da zatvaranje ima niz štetnih učinaka na javno zdravstvo i funkcioniranje društva, uključujući smanjenu kvalitetu života [885–894], povećanje društvenih nejednakosti [885, 892, 894–897], nezaposlenost [892, 894, 898–901], nasilje u obitelji [894, 902], ograničen pristup zdravstvenim uslugama [903–918], pojavu i pogoršanje postojećih kroničnih bolesti (kardiovaskularne bolesti [904–910, 919–932], dijabetes [933], rak [911–916], depresija i poremećaji tjeskobe [890, 891, 894, 895, 917, 934–981], ovisnosti [982–984] itd.), stres [985–993], smanjen pristup svježem zraku i sunčevoj svjetlosti [994], manjak vitamina D [994], povećan rizik od tzv. oportunističkih zaraza [37], manjak druženja i usamljenost [894, 935, 995], povećan rizik od samoubojstva [936, 940–942], smanjenje fizičke aktivnosti [929, 935, 953, 961, 962, 996–1000], bolove u kostima i mišićima zbog povećanog sjedenja [929, 1001], prekomjernu težinu i pretilost [1002] smanjenu kvalitetu sna [1003], povećan rizik od smrti [48, 1004–1006] itd., na što su djeca zbog nedovršenog razvoja i drugih čimbenika posebno osjetljiva [1007–1041].

Primjerice, jedna je analiza pokazala da je tijekom zatvaranja u Italiji rizik od infarkta miokarda bio uvećan za tri puta u usporedbi s istim razdobljem u 2019. [922] dok je druga analiza pokazala da je u Engleskoj i Walesu u prvoj polovici 2020. zabilježen porast broja smrtnih slučajeva od akutnih kardiovaskularnih bolesti za 35 % u usporedbi s onime što bi se očekivalo na temelju podataka iz razdoblja 2014.–2019. [923]. U Švicarskoj se predviđa da će ozbiljne posljedice zatvaranja na psihičko zdravlje dovesti do skraćenog životnog vijeka od ukupno 1.7 milijuna godina za 180 000 ljudi [937]; u Engleskoj se procjenjuje da jedno do tromjesečno odgađanje operacije kod onkoloških bolesnika u bilo kojem stadiju bolesti uzrokuje dodatnih 4 700 smrti godišnje [911]; i tako dalje. Navedeni su podaci vrlo uznemirujući, naročito ako u obzir uzmemo činjenicu da su svi navedeni čimbenici međusobno isprepleteni.

3.2. Zatvaranje škola

Djeca ograničeno sudjeluju u prijenosu novog koronavirusa i nemaju izražen rizik od teškog oblika bolesti i smrti pa je smislenost mjere zatvaranja škola i iz tog aspekta upitno (v. § 2.2).

Kao i cjelokupno zatvaranje, i zatvaranje škola odnosno onemogućavanje pojedinim razrednim zajednicama da održavaju nastavu u školi zbog sumnje na zarazu novim koronavirusom kod pojedinog učenika pokazano ima štetne učinke na zdravlje i razvoj djece te se u kontekstu covid-19 povezuje s pretiulošću i kratkovidnošću zbog smanjenog kretanja i povećanog gledanja u zaslone elektroničkih uređaja, usamljenošću, stresom, depresijom, povećanim rizikom od samoubojstva, tjeskobom, akutnim i kroničnim umorom, poremećenim spavanjem, usporenim razvojem jezika i govora, usporenim kognitivnim i emocionalnim razvojem, smanjenim učenjem, povećanim rizikom od odustajanja od škole, izrabljivanjem i zlostavljanjem djece, ranom trudnoćom itd. [37, 1007–1041, 1068–1085].

3.3. Nošenje maski

Nošenje maski i kod odraslih i kod djece također je kontroverzna tema u znanstvenoj literaturi. Trenutno ne postoje kvalitetna istraživanja na temelju kojih bi se moglo zaključivati o stupnju učinkovitosti maski u smanjenju prijenosa novog koronavirusa [1086, 1087]. Učinci na težinu simptoma i smrtnost u populaciji vrlo su slabo istraženi. Neka slabokvalitetna istraživanja provedena tijekom proglašene pandemije zaključila su da maske mogu doprinijeti smanjenju prijenosa novog koronavirusa u određenim kontekstima [1088–1091] dok su druga slabokvalitetna istraživanja zaključila da nošenje maski ima slab ili nikakav učinak na prijenos novog koronavirusa [1086, 1092–1103]. Prije proglašenja pandemije u znanstvenoj literaturi i službenim uputama relevantnih ustanova nije bilo govora da bi zdrave osobe nosile masku kako bi izbjegle zarazu ili kako osobe s “asimptomatskom” zarazom ne bi prenijele virus na druge [1100, 1104]. To je zato što su randomizirana kontrolirana istraživanja (u kojima se uspoređuju zdrave osobe koje nose masku s osobama koje ne nose) prije proglašenja pandemije pokazala da maske, a naročito kirurške i platnene, ne smanjuju prijenos virusa sličnih novome koronavirusu, a kamoli da smanjuju težinu simptoma i smrtnost u populaciji [1101, 1105–1024]. Trenutno nedostaju randomizirana kontrolirana istraživanja koja bi ispitala učinkovitost maski na kretanje novog koronavirusa u populaciji i razinu opasnosti koju ono predstavlja [1100, 1125].

Mnogo je istraživanja i rasprava istaknulo moguće štetne učinke nošenja maski, uključujući učinke na zdravlje, zbog čega razni autori smatraju da se i u slučaju da maske mogu doprinijeti suzbijanju covid-19 i/ili drugih virusa njihova opća uporaba ne preporuča [1086, 1095, 1096, 1099, 1100, 1126].

Maska predstavlja očitu prepreku između nosa/usta i vanjskog zraka te u istraživanjima postoji sporazum da nošenje maske dovodi do povećanja razina ugljikovog dioksida (tj. trenda prema tzv. hiperkapniji) i smanjenja razina kisika u tijelu (tj. trenda prema tzv. hipoksemiji) [1086, 1095, 1096, 1100, 1125–1149], poglavito zbog manje dostupnosti kisika tijelu i ponovnog udisanja dijela izdišenog ugljikovog dioksida [1086, 1126, 1131, 1149]. Kratkoročni učinci navedenih pojava uključuju otežano disanje [1095, 1129, 1130, 1050–1052], povišenu srčanu frekvenciju (broj otkucaja srca) [1129, 1134, 1136, 1148, 1153] i frekvenciju disanja (broj udisaja) [1129, 1134, 1136, 1148], zbunjenost, dekoncentraciju, dezorijentaciju i smanjene psihomotoričke sposobnosti [1132, 1136, 1142, 1145, 1153, 1154], vrtoglavicu [1142], smanjene kognitivne sposobnosti (razmišljanje) [1142, 1145, 1154–1158], glavobolju (i po četiri glavobolje dnevno, djelomično i zbog iritacije vratnih živaca uslijed zatezanja vrpce oko ušiju) [1115, 1140, 1159–1161] te umor i iscrpljenost [1095, 1133, 1148, 1161–1165]. Budući da je ljudskom organizmu za funkcioniranje potrebna pravilna izmjena kisika i ugljikovog dioksida, očekivano je da opetovano nošenje maske na dulja razdoblja (npr. nekoliko sati dnevno) može dovesti do ozbiljnih učinaka na zdravlje i pojave novih bolesti kao što su povišeni krvni tlak, arterioskleroza, koronarna bolest srca (začepljenje krvnih žila oko srca), astma, neurološki poremećaji zbog oštećenja žila koje vode u mozak itd. [1086, 1095, 1133, 1148, 1161]. Nošenje maski može biti povezano i s kliničkim razinama tjeskobe i depresije [1125, 1138, 1155, 1166–1172], paničnim napadajima [1172–1174], osjećajem gubitka slobode i autonomije [1086, 1152, 1175], štetnim učincima na trudnoću [1086, 1133, 1135, 1141, 1176], poteškoćama u verbalnoj i neverbalnoj komunikaciji [1086, 1126, 1152, 1177–1179], trajnim oštećenjem glasnica zbog opetovanog glasnog govorenja [1178], smanjenom kvalitetom života [1144], smanjenim vidnim poljem i zamagljivanjem naočala koje može povećati rizik od nesreća i smanjiti radnu učinkovitost [1126, 1152, 1180], poteškoćama u prepoznavanju lica [1086, 1126] i poteškoćama u razumijevanju emocija kod drugih [1086, 1126].

Nošenje maske pokazano dovodi i do povećanja temperature i vlage pod maskom [1086, 1100, 1142, 1152, 1153, 1149, 1181], čemu slijedi nakupljanje virusa, bakterija i gljivica i na vanjskoj i unutarnjoj površini maske [1182–1185] čime se povećava rizik od virusnih, bakterijskih i gljivičnih infekcija [1182–1189] te kožnih poremećaja poput perioralnog dermatitisa, akni, osipa i svrbeža [1153, 1154, 1190–1196], i u slučajevima kada se maska nosi “ispravno”. U slučaju postojeće zaraze, udisanje dijela već izdišenog zraka i izdisanje kontaminiranog zraka u oči može dovesti do produljenja i pogoršanja postojećih simptoma, i u slučaju covid-19 [1100, 1026, 1197]. Od kožnih poremećaja zabilježeni su i pojava prolazne ili trajne hiperpigmentacije (uočljivo tamnjenje kože u području nošenja maske) [1191, 1193] te kontaktni dermatitis u vezi s osjetljivošću na industrijske sastojke u maskama poput formaldehida i tirama [1176, 1192, 1198]. Formaldehid je karcinogeni biocid koji se koristi kao industrijsko dezinfekcijsko sredstvo, a tiram je originalno pesticid i koroziv [1086]. Udisanje polipropilenskih vlakana iz maski može dovesti do iritacije nosne sluznice te posljedično hunjavice i kihanja [1199]. Nošenje maske povezano je i sa smanjenim tokom slina i povećanim disanjem kroz usta što dovodi do suhoće ustiju i posljedično može povećati rizik od halitoze (smrad u ustima), gingivitisa (upala zubnih desni), kandidijaze (gljivična upala) i upale usana [1086, 1200, 1201].

Osobe koje nose masku imaju smanjenu radnu učinkovitost u usporedbi s osobama koje ne nose masku [1115, 1129, 1132, 1134, 1140, 1145, 1148, 1153, 1159, 1160, 1162, 1165, 1178, 1191, 1199, 1202].

Navedeni rizici mogu biti povećani kod djece [1086, 1095, 1126, 1139, 1148, 1203–1219]. Primjerice, jedno je istraživanje u kontekstu covid-19 provedeno na 25 930 djece ustanovilo da su maske bile povezane

s glavoboljom (kod 53 % djece), dekoncentriranošću (50 %), anhedonijom (klinički smanjenom motivacijom ili mogućnošću za doživljajem zadovoljstva; 49 %), poteškoćama u učenju (38 %), iscrpljenošću (37 %), a čak je 25 % djece zadovoljavalo uvjete za novu dijagnozu poremećaja tjeskobe uz visoku stopu prisutnosti noćnih mora [1206]. Očekivano je i da će mnogo djece imati zakašnjeli ili drugačije poremećeni razvoj govora i jezika, komunikacije, kognicije, obrade emocija i empatije ako su tijekom dojenačkog doba ili ranog djetinjstva kontinuirano bili izloženi bliskim osobama koje nose masku jer će, između ostalog, teško usvajati i prepoznavati glasove i nove riječi te teško usvajati i prepoznavati emocije te želje i namjere druge osobe, u oba slučaja jer je potrebno gledati govorniku u usta [1126]. Navedene su pojave karakteristične za neke psihijatrijske i neurološke razvojne poremećaje poput autizma [1220–1223]. Nošenje maske u učionici smanjuje usvajanje znanja i vještina jer maske ometaju komunikaciju i blokiraju emocionalne signale između nastavnika i učenika [1126].

Maske za odrasle u smanjenom izdanju koje se na raznim mjestima prodaju za djecu nisu odobrene za uporabu kod djece kao zaštitna medicinska oprema i nisu testirane za tu namjenu [1086, 1100, 1203].

S obzirom na navedeno, nejasno je zašto hrvatski zdravstveni djelatnici i dalje neutemeljeno inzistiraju na mjerama zatvaranja, zatvaranja škola odnosno održavanja tzv. e-nastave te nošenju maski ako je (1) učinkovitost takvih mjera u najmanju ruku sporna, (2) djeca nisu osjetljiva na covid-19, (3), djeca imaju smanjenu vjerojatnost da će zaraziti odrasle te (4) navedene mjere imaju vrlo zabrinjavajuće štetne učinke na zdravlje i razvoj djece, sugerirajući da će velik broj djece u Hrvatskoj u sljedećih nekoliko desetljeća patiti od raznih kroničnih oboljenja kao posljedica zatvaranja, zatvaranja škola i nošenja maski. Također je nejasno zašto zdravstveni djelatnici koji preko medija daju preporuke o zdravstvenom ponašanju ne informiraju javnost o mogućim ozbiljnim štetnim učincima tih mjera na aspekte javnog zdravstva i osobnog zdravlja nevezanog za covid-19, a u skladu sa Zakonom o zaštiti prava pacijenata [1224].

Ovo je bio samo kratki pregled nekih od problematičnih aspekata u trenutno proglašenoj pandemiji koji se ne tiču cjepiva. I druge pojave treba imati na umu u raspravama o djeci (i odraslima). Primjerice, povećana uporaba dezinfekcijskih sredstava za ruke i površine također može biti povezana s štetnim učincima na zdravlje [1225, 1226]. Moguć je razvoj kožnih reakcija poput iritantnog kontaktnog dermatitisa koji može dovesti do suhoće kože, svrbeža, eritema (upalno crvenilo) i krvarenja [1227–1229] te alergijskog kontaktnog dermatitisa koji može dovesti do pucanja kože od suhoće, ali i anafilakse [1230–1232]. Različiti su mehanizmi pretpostavljeni prema kojima uporaba dezinfekcijskih sredstava može dovesti do oboljenja, uključujući denaturaciju proteina u *stratum corneum* (najvišem sloju vanjskog sloja kože), promjene međustaničnih lipida, smanjenje kohezije korneocita i smanjenje mogućnosti *stratuma corneuma* da veže vodu [1225, 1233, 1234]. Opetovanim se korištenjem narušava lipidna barijera čime se omogućava sastojcima dezinfekcijskih sredstava da prodru dublje u slojeve kože i promjene floru kože, posljedično povećavajući prisutnost bakterijskih kolonija [1235–1239]. Uporaba dezinfekcijskih sredstava za ruke može dovesti do poremećaja sluznice nosa, usne šupljine i oči zbog diranja tih dijelova dezinficiranim rukama [1240–1241]. Veća dostupnost dezinfekcijskih sredstava u trenutno proglašenoj pandemiji povezana je s rastom slučajeva trovanja i oštećenja organa zbog nepravilne uporabe [1242–1246], čime su posebno pogođena djeca [1242, 1247]. Često pranje ruku sapunom u trenutno proglašenoj pandemiji također je povezano s dermatitisom [1248].

4. ZAKLJUČAK

U ovome kratkom pregledu odabrane literature vjerujem da sam dovoljno informacija i izvora za poticanje ozbiljne i javne rasprave o eventualnom cijepljenju djece protiv covid-19 i nastavku primjene tzv. mjera za suzbijanje pandemije. Očito je da postoje brojna pitanja o učinkovitosti i sigurnosti trenutnih cjepiva koja se moraju raspraviti kako bi se donijela smisljena i etična odluka.

Liječnici imaju dužnost obavijestiti osobe voljne cijepiti se o mogućim štetnim učincima na njihovo zdravlje. Obaviješteni pristanak pacijenta preduvjet je za primjenu terapije. Liječnici također moraju adekvatno reagirati u slučaju prisile pacijenta na cijepljenje.

Na državnoj bi se razini trebalo pod hitno započeti veliko istraživanje i kvalitetno skupljanje podataka o primjeni cjepiva kao i ostalih mjera.

Izjava o sukobu interesa

Autor izjavljuje da ne postoji sukob interesa.

Izjava o ograničenju odgovornosti

Svi stavovi u rukopisu su autorovi i ne predstavljaju nužno stavove Philippsovog sveučilišta u Marburgu.

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