Posodobljeno 28. avgusta 2021

Izobraževalno gradivo Združenja ameriških zdravnikov in kirurgov (The Association of American Physicians and Surgeons) AAPSonline.org

Vodič v domače zdravljenje COVIDne bolezni

ki vam lahko korak za korakom reši življenje

Glavna urednica:

Dr. Jane Orient, zdravnica interne medicine, izvršna direktorica Združenja ameriških zdravnikov in kirurgov, ter predsednica ustanove Zdravniki za pripravljenost na katastrofe

Gostujoči urednik:

Dr. Peter A. McCullough, MD, MPH, FACP, FACC, FCCP, FAHA, FNKF, FNLA, FCRSA
internist, kardiolog in epidemiolog, predsednik ameriškega Združenja za srce in ledvica

Urednica in avtorica:

Dr. Elizabeth Lee Vliet, specialist preventivne medicine, bivša direktorica Združenja ameriških zdravnikov in kirurgov in članica uredniškega odbora AAPS

Tehnični urednik:

Jeremy Snavely, poslovni direktor
Združenja ameriških zdravnikov in kirurgov

Izjava o omejitvi odgovornosti: Ta vodnik ne ponuja individualnih zdravniških nasvetov ali predpisuje zdravljenja, ampak je namenjena izobraževanju bolnikov in njihovih družin, da vedo, katere možnosti so na voljo in se pogosto uporabljajo pri številnih bolezenskih stanjih. Bolniki se morajo posvetovati s svojim izbranim zdravnikom glede individualne zdravniške ocene in priporočila za zdravljenje, prilagojeno individualnim potrebam.

Izobraževalno gradivo Združenja ameriških zdravnikov in kirurgov (The Association of American Physicians and Surgeons) AAPSonline.org

Kazalo

1. poglavje: Pregled - SARS-CoV-2 koronavirus in bolezen COVID-19
Kaj je koronavirus?
Kako smrtonosen je COVID?

2. poglavje: Imam gripi podobne simptome. Kaj naj naredim?
Kaj naj naredim najprej?
Simptomi COVID
Nujna priporočila za domačo nego
Ali naj se testiram za COVID?
Zgodnje zdravljenje je ključ uspeha
Kaj lahko pričakujem od obiska zdravnika?

3. poglavje: Navodila strokovnjakov za zgodnje domače zdravljenje
Prednosti domačega zdravljenja
Dostopna zdravila in njihova nova raba: Razlogi za njihovo kombiniranje pri COVID
Antibiotiki in antivirusna sredstva
Protivnetna zdravila - kortikosteroidi: Oralni in nebulizirani
Sredstva proti strjevanju krvi na recept: Zakaj so pri COVID-u ključna
Vitamini, prehranska dopolnila in kisik

4. poglavje: Novi pristopi k preventivi in zdravljenju
Monoklonska protitelesa
Rekonvalescentna plazma
Možnosti preventive: preprečevanje in cepiva

DODATKI

DODATEK I: Medicinski viri

DODATEK II: Contributors and Physician Resources for Treatment

DODATEK III: primeri vprašalnikov za klinično sledenje COVID-19

Opomba: Vsi zdravniki, ki so prispevali protokole zdravljenja opisane v tem vodniku, aktivno zdravijo bolnike s COVID-om in so osredotočeni na zgodnje, domače možnosti zdravljenja, razen v primerih, ko ti potrebujejo nujno bolnišnično zdravljenje. Sodelujoči zdravniki nimajo finančnih povezav z nobenim farmacevtskim podjetjem ali izdelkom, ki ga predlagajo v svojih protokolih zdravljenja.

Vsi sodelujoči so v teh izrednih razmerah prostovoljno vlagali svoj čas in strokovno znanje v splošno korist, da bi bolnikom predstavili njihove možnostih zdravljenja in preprečevanja, ki jih ocenjujejo strokovnjaki kot varne. Za svoje prispevke niso prejeli nikakršnega nadomestila. Mnenja, izražena v tem priročniku, so mnenja sodelujočih zdravnikov in ne nujno tudi ustanov, v katerih so zaposleni.

UVOD

Vodnik v domače zdravljenje COVID-a temelji na vse številčnejših strokovno pregledanih in objavljenih medicinskih raziskavah, ki so jih izvedli zdravniki z desetletji izkušenj pri zdravljenju bolnikov z najrazličnejšimi boleznimi.

Vodnik v domače zdravljenje COVID-a razkriva strokovno preverjene pristope k zgodnjemu zdravljenju, ki zagotavljajo razumno verjetnost uspeha proti tej pandemiji. Obstajajo peroralna zdravila, ki so odobrena za druga stanja, vendar ameriška uprava za hrano in zdravila še ni potrdila njihove učinkovitosti posebej pri COVID-19. V svetovni pandemični krizi obsežna randomizirana klinična preskušanja ob tako kritični bolezni namreč ni izvedljiva.

Ameriški državni inštitut za zdravje trenutno ne priporoča zdravljenja izven bolnišnice, z izjemo terapije REGEN-COV ™ (casirivimab z imdevimabom) pri bolnikih z visokim tveganjem za klinično napredovanje bolezni v bolnišnicah, ki niso hospitalizirane za COVID-19. Ravno tako ni potrjenih peroralnih zdravil, ki bi bila posebej odobrena za ambulantno zdravljenje COVID-19, čeprav je stopnja umrljivosti hospitaliziranih bolnikov nesprejemljivo visoka.

Zaradi naštetega mora biti zdravljenje, ki se izvaja zunaj bolnišničnega okolja, pod nadzorom zdravnika ali pooblaščenega zdravstvenega delavca, ki je seznanjen z uporabo zdravil in pristopom ambulantnega, domačega zdravljenja COVID-19, kot je opisan v tem vodniku. Bolniki, ki se jim stanje na kakršen koli način poslabša, morajo nemudoma poiskati nujno medicinsko pomoč.

Pri odzivu na pandemijo nalezljive bolezni moramo upoštevati štiri glavna področja delovanja:

1. Nadzor okužb (zaustaitev širjenja virusa)
2. Zgodnje ambulantno, domače zdravljenje
3. Zdravljenje poznega štadija v bolnišnicah
4. Cepljenje

Ta vodnik se osredotoča na področje zgodnjega ambulantnega, domačega zdravljenja, ki ga nadzoruje vaš zdravnik, pri katerem predpisuje kombinacijo dostopnih zdravil, ki so že potrjena za zdravljenje drugih obolenj ter v široki uporabi v vsakodnevni klinični medicini.

Zdaj nam je že znano, katera zdravila so učinkovita, kako in kdaj jih je potrebno uporabiti, kdo je izpostavljen največjemu tveganju, in katere strategije delujejo. Pozivamo vas, da berete ta vodnik odprtega duha. Napisali smo ga z namenom, da vam POMAGAMO in vas NAUČIMO, kako sodelovati s svojim zdravnikom.

Kot zdravnikom nam je jasno, da se moramo osredotočiti na zgodnje zdravljenje, saj je to najlažja pot zmanjšanja hospitalizacij in smrti. Ta vodnik naj vam razkrije, kakšne so vaše možnosti, in kako ga lahko s svojim izbranim zdravnikom uporabita skupaj.

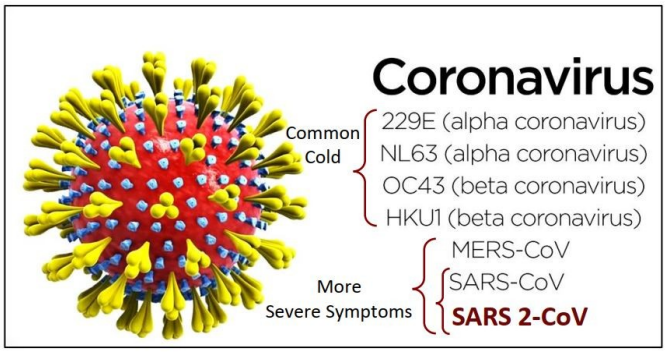
Pa začnimo!

1. poglavje

Pregled: koronavirus SARS-CoV-2

Kaj je koronavirus?

Koronavirusi so družina običajnih virusov dihal. Znanih je sedem različnih sojev koronavirusa. Štirje med njimi povzročajo simptome, ki jih večina ljudi zaznava kot navadni prehlad v jesensko-zimski sezoni: od običajnega 'prehlada' s kašljem in smrkavostjo, do gripi podobnih bolečin po telesu in celo manjše vročine.



SARS-1 (Hud akutni respiratorni sindrom), MERS (bližjevzhodni respiratorni sindrom) in najnovejši, SARS-2 COVID-19 so novejši koronavirusi, ki so se pojavili po letu 2002-2003, in lahko povzročijo resnejše obolenje.

Bolezni, ki se širijo na večjem področju označujemo za epidemijo, če so omejene predvsem na en predel sveta. Pandemija se nanaša na bolezen, ki se hitro širi iz nekega omejenega predela po vsem svetu. SARS-1 se je prvič pojavil na Kitajskem v letih 2002-2003. Čeprav se je razširil v 26 držav sveta, so ga kategorizirali kot epidemijo. Čeprav se je razširil izven meja Kitajske, ni veljal za dovolj nevarnega, da bi razglasili pandemijo. Njegova stopnja umrljivosti je bila nekako 9.6%.

SARS-1 je bil prisoten nekako dve sezoni, potem pa poniknil. In vendar so ga začeli zaradi njegovih kužnih značilnosti, iz različnih razlogov proučevati v mnogih raziskovalnih laboratorijih. Vse od takrat je virus iz različnih kitajskih laboratorijev ušel vsak šestkrat in povzročil nove izbruhe bolezni.

MERS so prvič zaznali leta 2012 v Saudski Arabiji. Poročila o njegovi kužnosti so bila podobna kot pri SARS-1, a je bila njegova stopnja smrtnosti veli višja, kar 34.4%. MERS je poniknil, saj so vse od prvega izbruha poročali o vsega nekaj posamičnih primerih.

SARS-2 COVID-19 je povsem drugačna zgodba. Resnični kužni virus je bil poimenovan SARS-2 ali SARS-CoV-2 (Severe Acute Respiratory Syndrome 2 oz. po naše hud akutni respiratorni sindrom 2) in je po poročilih 79% identičen po genskem zaporedju SARS 1. Po določenem času so poimenovali tudi 'bolezen' in sicer COVID-19 (kar je krajšava za Corona Virus Disease-2019 oz. po naše Koronavirusna bolezen-2019).

Virus SARS-2 in bolezen, COVID 19, sta označena za pandemijo zaradi hitrega, globalnega širjenja.

Kakšne vrste sezonskih sindromov respiratornih virusov poznamo?

Znanih je več virusov, ki prispevajo k vsakoletnemu kašlju, prehladu in gripi. Rhinovirusi povzročajo 35-70% vseh simptomov. Tem sledijo koronavirusi, ki povzročajo 12-15% vseh simptomov, tem pa sledijo adenovirusi in virusi gripe (7-12%). Stopnje pogostosti vsakega od teh sezonskih respiratornih virusnih sindromov se iz leta v leto spreminjajo. Gripa se vsako leto zelo spreminja po tem, kako hudi so njeni simptomi, kako hitro se prenaša in po svoji smrtnosti.

Kako smrtonosen je COVID 19?

Ko izbruhne resna kužna bolezen, nas povsen naravno zaskrbi, "Ali bom umrl?" Strah je povsem običajen odziv, zato se obrnemo na strokovnjake in vladne službe za informacije in navodila.

Veliko večino smrti zaradi COVID-a beležimo pri starih 75 let in več, pri čemer jih večina od njih boleha za katero drugo, predvsem kronično boleznijo ali več njih. Velik odstotek jih živi v domovih za ostarele A large percentage are in nursing care facilities, over 80 years old, and with an a, so starejši od 80 let in imajo 2,5 pridruženih bolezni, kot so debelost, diabetes, obolenja srca, ali bolezni pljuč in/ali ledvic. Te sočasne bolezni poimenujemo komorbidnosti, in

povečujejo možnosti za težak razvoj bolezni COVID.

Možnost, da bi nekdo mlajši od 50 let umrl za COVID-19, je 0,05%. Možnost, da bi nekdo mlajši od 18 let umrl za COVID-19 je praktično 0%. Pri tisti, ki kljub temu umrejo, so prisotne hude oblike sočasnih obolenj. Tako so izračunali, da nekako 7-krat vseč otrok umre za gripo, kot za COVID-19.

Ali če povemo drugače, kakšnih 99,9% posameznikov, ki se zbolijo za COVID-19, bo čutila blage do srednje hude simptome in se pozdravila, povsem enako kot pri gripi. Veliko večino smrti beležimo pri 0,62% prebivalstva, ki živi v domovih za ostarele.

Kaj torej to pomeni? Ta virus je podoben in tudi deluje zelo podobno kot gripa, vendar z eno pomembno RAZLIKO: Za razliko od običajne sezonske gripe se lahko razvije v različne nepredvidljive oblike hudega obolenja.

COVID-19 se lahko zelo hitro razvije v kritično obolenje iz dveh glavnih razlogov: ti virusi v telesu povzročijo DVA odziva, ki sta oba veliko hujša od sezonske gripe: prekomeren vnetni odziv, ki povzroči poškodbe ključnih organov in prekomerno strjevanje krvi, ki povzroča nastanek številnih krvnih strdkov v pljučih, možganih in drugih organih. Zdravniki so odkrili krvne strdke celo v velikih arterijah, kakršna je aorta.

Nadzor okužb ostaja prvi korak pri preprečevanju širjenja bolezni. Zdravstveni organi, kot so Ministrstvo za zdravstvo, Inštitut za varovanje zdravja, Ekspertna skupina in drugi izdajajo navodila, ki upoštevajo nova spoznanja in najnovejša spoznanja. Kot zdravniki, ki zdravimo bolnike, je naša odgovornost, da se osredotočamo na zdravljenje, kar je bil tudi namen našega sodelovanja pri pripravi tega vodnika.

Stroka priporoča, da se ob pojavu simptomov, posvetujete s svojim zdravnikom. Ta vodnik vam bo pomagal prepoznati simptome, kdaj je potrebno poklicati zdravnika, ter o kakšnih možnostih zgodnjega zdravljenja, ki so vam na voljo se velja pogovoriti s svojim zdravnikom.

2. poglavje

Imam gripi-podobne simptome: Kaj naj naredim?

Kaj naj naredim najprej?

Ob pojavu prvih simptomov COVID-19 se obrnite na svojega osebnega zdravnika. Če občutite hude, življenjsko nevarne simptome, pokličite 119 ali pa se napotite na pregled na najbližjo urgenco. Oteženo dihanje ali hude bolečine v prsnem košu sta znaka resnega obolenja in zahtevata takojšnjo zdravstveno pomoč.

Najpomembnejši razlog takojšnega obiska ali poziva zdravnika je v tem, da študije razkrivajo, da je zgodnje zdravljenje KLJUČ uspeha pri zdravljenju COVID-19. Zgodnje zdravljenje je še posebej ključno pri ljudeh z visokim tveganjem.

BOLNIKI Z VISOKIM TVEGANJEM: osebe starejše od 50 let, ki imajo eno ali več sočasnih obolenj:

- debelost
- diabetes ali pred-diabetes (“presnovni sindrom”)
- obolenje pljuč (kronična obstruktivna pljučna bolezen - COPD, pljučna fibroza, astma, cistična fibroza)
- obolenja ledvic
- visok krvni tlak
- avtoimunske motnje
- preživeto zdravljenje raka
- zgodovino rednega jemanja kortikosteroidov

Kakšni so simptomi COVID-19?

Pri večini ljudi se prvi simptomi ne razlikujejo veliko od tistih, ki so jih že doživeli ob pričetku prehlada ali gripe. Razlika je, da lahko COVID napreduje hitro in na nepričakovan način v zelo resne respiratorne težave, ki jih spremljajo z vnetji povzročene poškodbe in povečano tveganje nevarnih krvnih strdkov. Ti zadnji trije zapleti, ki jih beležimo pri COVID-19, se zelo razlikujejo od tistih, ki jih beležimo pri običajnem prehladu ali sezonski gripi, ter povzročajo najresnejše, potencialno smrtno nevarne poškodbe ključnih organov.

Trije majbolj kritični simptomi možnega COVID-a so **vročina, kratka sapa/oteženo dihanje/pritisk v prsnem košu in hud kašelj**. Kratka sapa lahko pomeni oteženo dihanje v mirovanju ali pri opravljanju običajnih dnevnih opravil.

O svojih simptomih vodite dnevnik. Ta bo pomagal zdravniku, ki ga boste obiskali, ugotoviti kaj se je dogajalo, saj bodo v dnevniku zapisani vsi simptomi z datumom in uro ter opisom vašega počutja oziroma vaše bolezni.

Takšen dnevnik vam lahko reši življenje, še posebej v urgentnem primeru, saj zdravniku takoj razkrije vaše simptome, kdaj so se začeli in kako dolgo so trajali, kako so se razvijali ter kako hudi so bili. Na ta način bo zdravnik lažje sprejel boljše odločitve glede za vas najprimernejšega zdravljenja.

Vročina: Najboljši način meritve telesne temperature je z uporabo staromodnega toplomerja za domačo rabo. Priskrbite si ga lahko v vsaki lokalni lekarni ali naročite prek spleta. Termometri za merjenje temperature na čelu so zelo priročni, vendar so precej dragi in ne tako zelo natančni. Pri majhnih otrocih je najboljše meriti temperaturo, tako da jim toplomer namestimo pod pazduho, saj ne moremo pričakovati, da ga bo lahko držal v ustih polne tri minute.

Tipični simptomi, ki jih lahko zaznavate (vendar ne pozabite, da skoraj nihče ne občuti vseh naštetih):

- smrkavost, kihanje
- nenaden pojav občutne utrujenosti
- izguba energije, slabo počutje
- bolečine po telesu, mišicah, glavobol
- kašelj, čeprav gre pri COVID za suh kašelj. Morda tudi ne bo izpljuvka (sputuma). Barva sputuma ni zanesljiv pokazatelj resnosti ali vrste obolenja
- če vaš kašelj povzroča kratko sapo ali vas moti pri spanju, to lahko pomeni slabšanje bolezni
- občutek ’vročičnosti’, četudi visoka temperatura (torej temperatura višja kot 38,3 stopinj Celzija) ni prisotna
- nočna mrzlica
- nenaden pojav potenja tekom dneva, ki ni povezan z naporom
- izguba okusa ali voha (ta se običajno pojavita, ko so drugi simptomi prisotni že 1-3 dni, čeprav se lahkopojavita tudi prej ali kasneje)
- izguba apaetita, slabost, gastrintestinalno nelagodje
- lahko se pojavi driska, čeprav to ni običajno. Če do nje pride, to lahko voi v dehidracijo in neravnovesje elektrolitov.
- po potem dnevu, ko se vnetje poslabša, bolnik pogosto zazna pritisk v pljučih, oteženo dihanje in kratko sapo
- upag kisika v krvi (merimo ga z oksimetrom na prstu, ki ga lahko kupite v lekarni) je znak resnih dihalnih težav
- pospešen utrip srca, palpitacije
- nezmožnost osredotočanja, težave s koncentracijo in spominom

Priporočila za takojšnje domače zdravljenje

Ob sumu okužbe ali ob pozitivnem COVID testu, se priporoča osamitev od drugih ljudi za zmanjšanje možnosti prenosa okužbe. Trajanje karantene naj bo med 7 in 14 dni, odvisno od bolnikovih simptomov, starosti in zdravstvenih tveganj.

Ustrezna higiena zavira širjenje virusa. Roke in telo si redno umivajte z milom in vodo. Izvajajte dezinfekcijo stanovanja ali sobe. Nasne prilke in ustne vodice, ki vsebujejo raztopino povidon joda so se izkazale odlično pri preprečevanju okužbe in širjenja COVID-19.

Sončni žarki in svež zrak sta ključni komponenti trdnega zdravja in obrambe pred COVID-om. Neposredna izpostavljenost sončnim žarkom 10-20 minut dvakrat dnevno predstavlja dober vir vitamina D (to v naših krajih pomeni med 15. junijem in 15. avgustom, ko je sonce dovolj visoko na nebu, sicer velja jemati dopolnilni vitamin D). Študije jasno kažejo, da je nizka raven vitamina D dejavnik tveganja za COVID, težji potek bolezni in večje tveganje za smrt. Vitamin D3 v oljnih kapsulah se boljše absorbira kot tisti v tabletah, zato predstavlja odličen vir dopolnilnega vitamina D, če nimate možnosti sončenja ali pa je vaša krvna raven vitamina D ekstremno nizka. V prihodnjih poglavjih bomo podrobneje navedli podatke o odmerkih in o tem, kako preveriti svoje krvni ravni vitamina D in druge laboratorijske preglede, ki vam lahko koristijo.

Pijte veliko tekočine, predvsem vodo in ne pijač bogatih s sladkorjem in dodatki. To je ključ do dobrega delovanja vašega imunskega sistema in ohranjanje kondicije vašega organizma, da se bo lažje ubranil virusa. Ustrezna hidracija je bistvenega pomena. Količina potrebne tekočine je odvisna od telesne teže, vendar je dobro merilo barva vašega urina, ki naj bi bil idealno barve svetle slame.

Če je vaš urin temno rumene ali zlate barve, to pomeni, da vode zagotovo ne pijete dovolj. Če je vaš urin brezbarven, je popijete preveč, kar lahko povzroči mineralno neravnovesje in omotičnost.

Zagotovo se pogovorite s svojim zdravnikom o povečanju uživanja vitaminov in mineralov, ki krepijo vaš imunski sistem. To so vitamin D, vitamin C, vitamin E, cink, selen in drugi, ki vam jih bo priporočil zdravnik.

Glede vročine oz. povišane telesne temperature: Pomembno je vedeti, da je **vročina tako opozorilni znak za vnetje, ki je lahko nevarno, kot tudi eden od obrambnih mehanizmov našega organizma**. Zato se tudi vsi zdravniki ne strinjajo, da je potrebna terapija za vsako povišano telesno temperaturo, saj lahko kaže na super-vnetje, ki zahteva agresivno zdravljenje z antibiotiki, ne zgolj zdravila za znižanje temperature.

Ob visoki vročini lahko izvajamo terapijo z acetaminofenom, ibuprofenom in/ali ledenimi obkladki. Uporaba slednjih je preprosta in dobra možnost zniževanja in ohrananja znižane temperature. Vrećko napolnite z ledom in si jo položite na hrbet, trebuh ali na bok.

Acetaminofen povzroča stranski učinek oksidacijskega stresa v jetrih. Neka znanstvena študija navaja tudi, da lahko povzroča zmanjšano nasičenost kisika v krvi.

Ena od možnosti je izmenjavanje ibuprofena in acetaminofena vsakih 4-6 ur. Na primer, ob 12-ih vzemite ibuprofen, nato pa, če je vročina še vedno prisotna, ob 18-ih vzemite acetaminofen. Pazite, da ne presežete na embalaži navedenega najvišjega dnevnega odmerka.

Ali naj se testiram za COVID?

Glede testiranja upoštevajte navodila NIJZ in ekspertne skupine za COVID. Ali naj se testirajo vsi ali zgolj tisti, ki kažejo simptome? Ali so testi natančni, in kaj se zgodi, če je rezultat pozitiven, a ne zaznavate simptomov? Ali naj grem v karanteno? S temi vprašanji nas bombradirajo mediji vse od izbruha COVID-a.

Glede na to, da je zgodnje zdravljenje COVID-a tako pomembno, se mnogi zdravniki odločajo za zdravljenje pacientov ob prisotnosti kliničnih simptomov, upoštevaje dejavnike tveganja in druge objektivnih pokazateljev, ko katerih so prišli s pregledom ali analizo krvi, da ne bi zgrešili ’časonega okna priložnosti’ za zgodnje zdravljenje, in čakali nekaj dni na rezultat testiranja za COVID.

To je vsekakor modra odločitev, saj so testi občasno težje dostopni, na rezultat pa je potrebno čakati več dni. Poleg tega je zanesljivost teh testov resen problem. Znani so primeri pacientov, pri katerih je bil test negativen, a so zaradi jasno izraženih glavnih simptomov kovidne bolezni nujno potrebovali takojšnje zdravljenje. V primeru, da imate glavne simptome kovidne bolezni, vaš rezultat testa pa je negativen, večina zdravnikov priporoča zgodnje zdravljenje v izogib morebitni hospitalizaciji.

Znanih je več različnih vrst testov:

1. **Diagnostični testi**: “antigenski” test in “molekularni” test. Antigenski test zaznava določene beljakovine na površini virusa, molekularni test, imenovan tudi RT-PCR ali rRT-PCR pa zaznava delce virusnega genetskega materiala. PCR testi z visokim številom ciklov pogost zaznajo ne-kužne virusne fragmente namesto aktivne okužbe s SARS-CoV-2.

2. **Test na protitelesa**: (po prebolelem COVID-u): S tem testom iščemo protitelesa, ki jih je ustvaril naš imunski sistem v odgovor na okužbo, denimo virusno obolenje. Protitelesa pomagajo premagovati okužbe, saj si protitelesa ’zapomnijo’, kako izgleda nek organizem, ki povzroči okužbo, s čemer pomagajo našemu organizmu v boju proti podobnim okužbam v prihodnje.

Testi na protitelesa se ne uporabljajo za diagnosticiranje aktivne okužbe. Ta test razkrije zdravniku, da ste preboleli bolezen in ste vzpostavili imunost. Običajni testi na protitelesa niso specifični za COVID. Pri ljudeh se lahko izraža podobni protitelesni odziv na druge virusne okužbe, kot denimo na koronavirus, ki povzroča navadni prehlad ali celo na virus gripe. Ta test nam lahko pove zgolj to, da smo imeli virusno okužbo, ne pa tudi za kateri specifični virus gre.

3. **Test na imunske celice** (T celice), ki je še v razvoju, označuje spomin na pretekle okužbe in sposobnost ustvarjanja imunskega odziva. Ta test je dostopen z dovoljenjem za uporabo v sili.

Torej, ali se morate testirati, ko se pojavijo simptomi COVID? To je izbira, ki jo imate na voljo s svojim zdravnikom. Če se boste odločili za test, je dobro poznati njihove pomanjkljivosti in omejitve.

Kakorkoli že, če se pojavijo simptomi, je ključnega pomena zgodnji pregled pri zdravniku in njegova ocena, ali spadate v skupino ljudi z visokim tveganjem, ki potrebuje zgodnje zdravljenje, da se zmanjša tveganje za hospitalizacijo ali resne zaplete.

Priporočamo vam upoštevanje korakov za ohranjanje zdravja, ki jih navajamo v tej brošuri, da se, kolikor je to možno, izogibate bolnih ljudi, in se seznanite z možnostmi zgodnjega domačega zdravljenja.

Zgodnje zdravljenje je ključ do uspeha

Poskrbite za zgodnje zdravljenje in se zanesite predvsem nase. Vsi v tej brošuri sodelujoči zdravniki prihajamo iz prvih zdravniških vrst ambulantnega zdravljenja bolnikov s prvimi znaki kovidne bolezni. Študije v ZDA in mnogih drugih državah po svetu jasno kažejo, da imajo bolniki, ki so deležni zdravljenja v prvih petih dneh odpojava prvih simptomov, boljše izglede, če so posežejo po kombinaciji zdravil, ki jih navaja spodnji protokol. Ob izostanku zgodnjega zdravljenja beležijo 12% smrtnost pri tistih, ki potrebujejo dodatni kisik, in celo 40% pri tistih, ki potrebujejo intenzivno nego. Te stopnje smrtnosti so nesprejemljivo visoke. Na podlagi naših izkušenj smo prišli do spoznanja, da lahko stopnje smrtnosti občutno znižamo z zgodnjim, ambulantnim zdravljenjem bolnikov z visokim tveganjem, ki so starejši od 50 let in eno spremljajočo boleznijo ali več njih.

Ne bojte se obiskati zdravnika, urgence ali nujne medicinske pomoči. Ne pozabite, da je naloga zdravnikov, da vam pomagajo in vam pridejo naproti. Nikar ne čakajte do konca, ker bo lahko prepozno.

Koraki, ki vas čakajo:

1. Bodite proaktivni.
2. Natisnite si protokol zdravljenja, ki ga najdete v naslednjem poglavju.
3. Preučite, katera zdravila so navedena v protokolu, in kdaj najboljše delujejo. Marsikatero od njih že poznate. Gre za običajna zdravila proti virusom, proti vnetjem in proti krvnim strdkom.
4. Za telefonski razgovor s svojim zdravnikom poskrbite še preden zbolite.
5. Poizvedite, ali vas je vaš zdravnik pripravljen zdraviti po navodilih tega strokovno recenziranega in objavljenega protokola, ki so ga skupa pripravili strokovnjaki vodilnih ameriških in italijanskih zdravstvenih centrov.
6. Če vas vaš zdravnik ni pripravljen zdraviti po navodilih tega protokola, ali se ne počuti sposobnega zdraviti vaše kovidne bolezni, si kar takoj poiščite takšnega, ki je pripravljen in se čuti sposobnega. Poiščite si takšnega, ki je pripravljen zdraviti vaš COVID skladno z agresivnim načrtom, ki ga najdte v naslednjem

poglavju. Viri za zdravnike iz ZDA so navedeni v DODATKU II. Potrebujete namreč zagovornika zagovornika, ki se bo potrudil, da se čim prej postavite na noge.

7. Pristop “čakanja in opazovanja” ne zadostuje pri pacientih z visokim tveganjem (torej tistih nad 50-im letom z eno ali več spremljajočo bolezijo). “Čakanje in opazovanje” je dejavnik, ki je v ZDA prispeval k visoki stopnji smrtnosti. Države z najnižjo stopnjo smrtnosti so tiste, ki zdravilo bolnike zgodaj na njihovem domu z zdravili iz tega protokola.

8. Naše medicinsko spoznanje o tem, kako zdraviti COVID, se spreminja in izboljšuje iz dneva v dan, zatorej ne oklevajte in si poiščite strokovno pomoč takoj ob pojavu prvih simptomov.

Kaj lahko pričakujete od konzultacije s svojim zdravnikom

Marsikateri od sodelujočih zdravnikov je pozval svoje paciente k izpolnjevanju vprašalnika in/ali razpredelnice simptomov, s katerima je natančno opisal svojo bolezen in njeno trajanje. Glej COVID SEZNAM DEJAVNIKOV TVEGANJA in PREGLEDNICA POTEKA IN ZDRAVLJENJA COVIDNE BOLEZNI v DODATKU III. Natisnite si ju in uporabite za beleženje vaših simptomov in napredovanja bolezni. Koristila bosta kateremukoli zdravniku, ki ga boste obiskali.

Zabeležite življenjske znake, kot so krvni tlak, pulz, višina, teža, indeks telesne mase, raven krvnega kisika. Morda bo potrebno tudi testiranje za COVID. Sodelujoči zdravniki običajno ne čakajo na rezultate testa in pričnejo z zdravljenjem, če je potrebno po njihovi zdravniški presoji, glede na simptome in dejavnike tveganja, nemudoma pričeti s terapijo.

Morda vas bo zdravnik napotil šena kakšen drug test, denimo katerega od naslednjih:: presnovni profil za glukozo, elektrolite, jetrne encime, itn., polno krvno sliko, pa C-reaktivni protein (splošni marker vnetij); D-Dimer (marker tveganja za krvne strdke); raven 25-OH vitamina D, raven serumskega cinka in feritin.

Morda vas bo napotil še na dodatne specialistične laboratorijske preizkave, kot denimo za markerje možnega napada srca, če bo zdravnik ocenil, da so potrebni.

Nekateri zdravniki priporočajo EKG za preveritev srčnega ritma in morebitne druge abnormalnosti. Zdravnik, ki ga skrbijo morebitne poškodbe pljuč ali prisotnost pljučnice lahko odredi rentgensko slikanje prsnega koša.

Večina sodelujočih zdravnikov priporoča svojim pacientom naprstno napravo za merjenje nasičenosti krvi s kisikom, imenovano oksimeter, ki se jo lahko kupi v lekarni ali na spletu od 20 EUR naprej.

Naslednji obiski zdravnika (osebno ali po telefonu) so običajno 3, 5 ali 7-10 dni po pričetku zdravljenja, kasneje pa v presledkih, ki jih določi zdravnik glede na pacientov odziv na zdravljenje in dejavnike tveganja.

3. poglavje

VODNIK V ZGODNJE DOMAČE ZDRAVLJENJE, KOT GA PRIPOROČAJO NAŠI ZDRAVNIKI

V državah po svetu so zdravniki spoznali, da zgodnje domače zdravljenje bolnikov s COVID-om ob pojavu prvih simptomov, vodi k boljšim izidom in dramatično nižji stopnji smrtnosti, kot v primeru, da zdravniki pošljejo paciente domov na čakanje, dokler ne zbolijo do takšne mere, da potrebujejo hospitalizacijo, intenzivno nego, priklop na ventilatorje in ob odpovedi ledvic celo dializo.

Smrtnost bolnišničnega zdravljenja kritično bolnih pacientov je veliko večja, veliko večje pa je tudi tveganje za dolgoročne pljučne, srčne, nevrološke in druge zaplete tistih, ki jim uspe preživeti.

Domače zdravljenje/nega je smiselno še iz drugega razloga: zmanjšuje širjenje bolezni, saj je COVID-19 zelo nalezljiv virus. Telefonska medicina omogoča varnejši pristop k oddaljenem ovrednotenju pacientovega stanja, oceno njegovih simptomov in življenjskih znakov (katere brez težav lahko izmerimo tudi doma). Ob današnji tehnologiji bolnim pacientom ni več potrebno osebno prihajati v zdravnikovo ordinacijo in s tem povzročati nevarnost, da bi okužili druge.

Prednosti domačega zdravljenja:

- Domača nega je varnejša saj zmanjša tveganje za okužbo s strani obolelih v bolnišnici.
- Domača nega poleg tega omogoča stike z drugimi člani družine, s tem pa njihovo ljubezen in podporo. Prav grozljivo je ležati v bolnišnici s težko boleznijo, še huje pa, ko nas ne morejo obiskovati svojci.
- V domači negi lahko hitro uporabimo splošno dostopna, poceni, generična oralna zdravila in se izognemo tveganim intravenskim zdravilom, ki jih potrebujejo kritično bolni v bolnišnicah.
- Zdravniki lahko na pacientovem domu predpišejo tudi terapijo s koncentratorjem kisika, ki jih lahko zagotavlja zdravstveni sistem. Koncentratorje kisika se lahko kupi na zdraviški recept na spletu ali od lokalnih dobaviteljev že za nekaj sto evrov.
- Vse modalitete zdravljenja, ki se izvajajo v bolnišnicah, razen uporabe mehanskih ventilatorjev, se lahko izvajajo tudi na pacientovem domu, in sicer hitreje in bolj prilagojene individualnim potrebam pacienta.
-

Včasih se je modro osredotočiti se na temeljna načela medicine:

- Širjenje virusa omejujemo doma z natančnimi dezinfekcijskimi postopki.
- Za zdravljenje specifičnih problemov, ki jih povzroča COVID-19, koristimo zdravila na recept in prehranska dopolnila.
- ZDRAVIMO ZGODAJ, saj pri okužbah takrat zdravila delujejo najboljše. Nobeno od znanih farmacevtskih zdravil ne deluje tako dobro v kritičnih, poznih fazah kovidne bolezni.
- Zdravljenje lahko pričnemo z ustreznimi zdravili ob pravem času, glede na potrebe pacienta.
- Vedno smo pripravljeni na intenzivno zdravljenje s celotno kombinacijo zdravil, da preprečimo kritični razvoj bolezni.

Dostopna zdravila in njihova nova namembnost: Razlogi za kombiniranje zdravil na recept

Bolezen COVID-19 lahko zelo hitro postane zelo resno in nepredvidljivo obolenje. Medtem, ko do kritičnega obolenja ne pride pri vsakomur, pa ni možno predvideti, pri kom bo do tega prišlo in kako hitro.

To nepredvidljivost in hitro napredovanje pri COVID-u povzročata DVA odziva na virus SARS-CoV-2 v telesu, ki sta veliko hujša od sezonske gripe:

- **Prekomern vnetni odziv**, ki povzroči poškodbe ključnih organov. V njegovi najhujši obliki ga imenujemo citokinska nevihta.
- **Prekomeren odziv v obliki krvnih strdkov**, ki vodi v nastanek številnih krvnih strdkov (trombov= v pljučih, možganih, ledvicah, črevesju in drugih ključnih organih. Ti krvni strdki lahko pri COVID-u nastanejo tako v venah kot tudi arterijah, kar je zelo nenavadno in potencialno smrtonosno, če ne zdravimo dovoj hitro.

Ta edinstvena vrsta škode, ki jo lahko povzroči COVID pomeni, da moramo hitro uporabiti kombinacijo zdravil na recept, da bi preprečili te nevarne učinke. Uporaba teh zdravil, ki jih obravnavamo v tem vodniku, mora biti klinično upravičena, nujna, predstavljati ustrezno 'alternativno' rabo teh izdelkov. "Alternativna" raba starejših farmacevtskih zdravil za nove namene se odvija vsak dan v zdravniških ordinacijah po celem svetu.

Dejstvo namreč je, da se kar nekako 20% od vseh receptov v ZDA piše za "alternativne" namene uporabe, če zdravnik oceni, da bo njihov učinek koristil njegovim pacientom. Ta povsem enak model se izvaja med pandemijo COVID-a, ko iščemo načine pomoči ljudem pri premagovanju bolezni in rešujemo življenja.

Kot pri vsakem drugem predpisanem zdravilu, se tudi pri teh priporoča seznanitev z varnostnimi informacijami in navodili, ki se nahajajo v embalaži, preden lahko ocenite tveganje in koristi posameznega zdravila.

Osnovne skupine zdravil na recept in drugih terapij, ki se koristijo pri COVID-19:

- Kombinacijo protivirusnih zdravil se prične jemati takoj o pojavu prvih simptomov.
- Dopolnjujemo jih z zdravili za umirjanje vnetij, kot so kortikosteroidi (imenovani tudi imunomodulatorji).
- Nadalje je potrebno pričeti z antikoagulantno terapijo, da se preprečuje nastajanje krvnih strdkov, ki lahko povzročijo možgansko kap, srčni infarkt, odpoved ledvic in smrt.
- Podporna terapija s prehranskimi dopolnili vključuje cink, vitamin D, vitamin C, napitke z elektroliti, kot denimo Pedialyte in podobne.
- Ne pozabite na dopolnjevanje kisika, denimo s koncentratorjem kisika. Morda ga krije celo zdravstveno zavarovanje, če vam recept zanj napiše zdravnik.

I. Antivirusna sredstva:

Z njimi je potrebno **pričeti hitro na PRVI STOPNJI (1-5 dan):**

Simptomi vključujejo boleče grlo, poln nos, utrujenost, glavobol, bolečine po telesu, izgubo okusa in vonja, izgubo teka, slabost, drisko, vročino.

Ta zdravila preprečujejo, da bi virus (1) prodrl v celice, in (2) da bi se znotraj celic razmnoževal, poleg tega pa zmanjšujejo invazijo bakterij v sinuse in pljuča:

- *Hydroxychloroquine (HCQ) z azitromycinom (AZM) ali doxycyclinom
  ALI
- Ivermectin z azithromycinom (AZM) ali doxycyclinom

Katerakoli od zgornjih kombinacij mora vključevati še cinkov sulfat ali glukonat, poleg tega pa še dopolnilni vitamin D in vitamin C. Nekateri zdravniki priporočajo tudi dopolnjevanjem z B kompleksom.

Cink je bistven, saj pomaga preprečiti razmnoževanje virusa. Hydroxychloroquine je prenašalec cinka V NOTRANJOST celic, kjer cink opravi svojo nalogo.

II. Protivnetna sredstva - kortikosteroidi (“steroidi”): Oralni in nebulizirani.

S protivnetnimi sredstvi pričnemo na DRUGI STOPNJI (3-14 dan) za umirjanje vnetij, ki povzročajo dodatno škodo pljučam in ključnim organom. Simptomi vključujejo vse hujši kašelj, oteženo dihanje, pritisk ali bolečine v prsnem košu.

Ker vnetje poškoduje sapnik, to poslabša normalno izmenjavo kisika in ogljikovega dioksida, zaradi česar upade nasičenost krvi s kisikom. To bolniki občutijo kot težave z osredotočanjem, omotičnost, zmedenost, težave s koncentracijo, pomanjkanje energije in hudo izčrpanost.

Prekomeren protivnetni odziv pri COVID-u še dodatno poveča tveganje za krvne strdke.

Zdravila na recept in druga sredstva, ki jih dodamo tistim na PRVI STOPNJI:

- nebulizirani budesonid za boljši prenos v pljuča in zmanjšanje vnetja
- oralni prednisone, methylprednisolon, dexamethasone
- colchicine – ravno tako umirja vnetja
- aspirin 325 mg za umirjanje vnetij in zmanjšanje tveganja nastajanja krvnih strdkov
- za izboljšanje nasičenosti krvi s kisikom bo morda potreben koncentrator kisika

III. Antikoagulanti oz. zdravila za redčenje krvi TRETJA STOPNJA (7 dan in naprej):

Simptomi, značilni za drugo stopnjo, se okrepijo. Težave z dihanjem postanejo ekstremne, vsebnost kisika v krvi drastičnu upade, poveča se nevarnost možganske kapi ali srčnega infarkta. Na tej točki govorimo o kritičnem obolenju.

Zdravila, ki jih dodamo že omenjenim na prvi in drugi stopnji, zdaj vključujejo:

- Aspirin 325 mg, razen če vam to odsvetuje vaš zdravnik

- In/ali injekcije heparina nizke molekularne mase (npr. enoxaparin [Lovenox])

ALI

- apixaban (Eliquis), ali rivaroxaban (Xarelto), ali dabigatran (Pradaxa) ali edoxaban (Savaysa) v standardnih odmerkih od 5 do 30 dni.

Če ti dodatni koraki ne prinesejo izboljšanja, ali pa postane bolnik nestabilen, nemudoma pokličite 112 za internistično prvo pomoč, kjer vas bodo pregledali in morebiti sprejeli v bolnišnico, kjer bodo lahko zagotovili bolj agresivna intravenska zdravila (denimo remdesivir, Regeneron in druga) in intenzivnejšo ventilacijo.

IV. Vitamini, dopolnila in kisik

- **Cinkov sulfat, glukonat ali citrat.** Te oblike so dostopne tako v lekarnah, trgovinah z zdravo hrano in v spletnih trgovinah. 220 mg cinkovega sulfata zagotavlja 50 mg elementarnega cinka, kar predstavlja ustrezen protivirusni odmerek. Cink v obliki pikolinata se ne priporoča, saj so raziskave izpred 20 let razkrile poškodbe jeter in tumorje. Na podlagi teh raziskav je nemška Komisija E, ki regulira prehranska dopolnila, ki jih uporabljajo v nemškem zdravstvu, to obliko cinka prepovedala.
- **Vitamin D3**, predvsem v oljni obliki v kapsulah za boljšo absorbcijo. Priporočeni odmerek za protivirusne koristi je od 5000 IU na dan ali več v trajanju 5-30 dni
- **Vitamin C** z bioflavonoidi za antioksidantne, protivnetne učinke. Priporočeni odmerki naših sodelujočih zdravnikov gredo od 1.000 mg (1 gram) en- do dvakrat na dan do 4- in večkrat na dan.
- Pa še beseda o **quercetinu**. Nekateri zdravniki priporočajo to dopolnilo za spopad z virusnimi obolenji, saj deluje quercetin kot cinkov ionofor, se pravi prenašalec cinka v celice. Je veliko manj močan transporter cinka od HCQ in ne dosega dovolj velike koncentracije v pljučnih celicah, kot jo HCQ. Quercetin lahko pomaga zmanjšati tveganje za virusno obolenje, v primeru, da ste v bistvu zdravi. A ni dovolj močan, da bi lahko nadomestil HCQ pri zdravljenju COVID-a, ko so enkrat simptomi že prisotni, po drugi strani pa se ne absorbira dovolj dobro v pljučno tkivo, če ne zaužijemo dovolj velikih odmerkov (3-5 gramov na dan), kar lahko povzroči črevesno nelagodje z drisko.

Dr. Peter McCullough je vodil skupino mednarodnih strokovnjakov in objavil prvi protokol ambulantnega zdravljenja bolnikov s COVID-19, ki je temeljil na njegovih izkušnjah zdravljenja pacientov v ZDA in Italiji, ki ga potrjuje vse več medicinske literature našega časa. Prvotni protokol je objavil spoštovani strokovni reviji *American Journal of Medicine*, dopolnjeni povzetek pa v *Reviews in Cardiovascular Medicine*.

Če ste sami ali vaši bližnji izpostavljeni tveganju za COVID-19, si preberite prispevek dr. McCullougha in sodelavcev iz vodilnih ameriških in italijanskih zdravstvenih centrov.

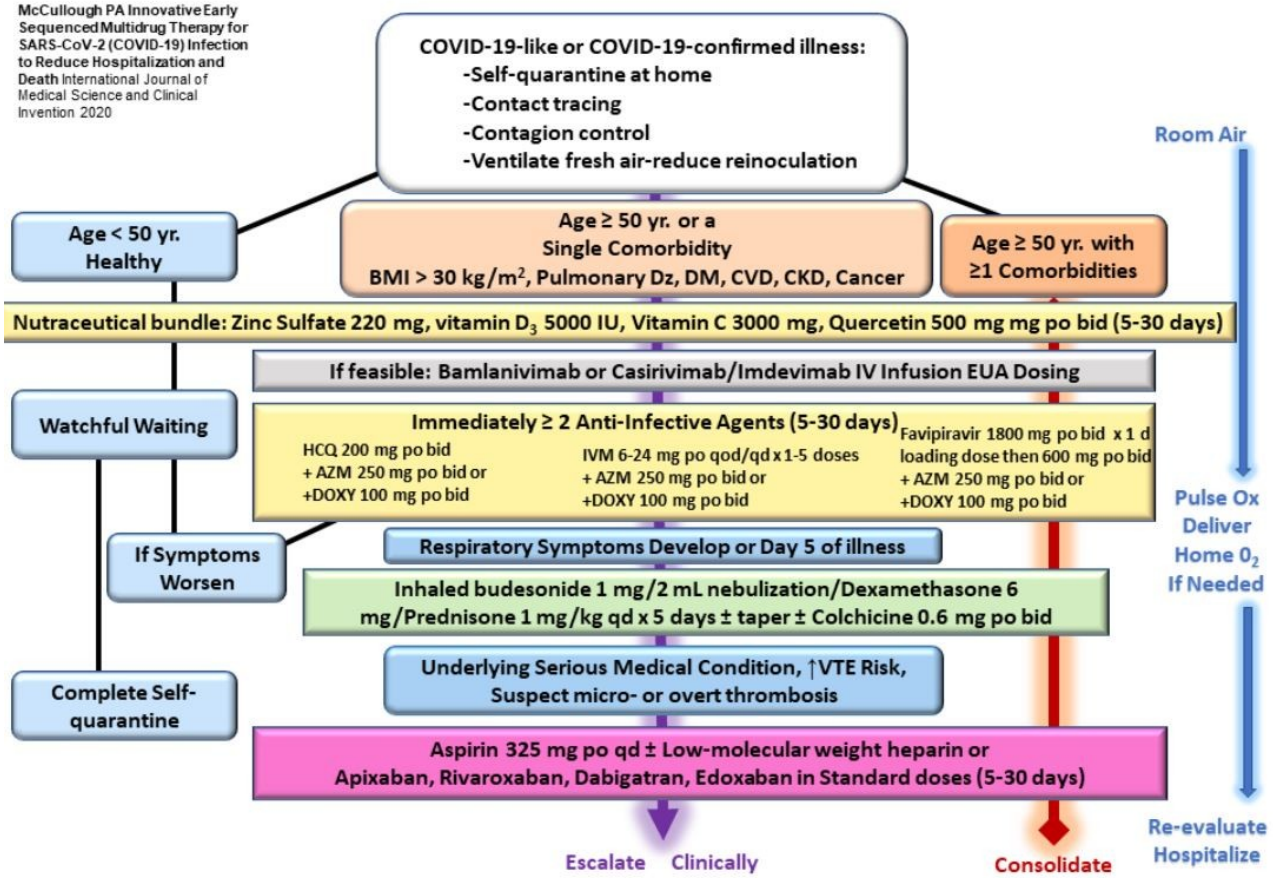
Natisnite si ta navodila za svojo prihodnjo rabo, kopijo le-teh pa odnesite svojemu zdravniku, da se bosta lahko pogovorila o vaših možnostih zdravljenja.

Za več informacij o varnosti HCQ in drugih zdravil, ki so vključena v naš protokol zdravljenja, si poglejte spletno stran c19study.com, kjer lahko najdete povzetek več kot 278 študij zdravljenja na podlagi HCQ, ki so še posebej pozitivne, če HCQ uporabimo v prvih nekaj dneh po pojavu simptomov COVID-19, kot sicer izrecno svetuje naš protokol zdravljenja.

Spletna stran C19study.com vsebuje tudi študije o koristih ivermectina, REGEN-COV, vitamina D, fluvoxamina, raztopine povidone-iodine, colchicina in mnogih drugih sredstev.

Za nadaljne informacije glej AAPS zbir prispevkov in študij o COVID-19.

*FDA svari pred uporabo hydroxychloroquina ali chloroquina pri COVID-19 izven bolnišnic ali v medicinskih študijah, in navaja tveganje za probleme z motnjo srčnega ritma. Prosimo, posvetujte se s svojim zdravnikom.



BMI=body mass index, Dz=disease, DM=diabetes mellitus, CVD=cardiovascular disease, CKD=chronic kidney disease, yr=years, HCQ=hydroxychloroquine, AZM=azithromycin, DOXY=doxycycline, IVM=Ivermectin, VTE=venous thrombo-embolic, EUA=Emergency Use Authorization (U.S. administration)

REVIEW McCullough PA, Kelly RJ, Ruocco G, Lerma E, Tumlin J, Wheelan KR, Katz N, Lepor NE, Vijay K, Carter H, Singh B, McCullough SP, Bhambi BK, Palazzuoli A, De Ferrari GM, Milligan GP, Safder T, Tecson KM, Wang DD, McKinnon JE, O'Neill WW, Zervos M, Risch HA. Pathophysiological Basis and Rationale for Early Outpatient Treatment of SARS-CoV-2 (COVID-19) Infection. Am J Med. 2020 Aug 7:S0002-9343(20)30673-2. doi: 10.1016/j.amjmed.2020.07.003. Epub ahead of print. PMID: 32771461; PMCID: PMC7410805.

THE AMERICAN JOURNAL of MEDICINE®

Pathophysiological Basis and Rationale for Early Outpatient Treatment of SARS-CoV-2 (COVID-19) Infection

Peter A. McCullough, MD, MPH,[a,b,c] Ronan J. Kelly, MD,[a] Gaetano Ruocco, MD,[d] Edgar Lerma, MD,[e] James Tumlin, MD,[f] Kevin R. Wheelan, MD,[a,b,c] Nevin Katz, MD,[g] Norman E. Lepor, MD,[h] Kris Vijay, MD,[i] Harvey Carter, MD,[j] Bhupinder Singh, MD,[k] Sean P. McCullough, BS,[l] Brijesh K. Bhambi, MD,[m] Alberto Palazzuoli, MD, PhD,[n] Gaetano M. De Ferrari, MD, PhD,[o] Gregory P. Milligan, MD, MPH,[a] Taimur Safder, MD, MPH,[a] Kristen M. Tecson, PhD,[b] Dee Dee Wang, MD,[p] John E. McKinnon, MD,[p] William W. O'Neill, MD,[p] Marcus Zervos, MD,[p] Harvey A. Risch, MD, PhD[q]

[a]Baylor University Medical Center, Dallas, Tex; [b]Baylor Heart and Vascular Institute, Dallas, Tex; [c]Baylor Jack and Jane Hamilton Heart and Vascular Hospital, Dallas, Tex; [d]Cardiology Division, Regina Montis Regalis Hospital, Mondovì, Cuneo, Italy; [e]Christ Advocate Medical Center, Chicago, Ill; [f]Emory University School of Medicine, Atlanta, Ga; [g]Johns Hopkins School of Medicine, Baltimore, Md; [h]Cedars Sinai Medical Center, Los Angeles, Calif; [i]Abrazo Arizona Heart Hospital, Abrazo Health System, Phoenix, Ariz; [j]Carter Eye Center, Dallas, Tex; [k]Cardiorenal Society of America, Phoenix, Ariz; [l]University of Texas McGovern Medical School, Houston, Tex; [m]Bakersfield Heart Hospital, Bakersfield, Calif; [n]University of Siena, Le Scotte Hospital Viale Bracci, Siena, Italy; [o]University of Torino, Torino, Italy; [p]Henry Ford Hospital, Detroit, Mich; [q]Yale University School of Public Health, New Haven, Conn.

Specialties

Internal Medicine
Critical Care
Nephrology
Cardiology
Electrophysiology
Infectious Diseases
Ophthalmology
Epidemiology
Biostatistics

ABSTRACT

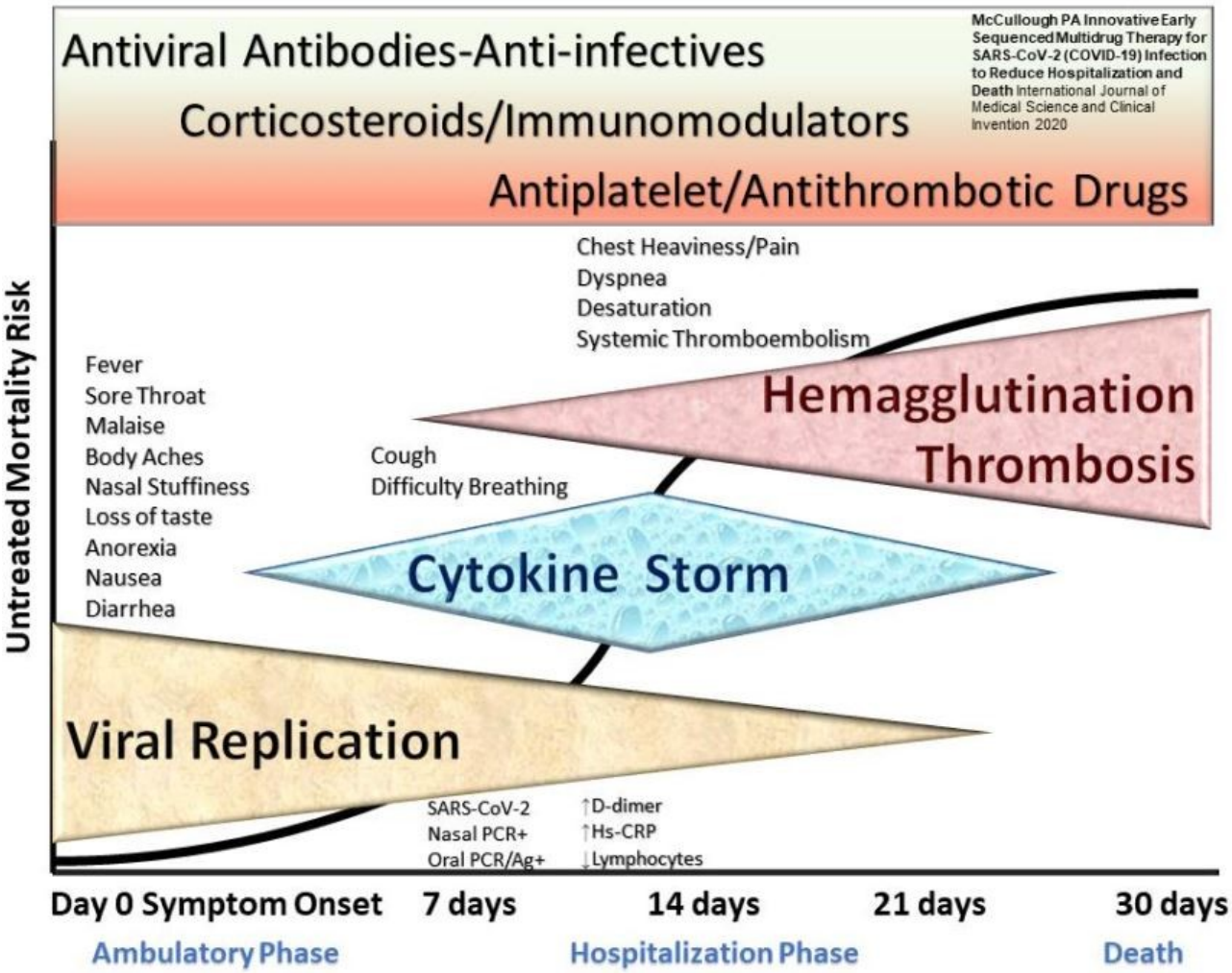
Approximately 9 months of the severe acute respiratory syndrome coronavius-2 (SARS-CoV-2 [COVID-19]) spreading across the globe has led to widespread COVID-19 acute hospitalizations and death. The rapidity and highly communicable nature of the SARS-CoV-2 outbreak has hampered the design and execution of definitive randomized, controlled trials of therapy outside of the clinic or hospital. In the absence of clinical trial results, physicians must use what has been learned about the pathophysiology of SARS-CoV-2 infection in determining early outpatient treatment of the illness with the aim of preventing hospitalization or death. This article outlines key pathophysiological principles that relate to the patient with early infection treated at home. Therapeutic approaches based on these principles include 1) reduction of reinoculation, 2) combination antiviral therapy, 3) immunomodulation, 4) antiplatelet/antithrombotic therapy, and 5) administration of oxygen, monitoring, and telemedicine. Future randomized trials testing the principles and agents discussed will undoubtedly refine and clarify their individual roles; however, we emphasize the immediate need for management guidance in the setting of widespread hospital resource consumption, morbidity, and mortality.

© 2020 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license. (http://creativecommons.org/licenses/by-nc-nd/4.0/) • The American Journal of Medicine (2020) 000:1–7

KEYWORDS: Ambulatory treatment; Anticoagulant; Anti-inflammatory; Antiviral; COVID-19; Critical care; Epidemiology; Hospitalization; Mortality; SARS-CoV-2

US/Italian Multicenter Collaboration

Academic Medical Centers
Public Heath
Integrated Health Systems
Community Practice
Biotech Industry



4. poglavje

Nove možnosti preventive in zdravljenja

Monoklonska protitelesa

Naravna protitelesa proizvaja telo v odgovor na tuje organizme, kot so virusi in bakterijea. Sintetična oz. umetna protitelesa pa so tista, ki jih proizvedejo v laboratoriju in naj bi posnemala tista, ki jih lahko proizvede telo. Ko takšne sintetične spojine, ki jim rečemo “monoklonska protitelesa”, proizvedejo v laboratoriju in so namenjena novemu zdravljenju v medicini, jih patentirajo kot nova terapevtska sredstva. To so takšne vrste eksperimentalnih sintetičnih monoklonskih protiteles, kakršne so opisovali v medijih, ki jih je prejel predsednik Trump v okviru svojega zdravljenja COVID-19 v bolnišnici Walter Reed.

Podjetje Regeneron je pričelo proizvajati zdravilo imenovano REGEN-COV2, ki je kombinacija dveh “monoklonskih protiteles”, ki so namenjeni boju proti virusu SARS-CoV-2, ki povzroča bolezen CoVID-19.

Pri razvoju REGN-COV2 so znanstveniki podjetja Regeneron uporabili protitelesa iz miši, ki so jih gensko spremenili za človekov imunski sistem, kot tudi protitelesa, ki so jih našli pri ljudeh, ki so preboleli COVID-19.

Končna učinkovitost tega novega Regeneronovega zdravljenja se bo pokazala v prihodnosti, saj je še vedno v eksperimentalni fazi in znjim izvajajo klinične raziskave. Dostopno je v različnih ustanovah z dovoljenjem za uporabo v sili. Daje se ga v obliki injekcije, zaželeno z intravensko infuzijo. Preverite pri svojem zdravniku, ali vam ga lahko predpiše in poizve, kje ga imajo.

Prebolevniška (konvalescentna) plazma

Prebolevniška plazma je serum iz krvi, ki so jo donirali ljudje, ki so imeli kužno bolezen, jo preboleli in so razvili protitelesa za ta kužni organizem, zaradi česar vsebuje ta protitelesa njihova kri, ki jo lahko v obliki prebolevniške plazme vbrizgamo intravensko v drugega bolnika s to boleznijo in s tem zdravimo okužbo. Prebolevniška plazma so

uporabljali med pandemijo gripe leta 1918, poleg tega pa v prvih destletjih 20. stoletja še za ošpice, mumps in poliomielitis. Ko je izbruhnila panedmija COVID-19, so začeli zdravniki razmišljati, da bi bila lahko to terapija, ki bi pomagala pri okrevanju bolnih.

Ameriška Uprava za hrano in zdravila (FDA) je prebolevniški plazmi za zdravljenje kovidnih bolnikov, podelila dovoljenje za uporabo v sili, in nekateri bolnišnični pacienti so je bili tudi deležni po intravenski poti. In vendar se ni izkazala pri preprečevanju napredovanja bolezni pri visoko-rizičnih pacientih s COVID-19, ki so jo prejeli v prvem tednu po pojavu simptomov. Tveganja za obolevnost za COVID-19 iz prebolevniške plazme niso preverili, a raziskovalci menijo, da je tveganje majhno, saj so darovalci popolnoma okrevali po okužbi.

Terapija s prebolevniško plazmo prinaša določeno tveganje, kot so alrgične reakcije, možne poškodbe pljuč in oteženo dihanje, ter možnost okužbe s HIV in hepatitisom B in C, čeprav je tveganje za te okužbe majhno, saj je donirana kri temeljito pregledana.

Možnosti preventive: Preventivna zdravila in cepiva

Vse od pojava virusa SARS-2, so se mediji osredotočali predvsem na razvoj cepiva, ki bo zaščitil ljudi, da bi se nalezli. In vendar je, poleg razvijanja cepiva, ki naj bi pomagalo preprečiti obolevanje za COVID-19, je v različnih državah po svetu v fazi oblikovanja, izvajanja in proučevanja več preventivnih protokolov.

Preventivni protokoli:

Preventiva zajema postopke, ki so usmerjeni v zmanjševanje tveganja za zbolevanje. To je temeljni pristop k preprečevanju bolezni, kot so malarija, herpes, HIV/AIDS in nekatere druge. Že zelo zgodaj med pandemijo COVID-19 so zdravniki v Indiji, Južni Koreji, na Japonskem, v Costa Rici, Turčiji in še v več drugih državah pričeli z uporabo varnega, široko dostopnega in zelo močnega proti-virusnega zdravila hidroksklorokin (HCQ) kot preventivno zdravilo proti COVID-19.

Indijski Svet za medicinske raziskave (ICMR) je marca 2020 objavil (osvežil maja 2020) državne smernice za Indijo z uporabo 400 mg HCQ enkrat tedensko za zdravstvene delavce, zdravnike, medicinske sestre, delavce prve pomoči, visoko rizične paciente, ter družinske člane tistih, ki so bili izpostavljeni ali pozitivni na testu za COVID-19. Države, ki so pristopile k razvejani preventivi in zgodnjemu zdravljenju s HCQ, imajo veliko nižjo stopnjo smrtnosti in hospitalizacij, od držav, v katerih preventivnih programov in zgodnjega zdravljenja z uporabo HCQ niso priporočali ali masovno izvajali.

Ekipa dr. McCullougha je v Dallasu izvedla študijo med svojimi zdravstvenimi delavci z uporabo preventivnih ukrepov s HCQ in razkrila, da so bili učinkoviti in varni, brez škodljivih srčnih epizod ali resnih stranskih učinkov.

Preventivni odmerki HCQ so veliko manjši, kot so odmerki, ki jih oboleli z trevmatoidnim artritisom, lupusom ali malarijo jemljejo vsak dan po več let. Ker so odmerki tako nizki, zdravilo pa se ne jemlje vsak dan, je tveganje za stranske učinke ekstremno nizko.

HCQ ima dolgo razpolovno dobo 22-tih dni, zato ga lahko dajemo le enkrat tedensko v trajanju 8-12 tednov, ali pa tudi dlje, če je nekdo nenehno izpostavljen COVID-u, kot denimo ljudje, ki delajo v bolnišnici. Novo poročilo, Zmanjševanje tveganja: Preventiva COVID-19 pred izpostavljenostjo obravnava preventivne ukrepe, ki so preprosti, prosto dostopni in poceni. V tem poročilu je HCQ predstavljen kot najboljši kandidat takšne preventivne strategije.

Preventivne prgrame, ki se razlikujejo po velikosti odmerkov in frekvenci doziranja, soustvarjalci tega vodnika redno priporočajo. Nekateri priporočajo protokol, ki ga je objavil Indijski Svet za medicinske raziskave (ICMR), drugi priporočajo 200 mg namesto 400 mg, spet tretji priporočajo doziranje na dva tedna namesto vsak teden, medtem ko nekateri predpisujejo HCQ za namen preventive celo samo enkrat na mesec.

Kot rezultat njegove varnosti in občutnega znižanja stopnje tveganja za obolevnosti s COVID-19, ti zdravniki pozivajo k bolj razširjenem izvajanju preventivnih protokolov s HCQ, ki so se tako dobro izkazali v drugih državah. Nekateri zdravniki prisegajo bolj na zdravilo proti parazitom, ivermectin , tako za preventivo, kot tudi zdravljenje. Sprva so priporočali odmerek 0,2 mg/kg, a so nekateri priporočali odmerke po 0,4 do 0,6 mg/kg. Ko bo na voljo več informacij, so bo tudi velikost odmerka verjetno spremenila.

Verjamemo, da je ob soočenju s svetovno zdravstveno krizo, potrebno razmišljati o pristopih, ki rešujejo življenja, in ki temeljijo na znanstveni logiki, razpoložljivih podatkih o varnosti in so klinično izvedljivi, četudi neizpodbitni rezultati še niso dostopni, saj še niso bile izvedene obsežnejše klinične študije.

Ravno tako verjamemo, da so preventivni protokoli najvarnejši in najbolj smotrn ukrep pomoči ljudem pri zmanjšanju tveganja, da zbolijo za COVID-19, ter lahko ohranimo odprte šole, podjetja in prostore druženja, da premagamo strah, si povrnemo našo svobodo živeti svoje življenje.

Cepiva

Vsa cepiva so prejela v ZDA s strani FDA 'Dovoljenje za uporabo v sili', verjetno pa bo temu kmalu sledila potrditev s strani FDA, čeprav dokončanje študij ni predvideno pred koncem leta 2022. Dve cepivi spadata v kategorijo mRNA, eno cepivo pa je vektorsko, vsa pa naj bi v telo vnesla gensko informacijo, ki naj bi v celicah izzvala proizvodnjo protiteles na virus SARS-CoV2 ("priklopno beljakovino"). Nato bi se nanjo naš imunski sistem odzval in vzpostavil odpornost na ta virus. Še več cepiv je v razvojni fazi.

Najpomembnejši zadržek pred potrditvijo cepiva za uporabo pri ljudeh je zagotovilo, da je cepivo varno in učinkovito. Razvoj varnih in nadzorovanih kužnih modelov za ljudi normalno zahteva več let večstopenjskega laboratorijskega testiranja, nato na živalih in končno na ljudeh. Mnogi zdravniki in znanstveniki so zaskrbljeni, saj proizvajalci cepiv ob podpori vlad pospešujejo ta proces na način, ki ne omogoča dovolj časa za izvedbo običajnih večstopenjskih laboratorijskih testov, ki vodijo v klinična testiranja na ljudeh.

Do sedaj še nobeno na RNA-temelječe cepivo nikoli ni bilo potrjeno za uporabo na ljudeh. Cepiva za RNA viruse so notorično velik izziv, njihov razvoj pa silno zapleten. Še vedno, po vseh teh letih od pojava AIDS-a v osemdesetih letih prejšnjega stoletja, nimamo cepiva za virus AIDS-a, ali koronavirus SARS-1, ki se je pojavil v letih 2002-2003, pa sta oba RNA virusa.

Bilo je kar nekaj poskusov ustvariti cepivo za koronavirus in druge respiratorne viruse, vendar nobeno od cepiv ni prestalo večstopenjskih laboratorijskih testiranj. Testiranje cepiva za SARS-1 iz leta 2003, denimo, je bilo opuščeno, saj je cepivo povzročalo po cepljenju pri testih na živalih po okužbi z naravnim virusom reakcije autoimunske preobčutljivosti.

Drug problem pa je, da virus SARS-CoV-2 že pokazal mnoge mutacije. Viruse se za preživetje namreč prilagajajo na okolje.

Celo najboljša cepiva proti gripi so le 30-60% učinkovita in se težko primerjajo z učinkovitostjo pri izboljšanju zdravstvenega stanja pri zgodnjem pričetku zdravljenja ambulantnih pacientov s COVID-19 z že predstavljenimi obstoječimi zdravili, ki dosegajo odstotke uspešnosti med 64% in celo nad 90%, kar razkriva več kot 100 najnovejših študij.

Zapozneli stranski učinki (npr. neplodnost, rak, avtoimunska obolenja) morda ne bodo vidni še leta. FDA je že objavila opozorila, ki se nanašajo na krvne srtdke, Guillain-Barré sindrom in miokarditis/perikarditis. Ti so morda res redki ali blagi, vendar moramo biti nanje pozorni, da lahko zagotovimo zgodnje zdravljenje. D-dimer in druge analize strjevanja krvi je potrebno budno nadzirati. Rahlo šibkost je potrebno jemati resno, saj lahko včasih zelo hitro napreduje v dihalno paralizo, ki zahteva mehanski ventilator. Pri diagnosticiranju vnetja srca je potrebno budno spremljati ravni troponina v krvi (encima, ki se sprošča ob poškodbah srčnih celic), izvajati ultrazvok ali MRI.

Paciente je potrebno informirati o potencialnih stranskih učinkih, le-te pa dosledno prijavljati ustreznim zdravstvenim organom.

V vse večjem številu se pojavljajo tudi okužbe med že cepljenimi, zato je tudi za cepljene treba predvideti terapevtske možnosti.

DODATEK I: Medicinski viri

Zgodnje domače zdravljenje Dr. Peter McCullough s sodelavci. Pregled algoritma s strani strokovne revije American Journal of Medicine in strokovnjakov

- Bela knjiga o HCQ: The Economic Standard

DODATEK II: SODELUJOČI in ZDRAVNIŠKI VIRI

- **Sodelujoči zdravniki**

  Stella Immanuel, MD, Family Physician rehobothmedicalcenter.com

  Lionel Lee, MD, FACOEP, Emergency Physician, Phoenix AZ; no website

  Peter A. McCullough, MD, MPH, FACP, FACC, FCCP, FAHA, FNKF, FNLA, FCRSA, Internist, Cardiologist and Epidemiologist

  Jane M. Orient, MD, Internist AAPSonline.org

  Sheila Page, DO, Neuromusculoskeletal Medicine, no website, retired

  Tom Reed, DPM, Foot and Ankle Surgeon, DAPBS, DABPM, FACFAS DrTomReed.com

  Elizabeth Lee Vliet, MD, Preventive & Climacteric Medicine ViveLifeCenter.com

- **Physician Resource List by State**
  aapsonline.org/covidearlytreatment

- Telemedicine Resources for COVID treatment
  www.c19protocols.com (click Facilities from menu)

  Medical and VIDEO Resources
  www.AAPSonline.org
  www.c19study.com
  www.CovidPatientGuide.com

DODATEK III: Primeri vprašalnikov za klinično sledenje COVID-19

- VIRUSNO OBOLENJE/COVID PRESEJALNI VPRAŠALNIK in SEZNAM DEJAVNIKOV TVEGANJA
- PREGLEDNICA POTEKA IN ZDRAVLJENJA COVIDNE BOLEZNI

VIRUSNO OBOLENJE/COVID PRESEJALNI VPRAŠALNIK

IME PACIENTA_____ DATUM:_____

Višina:_____ Teža:_____ Starost:_____Krvni tlak:_____ Pulz:_____RR: _____ O2%_____

❑ DA	❑ NE	1. Ste imeli vzadnjem času vročino nad 38,3° C ali se počutili vročični?
❑ DA	❑ NE	2. Ste v zadnjem času začeli kašljati ali pa se vam je obstoječi kašelj spremenil?
❑ DA	❑ NE	3. Ste imeli kratko sapo ali oteženo dihanje?
❑ DA	❑ NE	4. Ste v zadnjem času občutili mrzlico ali ponavljajoče tresavico z mrzlico?
❑ DA	❑ NE	5. Ste se v zadnjem času podnevi potili, kar ni bilo posledica telesnih naporov ali nočnega potenja?
❑ DA	❑ NE	6. Slabost, vzdraženo prebavo, bruhanje ali drisko?
❑ DA	❑ NE	7. Ste morda pred kratkim izgubili okus in voh?
❑ DA	❑ NE	8. So se vam pojavileali spremenile bolečine v mišicah ali sklepih?
❑ DA	❑ NE	9. Ste v zadnjem času občutili izgubo energije ali hudo izčrpanost?
❑ DA	❑ NE	10. Ste imeli v zadnjem času težave z osredotočanjem, spominom ali koncentracijo?
❑ DA	❑ NE	11. Ste v zadnjem času občutili kakšne druge gripi podobne simptome?
❑ DA	❑ NE	12. Ste v zadnjem času izgubili apetit ali shujšali?
❑ DA	❑ NE	13. Ste v zadnjih 14 dneh bili na področjih s pogostejšim COVID-19?
❑ DA	❑ NE	14. Ste bili v zadnjih 14 dneh v stiku s kom, ki je bil pozitiven na testu za COVID-19? Če ste bili, kdaj je to bilo? _____
❑ DA	❑ NE	5. Ali ste bili pozitivni na testu za COVID-19? Kdaj _____
❑ DA	❑ NE	16. Ali so vam diagnosticirali COVID-19?

(circle any that apply)		**SEZNAM DEJAVNIKOV TVEGANJA: ALI IMATE KATERO OD NAVEDENIH STANJ?**
❑ DA	❑ NE	Debelost, obolenje srca, prestani srčni infarkt, srčna aritmija, visok krvni tlak, prehodna ishemična motnja ali možganska kap?
❑ DA	❑ NE	Obolenje pljuč? (KOPB, astma, pljučna fibroza, cistična fibroza, kaj drugega?)
❑ DA	❑ NE	Obolenje ledvic? Vrsta:_____
❑ DA	❑ NE	Diabetes, presnovni sindrom/odpornost na insulin? Ali dobivate insulin? Da:_____ Ne:_____
❑ DA	❑ NE	Imate raka in se zdravite?
❑ DA	❑ NE	Imate kakšno avtoimunsko obolenje?
❑ DA	❑ NE	Ali redno jemljete kortikosteroidna zdravila?

© Vive! Life Center/Elizabeth Lee Vliet MD

PREGLEDNICA POTEKA IN ZDRAVLJENJA COVIDNE BOLEZNI

INITIAL SERVICE

DATUM_____

IME PACIENTA _____ ROJSTNI DATUM_____ SPOL_____

	Dan	1	3	5	7	KOMENTAR
1.	Vročina ali mrzlica 37,8° C ali višja					
2.	Kašelj					
3.	Kratka sapa					
4.	Izčrpanost					
5.	Bolečine v mišicah ali po telesu					
6.	Glavobol					
7.	Izguba okusa ali voha					
8.	Boleče grlo					
9.	Zamašen nos ali smrkavost					
10.	Slabost ali bruhanje					
11.	Driska					
12.	Pulz/nasičenost s kisikom (O_2)					
13.	Stranski učinki/Nova zdravila					

© Stella Emanuel MD

updated 2/2/2022

A Guide to Home-Based COVID Treatment

Step-By-Step Doctors' Plan That Could Save Your Life

Editors: Jane M. Orient, M.D. &
Elizabeth Lee Vliet, M.D.

A Guide to Home-Based COVID Treatment

Step-By-Step Doctors' Plan That Could Save Your Life

Senior Editor:

Jane Orient, MD, Internal Medicine Physician, Executive Director,
Association of American Physicians and Surgeons,
President, Doctors for Disaster Preparedness

Consulting Editor:

Peter A. McCullough, MD, MPH, FACP, FACC, FCCP, FAHA, FNKF, FNLA, FCRSA
Internist, Cardiologist, and Epidemiologist,
President, Cardiorenal Society of America

Editor/Writer:

Elizabeth Lee Vliet, MD, Preventive Medicine
Past Director, Association of American Physicians and Surgeons,
Member of AAPS Editorial Writing Team

Technical Editor:

Jeremy Snavely, Business Manager
Association of American Physicians and Surgeons

Disclaimer: This booklet does not provide individual medical advice or prescribe treatment but is provided as an educational service for patients and their families to know what options are available and widely used for many conditions. Patients should consult the physicians of their choice for individual medical evaluation and recommendations for treatment tailored to individual needs.

A Guide to Home-Based COVID Treatment

Step-By-Step Doctors' Plan That Could Save Your Life

Table of Contents

Chapter 1: Overview: SARS-CoV-2 Coronavirus and COVID-19 Illness
- What is a Coronavirus?
- How Deadly is COVID?

Chapter 2: I Have Flu-Like Symptoms: What Should I Do?
- What Should I Do First?
- Symptoms of COVID
- Immediate Home Care Recommendations
- Should I Get A COVID Test?
- Early Treatment Is Key to Success
- What to Expect At Your Physician Consultation

Chapter 3: The Experts Guide to *Early* Home Treatment
- Advantages of Home-Based Treatment
- Available Medicines, New Uses: Rationale for the Combination in COVID
- Antivirals and Antibiotics
- Anti-Inflammatories - Corticosteroids: Oral and Nebulized
- Prescription Anticoagulants ("Blood Thinners"): Why Crucial in COVID
- Vitamins, Supplements, and Oxygen

Chapter 4: Emerging Prevention and Treatment Options
- Monoclonal Antibodies
- Convalescent Plasma
- Prevention Options: Prophylaxis and Vaccines

APPENDICES

APPENDIX I: Medical Resources

APPENDIX II: Contributors and Physician Resources for Treatment

APPENDIX III: Sample Forms for Clinical Tracking in COVID

Disclosure: All physicians contributing to the treatment protocols in this guide for patients are actively treating COVID patients and are focused on early, home-based delivery of medical treatment options unless critical care in hospital is determined to be urgently needed. The contributors have no financial ties with any pharmaceutical company or product suggested in the treatment algorithms.

All contributors have volunteered their time and expertise as a community service in this time of national emergency to help inform patients of their options for research-based, peer-reviewed, safe treatments. They have received no remuneration for their contributions. The opinions expressed in this guide are those of the physician contributors and not those of their institutions listed.

INTRODUCTION

A Guide to Home-Based COVID Treatment is built on the rapidly accumulating peer-reviewed published medical research, written by practicing physicians with decades of experience treating patients with all kinds of illnesses.

We provide a step-by-step guide to medically sound early *treatments* that have a reasonable probability of success in this emergency pandemic. There are oral medications that are approved for other conditions, but not yet proven to be efficacious specifically for COVID-19 by the U.S. Food and Drug Administration. In the global pandemic emergency, large scale randomized clinical trials have not been feasible in the face of such critical illness. The National Institutes of Health was slow to recommend treatment outside of the hospital. And for the first nearly two years of the pandemic, there were no oral medications specifically approved for outpatient COVID-19 treatment, even though the mortality rate once patients require hospitalization is unacceptably high.

Thus, treatment administered outside of the hospitalized setting should be under the supervision of a physician or licensed medical professional who is knowledgeable in the use of the medications and the monitoring approach for ambulatory, home-based COVID-19 as described in this guide. Patients who worsen in any way should seek emergency room evaluation immediately.

There are four major pillars to infectious disease pandemic response:

1) Contagion control (stop the spread of the virus)
2) Early ambulatory, home-based treatment
3) Late-stage treatment in hospital
4) Vaccination

This guide will focus on the pillar of early, ambulatory, home-based medical treatment overseen by your physician, using a combination of available medicines, already FDA-approved for other medical conditions, and widely used in clinical medicine every day.

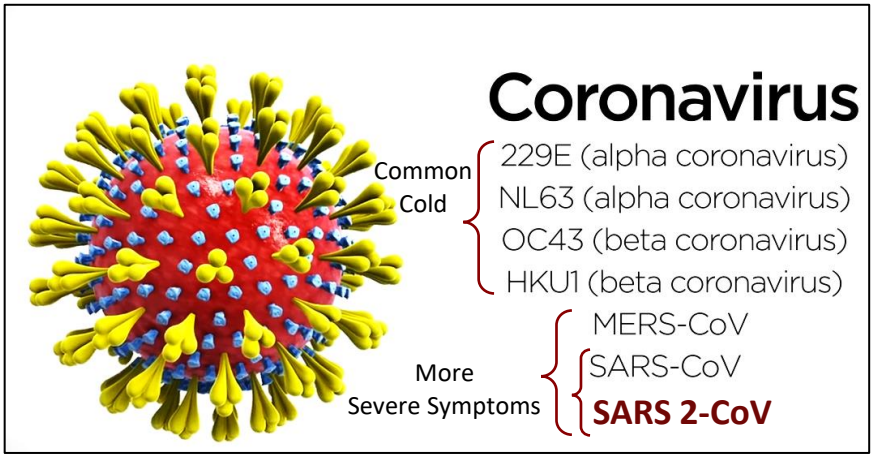
We have learned more about what medicines work, how to use them, when to use them, who is most at risk, and what strategies work. Please read this with an open mind. We are writing this to HELP you, to TEACH you how to work with your doctor.

As physicians, we know we need to focus now on ***early*** treatment to as the most immediate way to reduce hospitalizations and death. This is your guide to help you know your options, and to use with your personal physician.

Let's get started!

Chapter 1
Overview: SARS-CoV-2 Coronavirus

What Is Coronavirus?



Coronavirus is a family of common respiratory viruses. There are seven different strains of coronavirus. Four can cause symptoms many people experience in the fall/winter seasons: from the common "cold" with cough and runny nose to flu-like body aches and even a low-grade fever.

SARS-1 (Severe Acute Respiratory Syndrome), MERS (Middle East Respiratory Syndrome) and most recently, SARS-2 COVID-19 are newer coronaviruses that have emerged since about 2002-2003, and may cause more serious illnesses.

Diseases that spread widely are called an *epidemic* if they are mostly confined to one region of the world. *Pandemics* refer to diseases that rapidly spread out of a region, around the world. SARS-1 first appeared in China in 2002-2003. It was classified as an epidemic, even though it spread to 26 countries. SARS 1 did spread beyond China but was not considered serious enough to be a pandemic. It had a case fatality rate of about 9.6%.

SARS-1 lasted about two seasons, and then subsided. However, because of its infectious properties, various research labs began to study the SARS-1 virus for different reasons. During these years, the virus was known to have escaped at least six times from several labs in China, causing illness outbreaks.

MERS was first reported in Saudi Arabia in 2012. Contagion reports were similar to SARS-1, but the fatality rate was much more deadly at 34.4%. MERS subsided and there have been few cases reported since the outbreak.

SARS-2 COVID-19 has been a different story. The actual infecting virus has been named SARS-2 or SARS-CoV-2 (Severe Acute Respiratory Syndrome 2) and is reported to be 79% identical to the genetic sequence of SARS 1. The name that was finally given to the "disease" is COVID-19 (short for Corona Virus Disease-2019).

SARS-2 virus and the illness, COVID 19, are classified as a *pandemic* because of its rapid, global spread.

There are many viruses that contribute to the yearly cough, cold, flu, season. *Rhinoviruses* account for 35-70% of all symptoms, followed by *coronaviruses* at about 12-15% and then *adenoviruses*, and *influenza* viruses (7-12%). Rates for each type of seasonal respiratory virus syndrome vary year-to-year. Influenza varies widely each year in severity of symptoms, how easily it spreads to others, and death rates.

How Deadly Is COVID 19?

When a serious infectious disease breaks out, we naturally worry "Am I going to die?" Fear is a common response, so we turn to experts and our government agencies for information and guidance.

The vast majority of deaths from this COVID virus occur in those 75 years old and older, with most of those already sick with other illnesses. A large percentage are in nursing care facilities, over 80 years old, and with an average of 2.5 other medical conditions, such as obesity, diabetes, heart disease, lung and/or kidney disease. These other conditions are called *comorbidities,* and they increase the risk of serious illness with COVID.

The chances of someone *under 50 years old* with symptoms dying from COVID-19 is 0.05%.
The chances of someone under 18 years old dying from COVID is near 0%. Those that do are those with severe underlying medical conditions. There are roughly 7 times more children that die from the flu than COVID-19.

To put it another way, approximately 99.9%+ of individuals who contract COVID will have mild to moderate symptoms and recover, just like with the flu. The majority of deaths are coming from the 0.62% of the population who are in nursing home facilities.

The bottom line? This virus looks and acts very much like the flu, but with one CAVEAT: *Unlike the usual seasonal influenza*, COVID-19 illness can become profoundly serious in *unpredictable* ways.

COVID-19 can very rapidly become critical illness for two primary reasons: this viruses triggers TWO responses in the body much worse than seasonal flu: an *exaggerated inflammatory response* causing damage to critical organs, and an *exaggerated blood-clotting response* leading to multiple blood clots in the lungs, brain and other organs. Doctors have even found blood clots in large arteries like the aorta.

Contagion control remains the first step in reducing the spread of illness. Public health authorities such as CDC, WHO, and state and local health departments, issue guidelines as new information becomes available. As doctors treating patients, our responsibility is to focus on treatment, which is our purpose in writing this guide.

CDC recommends calling your doctor if you develop symptoms. This guide helps you recognize symptoms and when to call your doctor, and what options are available to discuss with your doctor for early treatment.

Chapter 2
I Have Flu-Like Symptoms: What Should I Do?

What should I do first?

Consult your primary physician with the **first onset** of COVID-19 symptoms.
If you are experiencing severe, life threatening symptoms call 911 or go to your nearest emergency department for evaluation. ***Difficulty breathing or severe chest pain is a sign of serious illness and needs medical attention promptly.***

The most important reason to contact your physician right away is that studies show ***early treatment*** is the KEY to success with COVID. *Early treatment is especially critical for people at high-risk.*

HIGH RISK PATIENTS: over age 50, with **one or more other medical conditions**:

- Obesity
- Diabetes, or pre-diabetes ("metabolic syndrome")
- Lung disease (COPD, pulmonary fibrosis, asthma, cystic fibrosis)
- Kidney disease
- Hypertension
- Autoimmune disorders
- History of cancer treatment
- History of taking corticosteroids regularly

What are the symptoms of COVID?

For most people, the first symptoms are not that different from those you have had before at the beginning of a cold or flu. The difference is that COVID can progress rapidly and in unpredictable ways into very severe *respiratory difficulties*, marked *inflammation damage*, and intensified risk of *serious blood clots*. These last three complications of COVID are different from what we see with typical colds or seasonal flu episodes, and are what cause the most serious, potentially life-threatening damage to critical organs.

The three most critical symptoms of possible COVID are ***fever, shortness of breath/difficulty breathing/ pressure in your chest, and severe cough***. Shortness of breath can mean shortness of breath at rest or even shortness of breath doing daily activities.

Keep a journal of your symptoms. It helps any doctors you consult know what has been happening if you keep a daily record of your symptoms by time and date and description of your illness.

Your journal can be life-saving when it comes time to see a doctor, especially in an emergency, since an accurate record of your symptoms, the timeline of when they started, how they progressed and how intense they are can help your doctor make better decisions about what you treatment you need.

***Fever**:* The most accurate way to check for fever is to use an old fashioned oral/mouth thermometer for home use. You can buy these inexpensively at any local pharmacy or on-line. Forehead digital thermometers are easy to use, but they are also expensive and are not as accurate. For young children, you can place the thermometer in the armpit, since it is difficult to have a sick child hold a thermometer in the mouth for three minutes.

Typical Symptoms You May Experience

(but keep in mind, not everyone has all of them):

- Runny nose, sneezing
- Sudden onset of marked fatigue
- Loss of energy, malaise
- Body aches, muscle aches, headaches
- Cough, though in COVID it is usually a *dry* cough. You may not produce mucus (sputum). Color of sputum is not necessarily a reliable indicator of severity or type of illness.
- If your cough is causing you to have increased shortness of breath or interfering with your sleep pattern, this could mean the disease is worsening.
- Feeling "feverish," even if fever (defined as temperature >101 degrees) is not present.
- Chills at night
- Sudden onset of sweats during the day that are unrelated to exercise
- Loss of taste or smell (tends to occur after the other symptoms have been there 1-3 days, but can occur earlier or later)
- Loss of appetite, nausea, GI upset
- Diarrhea may occur, though is not common. It can quickly lead to dehydration and electrolyte imbalances when it does happen.
- After about day 5, when the inflammation gets worse, there is often chest heaviness or tightness, difficulty breathing, shortness of breath.
- Drop in blood oxygen concentration (measured with a finger oximeter you can purchase at your local pharmacy) indicates serious respiratory problems
- Rapid heart rate, palpitations
- Loss of focus, difficulty with concentration and memory

Immediate home care recommendations

If you suspect COVID or have tested positive for COVID, isolate yourself from other people to minimize spread of the virus. Quarantine time ranges from 7-14 days, depending on the symptoms and your age and medical risks.

Good hygiene reduces spread of the virus. Remember to wash hands and body with soap and water. Maintain good disinfecting procedures throughout your room/home. Nasal sprays and mouthwashes containing dilute povidone iodine have been shown to help prevent infection or transmission of COVID-19.

Sunlight and fresh air are key components to good health and fighting COVID. Direct sunshine for 10-20 minutes twice a day is a good source of vitamin D. Studies are clear that low vitamin D is a risk factor for getting COVID and having a worse outcome and higher risk of dying. Vitamin D3 in oil in capsules is better absorbed than tablets and is an excellent source of supplemental vitamin D if you cannot be outside in the sunshine, or your blood level of vitamin D is too low. We will describe in upcoming chapters more about doses and how to check your blood levels of vitamin D and other laboratory studies that are helpful.

Plenty of fluids—preferably water, not beverages with sugars and additives—is key to keep your immune system working well and keeping your body healthier to fight off the virus. *Adequate hydration is crucial* – the amount will vary by body weight, but a good rule of thumb is that your urine should be the *color of pale straw.*

If your urine is *dark yellow or gold*, you are definitely not drinking enough water. If your urine is *colorless*, you are drinking too much plain water, and this can make you lightheaded or confused from electrolyte imbalance.

Healthy food intake also gives the vital nutrients for your immune system to work well. Fresh fruits and vegetables are good choices, along with healthy protein options like meats and beans. Avoid excess sugar, excess intake of "convenience" foods high in fat, sugars, salt and additives because these foods cause inflammation and weaken the immune system.

Make sure you talk with your physician about increasing your intake of immune-boosting vitamins and minerals: Vitamin D, vitamin C, zinc, and others as your physician may recommend.

For Fever: Remember, ***fever is both a warning of infection that could be serious, and one of our body's defenses against infection***. Not all physicians agree that every fever should be treated, since it may signal a superinfection that needs aggressive antibiotic treatment, not just a fever-reducing medicine.

For high fever, treatment can be with acetaminophen, ibuprofen, and/or ice packs. Ice packs are easy to use and a good option to keep fever down. Just fill a bag of ice and apply to your back/tummy/flank. Acetaminophen has side effects of oxidative stress on the liver. One study has suggested it may increase risk of oxygen desaturation.

One option is to alternate ibuprofen and acetaminophen every 4-6 hours. For example, use ibuprofen at 12 PM and then try acetaminophen at 6 PM, if the fever persists. Do not exceed recommended doses on the package.

Should I Get a COVID Test?

Follow the CDC recommendations on testing which currently state that COVID-19 testing is a decision to be advised by your doctor. Do we test everyone or just test those with symptoms? Are the tests accurate and what happens if you test positive but have no symptoms? Should I quarantine? The media has inundated us with these questions since the COVID outbreak began.

Because rapid treatment is so crucial in COVID, many outpatient physicians elect to treat their patients based on *clinical symptoms, risk factors, and other objective findings from a physical exam or blood work* and do not lose the "window of opportunity" for early treatment by waiting several days for a COVID test report. That is a very reasonable option, since the tests have been at times hard to get and may take too many days for results. Also, reliability of the tests has been a serious problem. We have patients who tested negative but had the cardinal features of the COVID illness and needed treatment. If you have all the symptoms of COVID illness, but a negative test result, most physicians still recommend early treatment to help reduce the risk of requiring hospitalization.

There are several basic types of tests:

1. *Diagnostic* tests: an "*antigen*" test and a "*molecular*" test. An antigen test detects certain proteins on the surface of the virus. A molecular test, called *RT-PCR or rRT-PCR* detects fragments of the virus' genetic material. PCR tests with a high cycle threshold may often be finding non-infectious viral fragments instead of active infection with SARS-CoV-2.

2. *Antibody tests: (after recovery from COVID):* These tests check for antibodies made by your immune system in response to an infection, such as a viral illness. Antibodies help fight infections and antibodies "remember" what the infection-causing organism looks like to help our bodies fight similar infections in the future.

   Antibody tests are *not* used to *diagnose an active infection*. These tests tell your doctor you had the illness and recovered and have developed immunity. Commonly used antibody tests are not specific to COVID. People may have similar antibody responses to other viral infections, such as the coronavirus that is responsible for the common cold and even the flu virus. The test can only say that you have had a viral infection, not the specific type of virus.

3. *Tests for immune cells (T cells)* , indicating memory of past infection and capacity to mount an immune response, are under development. The T-detect test is available under an emergency use authorization.

Should you get a COVID test when you develop symptoms? That is a choice between you and your doctor. If you do decide to test, be aware of the test's limitations.

But either way, if you develop symptoms, the key is to be evaluated by your physician promptly and decide whether you are in the high risk group that needs early treatment to reduce chance of having to be hospitalized or having serious complications.

We encourage you to follow the steps included here to keep yourself healthy, do your best to stay away from sick people, and learn about early treatment options.

Early Treatment Is the Key to Success

Seek early treatment and be your own advocate. All of the physicians contributing to this booklet are on the frontlines treating outpatients at the first signs of COVID illness. Studies in the US and many other countries clearly show that patients who are treated within the first 5 days of symptoms have better outcomes using the combination of medications in the algorithm below. Conversely the death rate is ~12% by the time oxygen is needed, and ~40% for those requiring the intensive care unit. These death rates are unacceptably high. We have found that death rates can be significantly lower with early, outpatient treatment for the high-risk patients over age 50, with one or more other medical conditions.

Do not be afraid to go to your doctor, an urgent care, or a local emergency department. Remember that our job as physicians is to take care of you. ***Do not wait until it is too late***.

Steps to Take:

1. Be proactive.
2. Print the treatment algorithm that we included in this chapter.
3. Study this algorithm of medicines used and when they work the best. You will recognize many. They are in common use as anti-virals, anti-inflammatories, and anti-coagulants.
4. Schedule a TeleMedicine appointment with your primary physician ahead of getting sick.
5. Find out if your physician is willing to treat you according to this peer-reviewed published protocol, developed by experts from major U.S. and Italian medical centers.
6. If your physician is not willing, or knowledgeable to treat you for COVID, start now to find one who is. Look for a physician who is willing to treat your COVID with an aggressive plan as shown in this chapter. Resources for physicians across the United States are listed in Appendix II. You need an advocate who will work to help you get well.
7. A "wait and see" approach is not adequate for high-risk patients (those over age 50 with one or more other medical conditions). "Wait and see" is a factor contributing to the high death rate in the United States. Countries with the lowest death rates are treating *early at home* with the oral medicines listed in the algorithm that follows in this chapter.
8. Our medical knowledge on how to treat COVID is changing and improving daily, so please do not be afraid to seek professional help promptly if you develop symptoms.

What To Expect at Your Physician Consultation

Many of our physician contributors have patients fill out a questionnaire and/or a flow sheet of their symptoms describing what they are experiencing and how long they have been sick. See the COVID Screening Checklist and COVID Illness Tracking Log in APPENDIX III. Print these and use them to track your symptoms and progress. They are helpful for any doctor you may see.

Vital signs (blood pressure, pulse, height, weight, BMI, blood oxygen levels) are checked and recorded. A COVID test may be recommended. Our physicians typically do not wait for the test results to start treatment if in their medical judgment, symptoms and risk factors mean *prescription medications* should be started rapidly.

Other laboratory tests may be ordered, and might include these basic tests: metabolic profile to check glucose, electrolytes, liver enzymes, etc; a complete blood count; C-reactive protein (general inflammatory marker); D-Dimer (a marker of blood clot risk); 25-OH vitamin D level; serum zinc level; and ferritin.

Additional specialty laboratory tests, such as markers of possible heart attack, may be ordered if the physician thinks necessary after evaluating the patient.

Some of our physicians recommend an EKG initially to check heart rhythm and look for any other abnormalities. Chest X-rays may be ordered if the physician is concerned lung damage or pneumonia may already be present.

Most of our physician contributors recommend patients purchase a device worn on the finger to measure blood oxygen saturation, called an *oximeter,* available at local pharmacies for about $40-50.00

Follow up appointments (in-person, telemedicine) are typically scheduled at about 3, 5 or 7-10 days from start of treatment, and thereafter at intervals determined by the physician, based on the patient's response and risk factors.

Chapter 3

PHYSICIANS' GUIDE TO EARLY HOME-BASED TREATMENT

In countries around the world, doctors have found that treating COVID patients at home quickly when symptoms develop leads to better outcomes, dramatically lower death rates than if doctors send people home to wait until they are so sick they need hospitalizations, ICU admissions, mechanical ventilators and even dialysis when kidneys fail.

Hospital care for critical patients has a much higher death rate, and far higher risk of long-term lung, heart, neurological, and other complications for those who survive.

Home-based treatment makes sense for another reason: *reducing the spread of the illness*. COVID-19 is a highly contagious virus. TeleMedicine allows us a safer option to evaluate patients remotely and assess how they look and sound in addition to evaluating their symptoms and vital signs (which can easily be taken at home). With today's technology, we no longer *need* to have sick patients come to the office in person and risk infecting others.

Advantages of Home-based Treatment:

- Home care is safer because it reduces the risk of picking up other infections from sick people in the hospital.
- Home care also allows people to have family members with them for love and support. It can be terrifying to be seriously ill in the hospital, and even worse to have family unable to visit.
- Home care can quickly use widely available, low cost, generic oral medicines and help avoid risks of IV medicines needed when people are critically ill in the hospital.
- Physicians can prescribe home-based oxygen therapy with oxygen concentrators available through home-health services. Oxygen concentrators can be purchased without prescription online or for cash payment from some local suppliers for as little as a few hundred dollars.
- All the treatment modalities used in hospitals, except for mechanical ventilators, can be implemented at home –faster, and better tailored to the individual patient.

It makes sense to go back to our basic principles in Medicine:

- Control spread of the virus with careful disinfecting procedures in the home.
- Use prescription medicines targeted to the specific problems COVID-19 causes.
- TREAT EARLY when medicines work best for infections.
  None of our medicines work *as well* in the critical late stages of COVID illness.
- Start with the right drugs at the right time, based on the patient needs.
- Be ready to treat intensively with full combination of medicines before critical illness occurs.

Available Medicines, New Uses: Rationale for the Combination of Rx Medicines

COVID-19 illness can become very serious, very rapidly, in *unpredictable* ways. While this does not happen to everyone, it is not possible to predict *who* will develop critical illness or how fast.

This unpredictability and rapid progression in COVID happen because the SARS-CoV-2 virus triggers TWO responses in the body that are much worse than seasonal flu:

- *An exaggerated inflammatory response,* causing damage to critical organs. In its most serious form, this is called c*ytokine storm*.

- *An exaggerated blood-clotting response,* leading to multiple blood clots (thrombi) in the lungs, brain, kidneys, intestines and other critical organs. These blood clots in COVID can occur in both veins *and arteries*, which is unusual and potentially life-threatening if not treated rapidly.

These unique kinds of damage from the COVID virus mean we must use a *combination* of prescription medicines rapidly to block these dangerous effects. The use of prescription medications discussed in this guide should be considered clinically indicated, medically necessary, and appropriate "off-label" use of these

products. “Off-label” use of older medicines for new uses occurs every day in doctors’ offices around the country.

In fact, about 20% of *all* prescriptions in the United States are written for “off-label” uses when a doctor thinks a medicine will benefit a patient. That is the same model being implemented in the emergency of the COVID pandemic as we seek ways to help people through this illness and save lives.

As with any medicine you are prescribed, we encourage you to read the safety information and US Food and Drug Administration approved package insert and patient guide before deciding on the risks and benefits of the medication. Patients should read the full prescribing information and patient guide provided with the medication upon pick-up at the pharmacy and ask questions of your physician for additional information/clarification. (Tip: Check GoodRx.com to comparison shop prices for your prescriptions).

The basic groups of prescription medicines and other therapies used in COVID-19:

- Combination *anti-viral* medicines started as soon as symptoms occur
- Medicines to decrease inflammation, such as *corticosteroids* (called *immunomodulators*)
- *Anticoagulant* therapy to prevent blood-clots that can cause strokes, heart attacks, kidney shut-down, and death.
- Non-prescription supportive treatments with zinc, vitamin D, vitamin C, electrolyte drinks such as Pedialyte, and others.
- Home-based oxygen support, such as with an oxygen concentrator. They might be covered by medical insurance plans if prescribed by a physician.

I. Antiviral Agents:

These must be started quickly at **STAGE I (Days 1-5)**:
Symptoms include sore throat, nasal stuffiness, fatigue, headaches, body aches, loss of taste and/or smell, loss of appetite, nausea, diarrhea, fever.

These medicines stop the virus from (1) entering the cells and (2) from multiplying once inside the cells, and they reduce bacterial invasion in the sinuses and lung:

- *Hydroxychloroquine (HCQ) with azithromycin (AZM) or doxycycline

OR

- Ivermectin with azithromycin (AZM) or doxycycline

Either combination above must also include zinc sulfate or gluconate, plus supplemental vitamin D, and vitamin C. Some doctors also recommend adding a B complex vitamin.

Zinc is critical. It helps block the virus from multiplying.
Hydroxychloroquine is the carrier taking zinc INTO the cells to do its job.

II. Anti-inflammatory Agents - Corticosteroids ("steroids"): Oral and Nebulized.

These are started at **STAGE II (Days 3-14)** to reduce *inflammation,* the cause of added damage to the lungs and critical organs. **Symptoms** include worsening cough, difficulty breathing, chest heaviness/tightness or chest pain.

As inflammation damages the airways interfering with normal oxygen-carbon dioxide exchange, blood oxygen levels drop and people experience loss of focus, drowsiness, confusion, difficulty concentrating, low energy and severe fatigue.

The exaggerated Inflammation response in COVID further increases the risk of blood clots.

Prescription medicines and other support *added* now to Stage I medicines are:

- nebulized budesonide to help penetrate the lungs and reduce inflammation
- oral prednisone, methylprednisolone, dexamethasone
- colchicine – may also be added to reduce inflammation
- full strength adult aspirin 325 mg to reduce inflammation and risk of blood clots
- home oxygen concentrator may be needed to improve oxygen levels

III. Prescription Anticoagulants ("blood thinners"): STAGE III (Day 7 and beyond):

Symptoms seen in Stage II intensify. Difficulty breathing becomes extreme, oxygen levels drop sharply, risk of heart attack or stroke increases. At this point, people are critically ill.

The medicines to be added to Stage I and II medicines now include:

- Aspirin 325 mg unless told not to take by your doctors
- And/or low molecular weight *heparin injections (e.g. enoxaparin [Lovenox])*
  OR
- apixaban (Eliquis), or rivaroxaban (Xarelto), or dabigatran (Pradaxa) or edoxaban (Savaysa) in standard doses for 5 to 30 days

If these added steps do not lead to improvement, or the patient becomes unstable, a 911 call is warranted for ER evaluation and hospital admission so that more aggressive IV medications (such as remdesivir, Regeneron, and others) may be considered, and more intensive ventilation regimens are possible in ICU settings.

IV. Vitamins, Supplements, and Oxygen.

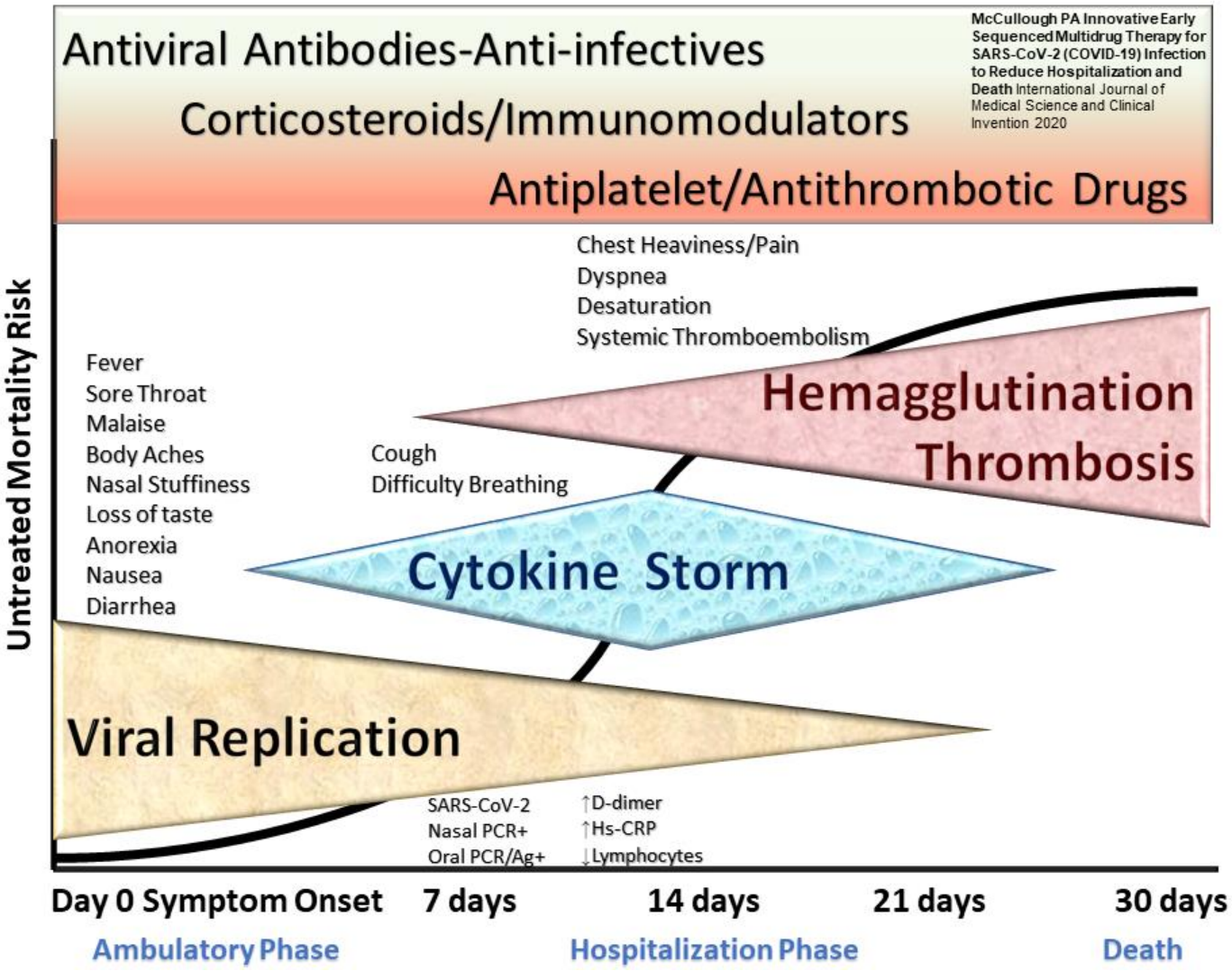
- **Zinc sulfate, gluconate or citrate**. These forms are available in pharmacies, health food stores, and sold online. Zinc sulfate 220 mg provides 50 mg elemental zinc, the recommended anti-viral dose. Zinc in the form of zinc picolinate form is not recommended following reports of liver damage and tumors from studies about 20 years ago. Following these reports, the German

Commission E that regulates supplements used in medical practice in Germany banned this form of zinc.

- **Vitamin D3**, preferable in oil in capsules for better absorption. Recommended doses for anti-viral benefit vary from 5000 IU or more for 5-30 days

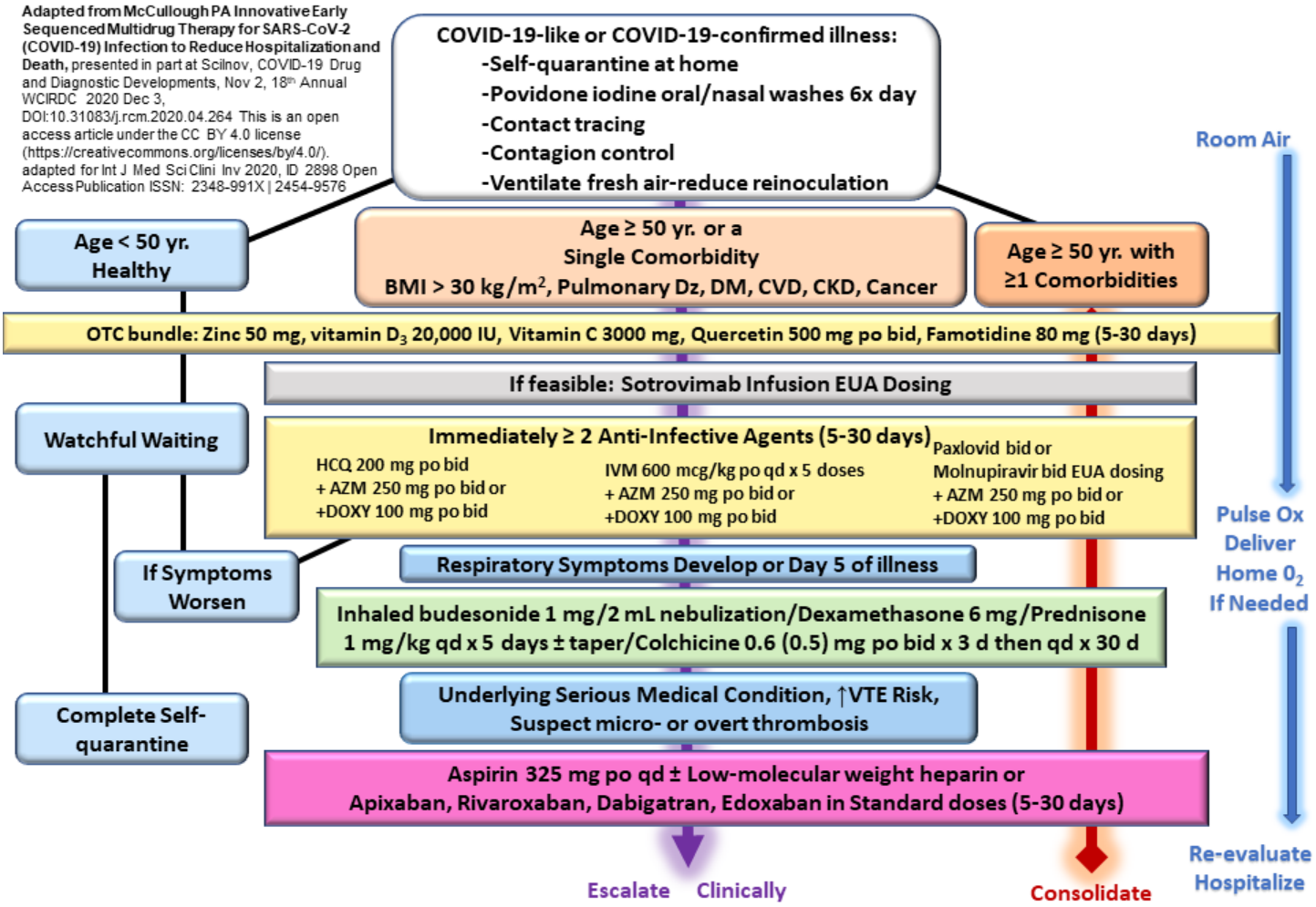
- **Vitamin C** with bioflavonoids for antioxidant, anti-inflammatory effects. Dose recommendations from our contributors vary from 1000 mg (1 gram) once or twice a day up to 4 or more times a day.

- A word about ***quercetin***. Some physicians are recommending this supplement to reduce viral illnesses because quercetin acts as a zinc ionophore to improve zinc uptake into cells. It is much less potent than HCQ as a zinc transporter, and it does not reach high concentrations in lung cells that HCQ does. Quercetin may help reduce risk of viral illness if you are basically healthy. But it is *not* potent enough to replace HCQ for *treatment* of COVID once you have symptoms, and it does not adequately get into lung tissue unless you take massive doses (3-5 *grams* a day), which cause significant GI side effects such as diarrhea.



V. Other Re-Purposed Drugs

To name a few, fenofibrate, cyproheptadine, famotidine, colchicine, anti-androgens, fluvoxamine, and melatonin have been investigated. Studies are compiled at c19study.com.



BMI=body mass index, Dz=disease, DM=diabetes mellitus, CVD=cardiovascular disease, CKD=chronic kidney disease, yr=years, HCQ=hydroxychloroquine, AZM=azithromycin, DOXY=doxycycline, IVM=Ivermectin, VTE=venous thrombo-embolic, EUA=Emergency Use Authorization (U.S. administration)

Dr. Peter McCullough led a team of international experts and published the first treatment protocol for ambulatory COVID-19 patients developed from experience treating patients in the US. and Italy and supported by the expanding medical literature at the time. The initial protocol was published in the highly respected *American Journal of Medicine*.

If you or a loved one are ill or exposed to risk of COVID-19, read the article (shown in image below) by Dr. McCullough and colleagues from leading US and Italian medical centers, which was published in the American Journal of Medicine (link above) and the updated summary in *Reviews in Cardiovascular Medicine*. ***Print these resources for your medical records and take a copy to your physician to discuss these treatment options.***

REVIEW McCullough PA, Kelly RJ, Ruocco G, Lerma E, Tumlin J, Wheelan KR, Katz N, Lepor NE, Vijay K, Carter H, Singh B, McCullough SP, Bhambi BK, Palazzuoli A, De Ferrari GM, Milligan GP, Safder T, Tecson KM, Wang DD, McKinnon JE, O'Neill WW, Zervos M, Risch HA. Pathophysiological Basis and Rationale for Early Outpatient Treatment of SARS-CoV-2 (COVID-19) Infection. Am J Med. 2020 Aug 7:S0002-9343(20)30673-2. doi: 10.1016/j.amjmed.2020.07.003. Epub ahead of print. PMID: 32771461; PMCID: PMC7410805.

THE AMERICAN JOURNAL of MEDICINE®

Pathophysiological Basis and Rationale for Early Outpatient Treatment of SARS-CoV-2 (COVID-19) Infection

Peter A. McCullough, MD, MPH,[a,b,c] Ronan J. Kelly, MD,[a] Gaetano Ruocco, MD,[d] Edgar Lerma, MD,[e] James Tumlin, MD,[f] Kevin R. Wheelan, MD,[a,b,c] Nevin Katz, MD,[g] Norman E. Lepor, MD,[h] Kris Vijay, MD,[i] Harvey Carter, MD,[j] Bhupinder Singh, MD,[k] Sean P. McCullough, BS,[l] Brijesh K. Bhambi, MD,[m] Alberto Palazzuoli, MD, PhD,[n] Gaetano M. De Ferrari, MD, PhD,[o] Gregory P. Milligan, MD, MPH,[a] Taimur Safder, MD, MPH,[a] Kristen M. Tecson, PhD,[b] Dee Dee Wang, MD,[p] John E. McKinnon, MD,[p] William W. O'Neill, MD,[p] Marcus Zervos, MD,[p] Harvey A. Risch, MD, PhD[q]

[a]Baylor University Medical Center, Dallas, Tex; [b]Baylor Heart and Vascular Institute, Dallas, Tex; [c]Baylor Jack and Jane Hamilton Heart and Vascular Hospital, Dallas, Tex; [d]Cardiology Division, Regina Montis Regalis Hospital, Mondovì, Cuneo, Italy; [e]Christ Advocate Medical Center, Chicago, Ill; [f]Emory University School of Medicine, Atlanta, Ga; [g]Johns Hopkins School of Medicine, Baltimore, Md; [h]Cedars Sinai Medical Center, Los Angeles, Calif; [i]Abrazo Arizona Heart Hospital, Abrazo Health System, Phoenix, Ariz; [j]Carter Eye Center, Dallas, Tex; [k]Cardiorenal Society of America, Phoenix, Ariz; [l]University of Texas McGovern Medical School, Houston, Tex; [m]Bakersfield Heart Hospital, Bakersfield, Calif; [n]University of Siena, Le Scotte Hospital Viale Bracci, Siena, Italy; [o]University of Torino, Torino, Italy; [p]Henry Ford Hospital, Detroit, Mich; [q]Yale University School of Public Health, New Haven, Conn.

Specialties

Internal Medicine
Critical Care
Nephrology
Cardiology
Electrophysiology
Infectious Diseases
Ophthalmology
Epidemiology
Biostatistics

ABSTRACT

Approximately 9 months of the severe acute respiratory syndrome coronavius-2 (SARS-CoV-2 [COVID-19]) spreading across the globe has led to widespread COVID-19 acute hospitalizations and death. The rapidity and highly communicable nature of the SARS-CoV-2 outbreak has hampered the design and execution of definitive randomized, controlled trials of therapy outside of the clinic or hospital. In the absence of clinical trial results, physicians must use what has been learned about the pathophysiology of SARS-CoV-2 infection in determining early outpatient treatment of the illness with the aim of preventing hospitalization or death. This article outlines key pathophysiological principles that relate to the patient with early infection treated at home. Therapeutic approaches based on these principles include 1) reduction of reinoculation, 2) combination antiviral therapy, 3) immunomodulation, 4) antiplatelet/antithrombotic therapy, and 5) administration of oxygen, monitoring, and telemedicine. Future randomized trials testing the principles and agents discussed will undoubtedly refine and clarify their individual roles; however, we emphasize the immediate need for management guidance in the setting of widespread hospital resource consumption, morbidity, and mortality.

© 2020 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license. (http://creativecommons.org/licenses/by-nc-nd/4.0/) • The American Journal of Medicine (2020) 000:1–7

KEYWORDS: Ambulatory treatment; Anticoagulant; Anti-inflammatory; Antiviral; COVID-19; Critical care; Epidemiology; Hospitalization; Mortality; SARS-CoV-2

US/Italian Multicenter Collaboration

Academic Medical Centers
Public Heath
Integrated Health Systems
Community Practice
Biotech Industry

For more information on safety of HCQ and other medicines *in the algorithm,* check the c19study.com website that summarizes more than 278 studies of HCQ-based treatment, which are particularly favorable when HCQ is used in the first few days of COVID-19 symptoms as recommended in the above algorithm.

C19study.com also includes studies of ivermectin, REGEN-COV, vitamin D, fluvoxamine, dilute povidone-iodine, colchicine, and many other therapies.

For further information, see AAPS compendium of articles and studies on COVID-19.

*FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial, citing risk of heart rhythm problems. Please consult with your physician before use.

Chapter 4
Emerging Prevention and Treatment Options

Monoclonal antibodies

Natural Antibodies are produced by the body in response to foreign organisms, such as viruses and bacteria. Synthetic antibodies are those produced in a laboratory to mimic ones the body can make. When these synthetic compounds, referred to as "monoclonal antibodies," are made in the lab targeted for a new treatment in medicine, they are patented as new therapeutic agents. This is the type of experimental synthetic monoclonal antibody you heard described on the news that was given to President Trump as part of his treatment for COVID-19 when he was in the hospital at Walter Reed.

The company Regeneron has produced a drug, called REGEN-COV2, that is a combination of two "monoclonal antibodies" intended to fight off the virus SARS-CoV-2 that causes the illness we call CoVID-19. To develop REGN-COV2, Regeneron scientists use antibodies from mice that have been genetically modified to have a human immune system, as well as antibodies identified from humans who have recovered from COVID-19.

The overall effectiveness of Regeneron as a new treatment remains to be seen, since it is still in the experimental stage and is undergoing clinical trials. It is available under an Emergency Use Authorization in many facilities. It needs to be given by injection, preferably intravenous infusion. Check with your local health authorities about qualifications to receive it and the most convenient locations.

The Emergency Use Authorization for Regeneron was withdrawn. An EUA was issued for sotrovimab, claimed to be the only type effective against the Omicron variant, which is contingent on the federal government controlling the distribution. Supply is extremely limited. Check with your local health authority about availability.

Convalescent Plasma

Convalescent plasma, or CP, is the serum from blood donated by people who have had an infectious disease, recovered, and developed antibodies to the infectious organism so that their blood contains those antibodies that can be administered intravenously to a another person with that disease to treat the infection. CP was using during the 1918 flu pandemic, and has also been used for measles, mumps, and polio early in the 20th century. When the COVID pandemic hit, physicians began considering this could be a therapy to help ill patients recover. The FDA approved an Emergency Use Authorization to use CP to treat COVID patients, and it has been given intravenously to COVID patients in the hospital. It has not been shown prevent disease progression in high-risk outpatients with COVID-19, when administered within the first week of their symptoms. The risk of getting COVID-19 from convalescent plasma has not been tested, but researchers believe that the risk is low because donors have fully recovered from the infection.

Convalescent plasma therapy has some risks, such as allergic reactions, possible lung damage and difficulty breathing, and infections such as HIV and hepatitis B and C though the risk of these infections is low because donated blood is tested for safety.

Prevention Options: Prophylactic Medications and Vaccines

Since SARS-2 virus first appeared, there has been much media focus on developing a vaccine that will protect people from contracting the SARS 2 virus. But in addition to working on a vaccine to help prevent people from becoming ill with COVID, there are already several *prophylactic,* or preventive, medication protocols in use in various countries and in controlled trials in the United States.

Prophylaxis Regimens:

Prophylaxis means treatment designed to reduce risk of getting an illness. It is a basic approach to prevention, particularly with illnesses like malaria, herpes, HIV/AIDS and some other illnesses. Very early on in the COVID pandemic, physicians in India, South Korea, Japan, Costa Rica, Turkey and several other countries began using the safe, widely available and very potent anti-viral medicine *hydroxychloroquine (HCQ)* as a *prophylactic* (preventive) medicine in COVID-19.

The India Council on Medical Research (ICMR) published in March 2020 (updated in May, 2020) their national guidelines for India using HCQ 400 mg once a week for health care workers, physicians, nurses, first responders, high risk patients, and family members of exposed or COVID-positive individuals. Nations that employed widespread prophylaxis and early treatment with HCQ have had death and hospitalization rates much lower than nations where prophylactic and early treatment use of HCQ has not been recommended or widely available.

Dr. McCullough's team in Dallas did a study in their health care workers using HCQ prophylaxis and found it to be effective and safe, with no adverse cardiac events or serious side effects.

The doses of HCQ for prophylaxis are far lower than doses patients with rheumatoid arthritis or lupus or malaria take daily for many years. Because the doses are so low, and not taken daily, risk of side effects is extremely low.

HCQ has a long half-life of about 22 days, so it can be given just once weekly for 8-12 weeks, or longer if someone is continually exposed to COVID, such as people working in hospitals. A new report, *Flattening the Risk: Pre-exposure Prophylaxis for COVID-19* examines this prophylactic treatment that is easy to use, already available, and inexpensive. They make the case for HCQ as the best candidate for this prevention strategy.

Prophylactic regimens are often recommended by the contributors to this guide, who are using several different dose and frequency regimens. Some use the regimen published by the India Council on Medical Research (ICMR), some use 200 mg instead of 400 mg, some recommend the dosing every two weeks instead of once a week, and some doctors even use HCQ for prophylaxis only once a month.

As a result of the safety and significant reduction in risk of becoming ill with COVID-19, physician contributors to this guide are recommending more widespread use of the prophylactic regimens with HCQ that are working so well in other countries. Some physicians prefer the anti-parasitic drug ivermectin for both prophylaxis and treatment. The initial dose recommendation was 0.2 mg/kg, but some are suggesting 0.4 to 0.6 mg/kg. As more information becomes available, recommendations may change.

We believe that in the face of a public health crisis, it is important to consider life-saving approaches based on scientific logic, available safety data, and clinical availability, even if definitive results are not yet available pending more extensive clinical trials.

We also believe that prophylactic therapy is the safest and most expedient way to help Americans reduce risk of getting sick with COVID, and be able to open schools, businesses and churches so we can overcome fear, and regain our freedom to live our lives again.

Vaccines

Three vaccines have received Emergency Use Authorization in the U.S., and FDA approval may come very soon even though studies are not scheduled to be completed before the end of 2022. Two use messenger RNA and one uses a DNA virus vector to introduce genetic information that causes your cells to produce a SARS2-like viral antigen ("spike protein"). Your immune system then reacts to that to develop immunity to the virus. More vaccines are under development. Although studies are not scheduled to be completed before the end of 2022, FDA granted approval to two mRNA vaccines, BioNTech's Comirnaty™ (said to be interchangeable with the Pfizer product) and Moderna's SpikeVax™. These brand-name products are not currently available in the U.S., and the EUAs are extended for the available Pfizer and Moderna products.

The most important consideration before approving a vaccine for human use is to make sure that the vaccine is safe and effective. Developing safe and controlled infection models for humans normally takes many years of phased testing in the lab, in animals, and then in humans. Many physicians and scientists have been concerned that vaccine manufacturers, with government support, are speeding up this process in ways that are not allowing adequate time for the usual phased testing leading up to human clinical trials.

No RNA-based vaccines were previously approved for human use. Vaccines for RNA viruses are notoriously challenging and difficult to develop. We still, after all these years since AIDS emerged in the 1980s, do not have a vaccine for the AIDS virus, or the SARS-1 coronavirus that emerged in 2002-2003, and both are RNA viruses.

Several attempts have been made to create vaccines for coronavirus and other respiratory viruses but none of the vaccines have survived the testing phases. The vaccine trial for SARS-1 from 2003, for example, was shut down because it produced autoimmune hypersensitivity reactions when exposed to the natural virus after immunization in animal studies.

Another problem is that the SARS-CoV-2 virus already has many variants, against which vaccines may be less effective.

Even the best vaccines for flu are only about 30-60% effective. Compare that with an effectiveness for improvement ranging from 64% to more than 90% in more than 100 new studies showing early, outpatient treatment for COVID-19 with our existing medications described in chapters.

Delayed side effects (e.g., infertility, cancer, autoimmune diseases) may not be seen for years. FDA has already issued warnings concerning blood clots, Guillain-Barré syndrome, and myocarditis/pericarditis. These may be rare or mild, but vigilance is needed so that early treatment can be offered. D-dimers and other blood coagulation tests should be monitored. Mild weakness should be taken seriously because it sometimes

progresses rapidly to respiratory paralysis requiring mechanical ventilation. Blood troponin levels (an enzyme released when heart cells are damaged), ultrasound, or MRI help to diagnose heart inflammation.

Patients need to be informed of potential adverse effects, and they need to be reported to the Vaccine Adverse Events Reporting System (VAERS).

Breakthrough infections are occurring, so early treatment options are also needed in vaccinated persons.

New Drugs

FDA has issued EUAs for two new oral drugs that show some benefit for early treatment. Both are quite expensive, though the government may provide them at taxpayer expense. Supplies are extremely limited. However, hospitals and employed physicians might be willing to prescribe them to patients meeting risk criteria, while denying access to older, long approved re-purposed drugs.

Paxlovid™ by Pfizer is a combination of a protease inhibitor and the HIV drug ritonavir, which is needed to prevent its rapid breakdown but has many serious adverse effects. Ivermectin is also a protease inhibitor and has numerous other mechanisms of action. Paxlovid takes months to manufacture.

Molnupiravir by Merck is, like remdesivir, a nucleoside analog. It can be made available more quickly, but its mutagenic action poses a risk of birth defects.

.

APPENDIX I: Medical Resources

- Early Home-based Treatment Dr. Peter McCullough and colleagues American Journal of Medicine review and peer-reviewed algorithm
- HCQ White Paper: The Economic Standard
- Dr. Brian Tyson's First Person Account of Treating COVID-19 with Hydroxychloroquine

APPENDIX II: CONTRIBUTORS and PHYSICIAN RESOURCES

- Physician Contributors

Stella Immanuel, MD, Family Physician rehobothmedicalcenter.com
Lionel Lee, MD, FACOEP, Emergency Physician, Phoenix AZ; no website
Peter A. McCullough, MD, MPH, FACP, FACC, FCCP, FAHA, FNKF, FNLA, FCRSA, Internist, Cardiologist and Epidemiologist
Jane M. Orient, MD, Internist AAPSonline.org
Sheila Page, DO, Neuromusculoskeletal Medicine, no website, retired
Tom Reed, DPM, Foot and Ankle Surgeon, DAPBS, DABPM, FACFAS DrTomReed.com
Elizabeth Lee Vliet, MD, Preventive & Climacteric Medicine ViveLifeCenter.com

- Physician Resource List by State
  aapsonline.org/covidearlytreatment
- Telemedicine Resources for COVID treatment
  www.c19protocols.com (click Facilities from menu)
- Medical and VIDEO Resources
  www.AAPSonline.org
  www.c19study.com
  www.CovidPatientGuide.com

APPENDIX III: Sample Forms for Clinical Tracking in COVID

- COVID Screening Questionnaire and Risk Factor Checklist
- COVID Clinical Tracking Form

(SAMPLE) VIRAL ILLNESS/COVID SCREENING QUESTIONNAIRE
PATIENT NAME_____ DATE:_____

Height:_____ Weight:_____ Age:_____ BP:_____ Pulse:_____RR: _____ O2%____

❑ YES ❑ NO 1. Have you had a fever >101, or felt feverish lately?
❑ YES ❑ NO 2. Have you had a new or different type cough lately?
❑ YES ❑ NO 3. Have you had shortness of breath, difficulty breathing?
❑ YES ❑ NO 4. Any chills or repeated episodes of shaking with chills?
❑ YES ❑ NO 5. Any daytime sweats unrelated to exercise, or night sweats?
❑ YES ❑ NO 6. Any nausea, GI upset, vomiting or diarrhea?
❑ YES ❑ NO 7. Have you had recent loss of taste or smell?
❑ YES ❑ NO 8. Do you have new or different muscle/joint aches?
❑ YES ❑ NO 9. Have you felt loss of energy, or severe fatigue lately?
❑ YES ❑ NO 10. Have you had trouble with focus, memory or concentration?
❑ YES ❑ NO 11. Have you had any other flu-like symptoms?
❑ YES ❑ NO 12. Have you lost appetite and or lost weight?
❑ YES ❑ NO 13. Any travel to COVID-19 areas in last 14 days?
❑ YES ❑ NO 14. Any contact within last 14 days with someone who tested positive for COVID-19? If so when? _____
❑ YES ❑ NO 15. Have you tested positive for COVID-19? When_____
❑ YES ❑ NO 16. Have you been clinically <u>diagnosed</u> with COVID-19?

<u>RISK FACTORS CHECKLIST: DO YOU HAVE ANY OF THESE CONDITIONS?</u>

❑ YES ❑ NO Obesity, Heart disease, history of heart attack, arrhythmias, high blood pressure, TIA, or stroke? (circle any that apply)
❑ YES ❑ NO Lung disease? (COPD, asthma, pulmonary fibrosis, CF, other?)
❑ YES ❑ NO Kidney disease? Type:_____
❑ YES ❑ NO Diabetes, Metabolic Syndrome/Insulin Resistance?
Are you taking insulin? Yes:_____ No:_____
❑ YES ❑ NO Any kind of cancer, undergoing treatment?
❑ YES ❑ NO Any type of autoimmune disease?
❑ YES ❑ NO Do you regularly take corticosteroid medicines?

© Vive! Life Center/Elizabeth Lee Vliet MD

(SAMPLE) COVID TREATMENT FLOW SHEET INITIAL SERVICE

DATE_____

Name _____ DOB _____ SEX _____

	Day	1	3	5	7	Comments
1.	Fever or chills. 100° F or higher.					
2.	Cough					
3.	Shortness of breath					
4.	Fatigue					
5.	Muscle or body aches					
6	Headache					
7.	New loss of taste or smell					
8.	Sore throat					
9.	Congestion or runny nose					
10	Nausea or vomiting					
11	Diarrhea					
12.	Pulse Rate/O2 sats					
13.	Side effects/New meds					

© Stella Emanuel MD