17 April 2020

To: Board of Health, Health Officer, COVID-19 Incident Management Team, and Ravalli County Commissioners.

From: James R. Olsen

Subject: Potential Treatments; Supplements; Testing; Coexisting Diseases

Potential Treatments. In the March 23 input, several possible treatments that were mentioned. Over 600 trials and studies are listed by the NIH for COVID-19.[1] The status I can find is:

> **Chloroquine (CQ) and hydroxychloroquine.** Primarily used for malaria, the FDA has authorized its use for COVID-19; there are numerous reports of physicians using it for both a treatment and prophylaxis (a preventative).
>
> There are several trials in progress in various countries. The U. S. military is doing major trial. It seems that that the dose is extremely important to avoid negative effects. Many studies use it in combination.[2] Some trials show success and some do not.[3]
>
> A Brazilian trial was halted because the "high dose" (600mg CQ twice daily CQ) used caused an increase in fatality. The trial also included a low dose (450mg for 5 days, twice daily only on the first day). The trial was for infected patients who were also given antibiotics.[4]
>
> A French study which appeared to have initiated political recommendations has been questioned because of its methodology.[5] There have also been questions about the design of one of two Chinese trials cited.
>
> There are many attempts around the world searching for right application. An interesting trial in Turkey uses Chloroquine in combination with Zinc.[6]
>
> **Remdisivir.** Things have gotten promising for Remdivir, a treatment for Ebola, and had been approved for compassionate use on COVID-19 by the FDA. Double-blind trials were begun on April 1 by the National Institute of Allergy and Infectious Diseases

---

[1] Clinical Trials.gov. https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=&cntry=&state=&city=&dist=
[2] Lewis, "Here's What We Know about the Most Touted Drugs Tested for COVID-19."; Harvard Health Publishing. "Treatments for COVID-19."
[3] Chen, "Efficacy of hydroxychloroquine…"; Lewis, "Here's What We Know about the Most Touted Drugs Tested for COVID-19."
[4] Borba,. "Chloroquine diphosphate in two different dosages…"; Rettner, "Trial of chloroquine to treat COVID-19 stopped…"
[5] Darren, "Statistical review of Hydroxychloroquine…"
[6] Weintraub, "Chloroquine, Zinc Trials Underway for COVID-19 Prophylaxis."

(NIAID) (Rocky Mountain Laboratories is part of NIAID). Two other trials in China began on February 6 and February 12.[7]

There are promising results, especially when delivered early.[8]

Ritonavir – Kaletra (ritonavir plus lopinavir). This showed no benefit for COVID-19.[9]

Interferon. The vote is still out, with trials going on, but can find no results.[10]

Favipiravir. This showed no benefit for COVID-19.[11]

Tocilizumab (Actemra). This has shown promise in early trials for COVID-19 severae pneumonia and has been approved for Phase III trials.[12]

Kevzara. Is in overseas trials, generally for cases of overactive immune response against lungs and other organs.[13]

Another treatment that is approved for serious COVID-19 symptoms is Convalescent Plasma. The effectiveness is under trial.[14]

Supplements.

THE FOLLOWING IS REPEATED FROM THE MARCH 23 INPUT (with additional citations)

Supplements are recognized by the NIH are: Vitamin C, Selenium, Vitamin E, Zinc, avoiding B-6 and folic acid deficiency, D-3 (esp. respiratory disease).[15]

You have solicited substantive comments from the public and you have gotten at least two of them on this subject including a call-in comment. I find the answer given at the April 8 meeting to "follow the guidelines of the CDC" unsatisfactory as a reason not to put something like this out to the public. The fact is that these supplements ARE recognized by the NIH and the public should be told.

I would like a better explanation for not doing it.

---

[7] Clinical Trials.gov: https://clinicaltrials.gov/ct2/show/NCT04257656; https://clinicaltrials.gov/ct2/show/NCT04252664?term=remdesivir&draw=2

[8] Feuerstein, "Early peek at data …."; Grein, "Compassionate Use of Remdesivir …"; Lewis, Tanya. "Here's What We Know about the Most Touted Drugs Tested for COVID-19."

[9] Cao, "A Trial of Lopinavir–Ritonavir…"

[10] Sallard, "Type 1 interferons …"

[11] Cai, "Experimental Treatment with Favipiravir…"

[12] Cennimo, "What is the role of the IL-6 inhibitor tocilizumab…"

[13] Keown, "Sanofi and Regeneron Launch Second Kevzara…"

[14] Harvard Health Publishing. "Treatments for COVID-19."; Clinical Trials.gov: https://clinicaltrials.gov/ct2/show/NCT04342182

[15] Yamshchikov, "Vitamin D…"; Beck, "Selenium and vitimine E…"; Hulisz, Darrell. "Efficacy of Zinc Against Common Cold Viruses: An Overview." (the common cold virus is a coronavirus).

The Testing Trap. In Montana, 10,244 tests for COVID-19 have been done with 422 positives — 4%. It appears that testing is done if 1) a person has symptoms and 2) they have been in contact with someone who tested positive. The criteria is actually not clear and seems to be subjective. No one seems to have a handle on false negatives. Is this the right protocol?

There is finally a report of the outcome of universal testing — albeit for only 215 pregnant women of whom 33 (13%) tested positive for COVID-19

29 of the women who tested positive had no symptoms. ***88% who tested positive had no symptoms***. Apparently, 100% of the people who had symptoms (this was in the heart of the New York epidemic) were positive.[16]

What does all this mean?

- The data implies that testing people who have been exposed to COVID-19 makes a lot of sense and quarantine in place regardless of the test results makes sense.

- Testing people with symptoms makes sense.

- Limiting testing for other people only if they exhibit symptoms makes no sense.

The impression given to the public that CDC guidelines are the best medical practice is a false narrative. These guidelines are the result of the delay in the United States and, thus, Montana, to get test kits in place. ***The best practice is widespread testing, which has the best results.***

It is hard to see how following CDC guidelines for testing can be said to be the best medical practice.

Not just lungs, but the heart. The very large percentage of COVID-19 fatalities are patients with some other disease. I won't include references for this comment, but more and more research trials as well commentary on the right medical intervention deal with heart function; a good percentage of the fatalities due to heart failure. Further the majority of cases that are put on an invasive ventilator do not recover.

Thus, it seems that some preparatory thinking would be in order for serious COVID-19 cases – since the treatment may well be as much or more for the coexisting disease as for COVID-19. Which, in turn, suggests that specialists should be brought into the medical team treating COVID-19 patients if this is not already the case.

Best Regards,

James R. Olsen

[16] Sutton, "Universal Screening for SARS-CoV-2 in Women Admitted for Delivery."

References:

Beck, MA. "Selenium and vitamin E status: impact on viral pathology." May 2007. *Journal of* Nutrition, Vol, 137, Issue 5, pages 1338-1340. Oxford. DOI: https://doi.org/10.1093/jn/137.5.1338

Borba, Mayla Gabriela Silva, et. al. "Chloroquine diphosphate in two different dosages as adjunctive therapy of hospitalized patients with severe respiratory syndrome in the context of coronavirus (SARS-CoV-2) infection: Preliminary safety results of a randomized, double-blinded, phase IIb clinical trial (CloroCovid-19 Study)." 16 April 2020. [not peer reviewed] *MedRxiv*. doi: https://doi.org/10.1101/2020.04.07.20056424

Cao, Bin, et. al. "A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19." 18 March 2020. *The New England Journal of Medicine*. https://www.nejm.org/doi/10.1056/NEJMoa2001282

Cai, Qingxian, et. al. "Experimental Treatment with Favipiravir for COVID-19: An Open-Label Control Study." 18 March 2020. https://doi.org/10.1016/j.eng.2020.03.007

Cennimo, David. "What is the role of the IL-6 inhibitor tocilizumab (Actemra) in the treatment of coronavirus disease 2019 (COVID-19)?" 15 April 2020. *MedScape*, https://www.medscape.com/answers/2500114-197457/what-is-the-role-of-the-il-6-inhibitor-tocilizumab-actemra-in-the-treatment-of-coronavirus-disease-2019-covid-19

Clinical Trials.gov. https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=&cntry=&state=&city=&dist=

Chen, Zhaowei, et. al. "Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial." 10 April 2020 [Not peer reviewed]. Wuhan University. *Medrxiv.* doi: https://doi.org/10.1101/2020.03.22.20040758

Darren, Dahly, et. al. [Three PhD statisticians working with clinical trials]. "Statistical review of Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial." 23 March 2020. *Zenodo* Open Blog. https://zenodo.org/record/3725560#.XplJdS-z3UI. DOI: 10.1056/ NEJMoa2007016

Feuerstein, Adam. "Early peek at data on Gilead coronavirus drug suggests patients are responding to treatment." 16 April 2020. *STAT*. https://www.statnews.com/2020/04/16/early-peek-at-data-on-gilead-coronavirus-drug-suggests-patients-are-responding-to-treatment/

Furst, Jay. "False-negative COVID-19 test results may lead to false sense of security." 9 April 2020. *Mayo Clinic*. https://newsnetwork.mayoclinic.org/discussion/false-negative-covid-19-test-results-may-lead-to-false-sense-of-security/

Grein, Jonathan, et. al. "Compassionate Use of Remdesivir for Patients with Severe Covid-19." 10 April 2020. *The New England Journal of Medicine.* https://www.nejm.org/doi/full/10.1056/NEJMoa2007016

Harvard Health Publishing. "Treatments for COVID-19." 9 April 2020. *Harvard Medical School*. https://www.health.harvard.edu/diseases-and-conditions/treatments-for-covid-19

Hulisz, Darrell. “Efficacy of Zinc Against Common Cold Viruses: An Overview.” *JAPhA – Journal of American Pharmacists Association*, Sept-Oct 2004, Vol. 44, Issue 5. Pages 594-603. DOI: https://doi.org/10.1331/1544-3191.44.5.594.Hulisz

Keown, Alex. “Sanofi and Regeneron Launch Second Kevzara Trial Against COVID-19.” 1 April 2020. https://www.biospace.com/article/sanofi-and-regeneron-launch-second-kevzara-trial-against-covid-19/

Lewis, Tanya. “Here’s What We Know about the Most Touted Drugs Tested for COVID-19.” 16 April 2020. *Scientific America*. https://www.scientificamerican.com/article/heres-what-we-know-about-the-most-touted-drugs-tested-for-covid-191/

Lowe, Derek. “Comparing HydroxyChloroquine Trials.” 31 March 2020. Science Translational Medicine, *Science Magazine*. https://blogs.sciencemag.org/pipeline/archives/2020/03/31/comparing-chloroquine-trials

Montana Response: COVID-19. https://montana.maps.arcgis.com/apps/MapSeries/index.html?appid=7c34f3412536439491adcc2103421d4b

Rettner, Rachael. “Trial of chloroquine to treat COVID-19 stopped early due to heart complications.” 14 April 2020. *LiveScience*. https://www.livescience.com/coronavirus-chloroquine-study-stopped-early.html

Sallard, Erwan. “Type 1 interferons as a potential treatment against COVID-19.” 9 April 2020. Antiviral Research, *PMC-NIH*. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7138382/

SeliWeintraub, Karen. “Chloroquine, Zinc Trials Underway for COVID-19 Prophylaxis.” 9 April 2020. https://www.medscape.com/viewarticle/928472#vp_2

Sutton, Desmond, et. al. “Universal Screening for SARS-CoV-2 in Women Admitted for Delivery.” 13 April 2020. *New England Journal of Medicine*. https://www.nejm.org/doi/full/10.1056/NEJMc2009316

Yamshchikov, Alexandra et. al. “VITAMIN D FOR TREATMENT AND PREVENTION Of INFECTIOUS DISEASES: A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS.” 15 Apr 2010. HHS Author Manuscripts, NIHMS187181. doi: 10.4158/EP09101.ORR https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2855046/