

Release Notes 2021-08-17: : This is a draft of a table I expect to put into my updated notes on covid-19 and aging. Comments or questions welcome but caveat emptor. So far, I'm pleased that results do not appear to be trivially wrong or misdirected and wrong predictions may be informative. Note that this is a draft of an excerpt from a larger more detailed work in preparation on a controversial unresolved medical problem and should not be used for any particular purpose.

(To cite, see **BibTex** at end)

I posted a set of notes around July 2020 on **LinkedIn** [10] that included a list of nutrients predicted to help covid-19 patients based on a developing theory of aging and experience optimizing vitamins for dogs. The following is a table I intend to put in my updated "Age Distribution of covid-19 " notes that compares the original ideas to recent developments. I try to compare expectations, falling somewhat short of explicit predictions, from the original notes to results and observations obtained over the last year. With no obvious effective cure in sight and problems with vaccines, the additional information obtained over this time make the original ideas more compelling as they pertain to both covid-19 and aging.

Prior Expectations and New Results			
Expectation [10]	Supporting	Refuting	Follow up
Acute ↓Arg	Observed [21]		
Acute ↓Citrate	Observed [2] [18]		
Acute ↓Trp	Observed [21]		
Chronic ↓Trp		Rarely Observed [6]	Look at Dynamics[16]
Chronic Membrane Leak	↑Taurine in Long covid [6]		Find HIT
↑Phe	Observed [21]		
↑Tyr live longer	Drosophila [19]		
↓Tyr		Generally ↑[21] [15] [1]	Isomer Specific Assay
Citrate Helpful	vs oral Gln [13] (non-covid [5])		GS ↓(?) [23]
Citrate Helpful	Gln small benefit [4]		GS ↓(?) [23]
Citrate Helpful	elevated Glu/Gln ratio [6]		GS ↓(?) [23]
Copper over Zinc	Zn failed [24] [25] or harmful [22]		direct Cu test
VK for ET	Ubiquinol, CoQ help [20]		
Going Forward: Tests and Predictions			
New Prediction	Tests or Analysis		Trial solution
Vitamin D small effect	correlate, not primary cause [see text]		distraction
Tyr isomers ↑	isomer resolving assay		VK, Tyr maybe Phe
Taurine ↑due to HIT	speed up protein cycling		essential amino acids
anticoagulant fail [12] [11]	assay damaged fibrinogen		VK and citrate
VK for Gln	sequester ROS generators [9].		VK and citrate
Histidine helpful	personal observations, found ↓[8]		histidine
Trp helpful	Trp in cancer sarcopenia[16]		Trp

TABLE I: Summary of literature reports since initial suggestions from July 2020. Generally, vitamin K is used as an anti-oxidant due to like sequestration of ROS generators. GS may be sensitive to a lot of disease related effects like ROS and TCA depletion. TAT remains as a big unknown here. **ET** : Electron Transport, **GS** : Glutamine synthetase, **HIT** : High-Infidelity Translation, **TAT** : Tyrosine AminoTransferase, **VK**: Vitamin K

The most important failure so far is the lack of obvious consistent measured tyrosine depletion. This may just be balanced dynamics with BH4, breakdown of blood or muscle, and tyrosine aminotransferase but the important possibility remains that analogs of p-tyrosine are produced [14] [7] [3] . Further, correlation with clotting status could make a nice theory regarding clots sequestering ROS generators. As roles for m-tyrosine and tyrosine aminotransferase in other conditions are research topics, much potential exists for synergies with these other areas for any related investigations.

I'm posting this because I think the original hypothesis is still competitive but also think that specific investigations would be useful for assessing this theory or related ones. In the absence of even informal testing, beyond a few patients taking a drink containing citrate and nitrate while on a pulse oximeter [17], the clinical and lab results combined with my own continued experience feeding dogs, points to increased likelihood of producing informative results in more controlled tests.

Some tests would include,

1. Actually try the nutrients on covid-19 patients
2. Informal testing of at least components while on heart monitor or pulse oximetre [17]

3. Determine if covid-19 "tyrosine" contains significant isomer content or analogs.
4. Measure p-tyrosine isomers/analogues as function of coagulation status.
5. Consider citrate as an alternative to glutamine to stimulate glutamine synthetase.
6. Determine a dose response curve for vitamin K

Citation information, may need to manually insert url or find software like *TooBib* that can do that (although I'm not sure *TooBib* can always get this from **LinkedIn** url's),

```
@TECHREPORT{mmarchywka-MJM-2021-007-1-table,
AUTHOR = {M.J. Marchywka},
TITLE = { Update to Covid-19 Age Distribution Notes },
NUMBER = {MJM-2021-007},
VERSION = {.1},
INSTITUTION = { not institutionalized , independent},
ADDRESS = {306 Charles Cox , Canton GA 30115},
NOTE = {Version .1, may change significantly if less than 1.00 },
DATE = {August 17, 2021},
DAY = {17},
MONTH = {8},
YEAR = {2021},
AUTHOR1EMAIL = {marchywka@hotmail.com},
AUTHOR1ID = {orcid.org/0000-0001-9237-455X},
PAGES = { 4 },
CONTACT = {marchywka@hotmail.com},
FILENAME = {MJM-2021-007-table-2021-08-13}
}
```

1. BIBLIOGRAPHY

-
- [1] Laura Ansone, Monta Ustinova, Anna Terentjeva, Ingus Perkons, Liga Birzniece, Vita Rovite, Baiba Rozentale, Ludmila Viksna, Oksana Kolesova, Kristaps Klavins, and Janis Klovins. Tryptophan and arginine metabolism is significantly altered at the time of admission in hospital for severe COVID-19 patients: findings from longitudinal targeted metabolomics analysis. apr 2021. URL: <https://doi.org/10.1101/2F2021.03.31.21254699>, doi:10.1101/2021.03.31.21254699.
 - [2] Eva Baranovicova, Anna Bobcakova, Robert Vysehradsky, Zuzana Dankova, Erika Halasova, Vladimir Nosal, and Jan Lehotsky. The ability to normalise energy metabolism in advanced covid-19 disease seems to be one of the key factors determining the disease progression a metabolomic nmr study on blood plasma. *Applied Sciences*, 11(9), 2021. URL: <https://www.mdpi.com/2076-3417/11/9/4231>, doi:10.3390/app11094231.
 - [3] Céline Bertin, Leslie A. Weston, Tengfang Huang, Georg Jander, Thomas Owens, Jerrold Meinwald, and Frank C. Schroeder. Grass roots chemistry: meta-tyrosine, an herbicidal nonprotein amino acid. *Proceedings of the National Academy of Sciences*, 104(43):16964–16969, 2007. URL: <https://www.pnas.org/content/104/43/16964>, arXiv:<https://www.pnas.org/content/104/43/16964.full.pdf>, doi:10.1073/pnas.0707198104.
 - [4] Mahir Cengiz, Betül Borku Uysal, Hande İkitimur, Erkan Özcan, Mehmet Sami Islamolu, Emre Aktepe, Hakan Yavuzer, and Serap Yavuzer. Effect of oral l-glutamine supplementation on covid-19 treatment. *Clinical Nutrition Experimental*, 33:24–31, 2020. URL: <https://www.sciencedirect.com/science/article/pii/S2352939320300166>, doi:<https://doi.org/10.1016/j.clnex.2020.07.003>.
 - [5] Daren Heyland, John Muscedere, Paul E. Wischmeyer, Deborah Cook, Gwynne Jones, Martin Albert, Gunnar Elke, Mette M. Berger, and Andrew G. Day. A randomized trial of glutamine and antioxidants in critically ill patients. *New England Journal of Medicine*, 368(16):1489–1497, apr 2013. URL: <https://doi.org/10.1056/2Fnejmoa1212722>, doi:10.1056/nejmoa1212722.

- [6] Elaine Holmes, Julien Wist, Reika Masuda, Samantha Lodge, Philipp Nitschke, Torben Kimhofer, Ruey Leng Loo, Sofina Begum, Berin Boughton, Rongchang Yang, Aude-Claire Morillon, Sung-Tong Chin, Drew Hall, Monique Ryan, Sze-How Bong, Melvin Gay, Dale W. Edgar, John C. Lindon, Toby Richards, Bu B. Yeap, Sven Pettersson, Manfred Spraul, Hartmut Schaefer, Nathan G. Lawler, Nicola Gray, Luke Whiley, and Jeremy K. Nicholson. Incomplete systemic recovery and metabolic phenoreversion in post-acute-phase nonhospitalized covid-19 patients: Implications for assessment of post-acute covid-19 syndrome. *Journal of Proteome Research*, 20(6):3315–3329, 2021. PMID: 34009992. URL: <https://doi.org/10.1021/acs.jproteome.1c00224>, arXiv:<https://doi.org/10.1021/acs.jproteome.1c00224>, doi:10.1021/acs.jproteome.1c00224.
- [7] Brett R. Ipson and Alfred L. Fisher. Roles of the tyrosine isomers meta-tyrosine and ortho-tyrosine in oxidative stress. *Ageing research reviews*, pages 93–107, 03 2016. URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4841466/>, doi:10.1016/j.arr.2016.03.005.
- [8] Nathan G. Lawler, Nicola Gray, Torben Kimhofer, Berin Boughton, Melvin Gay, Rongchang Yang, Aude-Claire Morillon, Sung-Tong Chin, Monique Ryan, Sofina Begum, Sze How Bong, Jerome D. Coudert, Dale Edgar, Edward Raby, Sven Pettersson, Toby Richards, Elaine Holmes, Luke Whiley, and Jeremy K. Nicholson. Systemic perturbations in amine and kynurenine metabolism associated with acute sars-cov-2 infection and inflammatory cytokine responses. *Journal of Proteome Research*, 20(5):2796–2811, 2021. PMID: 33724837. URL: <https://doi.org/10.1021/acs.jproteome.1c00052>, arXiv:<https://doi.org/10.1021/acs.jproteome.1c00052>, doi:10.1021/acs.jproteome.1c00052.
- [9] R L Levine. Oxidative modification of glutamine synthetase. i. inactivation is due to loss of one histidine residue. *Journal of Biological Chemistry*, 258(19):11823–11827, 1983. URL: <https://www.sciencedirect.com/science/article/pii/S0021925817443055>, doi:[https://doi.org/10.1016/S0021-9258\(17\)44305-5](https://doi.org/10.1016/S0021-9258(17)44305-5).
- [10] M.J. Marchywka. On the age distribution of sars-cov-2 patients. Technical Report MJM-2020-002-0.10, not institutionalized , independent, 306 Charles Cox , Canton GA 30115, 7 2020. Version 0.10 , may change significantly if less than 1.00. URL: https://www.linkedin.com/posts/marchywka_notes-on-aging-as-it-relates-to-covid19-activity-6684083706170265601-JMnN.
- [11] M.J. Marchywka. Considering alternative fibrinogen fates in diseased states. Technical Report MJM-2021-006, not institutionalized , independent, 306 Charles Cox , Canton GA 30115, 07 2021. Version 0.50 , may change significantly if less than 1.00. URL: https://www.researchgate.net/publication/353314699_Considering_Alternative_Fibrinogen_Fates_in_Diseased_States.
- [12] M.J. Marchywka. A proposed qualitative non-monotonic paradox resolving actvitiy-coagulability curve for vitamin k. Technical Report MJM-2021-004, not institutionalized , independent, 306 Charles Cox , Canton GA 30115, 6 2021. Version 0.90 , may change significantly if less than 1.00. URL: https://www.researchgate.net/publication/352020800_A_Proposed_Qualitative_Non-monotonic_Paradox_Resolving_Actvitiy-Coagulability_Curve_for_Vitamin_K.
- [13] L.V. Marino, F.V. Valla, L.N. Tume, C. Jotterand-Chaparro, C. Moullet, L. Latten, K. Joosten, and S.C.A.T. Verbruggen. Considerations for nutrition support in critically ill children with covid-19 and paediatric inflammatory multisystem syndrome temporally associated with covid-19. *Clinical Nutrition*, 40(3):895–900, 2021. URL: <https://www.sciencedirect.com/science/article/pii/S0261561420305343>, doi:<https://doi.org/10.1016/j.clnu.2020.10.007>.
- [14] Gerg A. Molnr, Szilrd Kun, Eszter Slley, Melinda Kertsz, Lvia Szlig, Csaba Csontos, Katalin Bddi, Lajos Bogr, Attila Miseta, and Istvn Wittmann. Role of tyrosine isomers in acute and chronic diseases leading to oxidative stress - a review. *Current Medicinal Chemistry*, pages 667–85, 2016. URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4997921/>, doi:10.2174/0929867323666160119094516.
- [15] Michele Mussap and Vassilios Fanos. Could metabolomics drive the fate of COVID-19 pandemic? a narrative review on lights and shadows. *Clinical Chemistry and Laboratory Medicine (CCLM)*, 0(0), jul 2021. URL: <https://doi.org/10.1515%2Fccclm-2021-0414>, doi:10.1515/ccclm-2021-0414.
- [16] Soranobu Ninomiya, Nobuhiko Nakamura, Hiroshi Nakamura, Taku Mizutani, Yuto Kaneda, Kimihiro Yamaguchi, Takuro Matsumoto, Junichi Kitagawa, Nobuhiro Kanemura, Makoto Shiraki, Takeshi Hara, Masahito Shimizu, and Hisashi Tsurumi. Low levels of serum tryptophan underlie skeletal muscle atrophy. *Nutrients*, 12(4):978, apr 2020. URL: <https://doi.org/10.3390%2Fnu12040978>, doi:10.3390/nu12040978.
- [17] Sergej M. Ostojic, Aleksandra Milovancev, Patrik Drid, and Alexandros Nikolaidis. Oxygen saturation improved with nitrate-based nutritional formula in patients with COVID-19. *Journal of International Medical Research*, 49(4):030006052110123, apr 2021. URL: <https://doi.org/10.1177%2F03000605211012380>, doi:10.1177/03000605211012380.
- [18] José C. Páez-Franco, José J. Torres-Ruiz, Víctor A. Sosa-Hernandez, Rodrigo Cervantes-Díaz, Sandra Romero-Ramírez, Alfredo Pérez-Fragoso, David E. Meza-Sánchez, Juan Manuel Germán-Acacio, José L. Maravillas-Montero, Nancy R. Mejía-Domínguez, Alfredo Ponce de León, Alfredo Ulloa-Aguirre, Diana Gómez-Martín, and Luis Llorente. COVID-19 metabolomic profile: A link between lung dysfunction markers and altered amino acid metabolism. oct 2020. URL: <https://doi.org/10.21203%2Frs.3.rs-92697%2Fv1>, doi:10.21203/rs.3.rs-92697/v1.
- [19] Andrey A Parkhitko, Divya Ramesh, Lin Wang, Dmitry Leshchiner, Elizabeth Filine, Richard Binari, Abby L Olsen, John M Asara, Valentin Cracan, Joshua D Rabinowitz, Axel Brockmann, and Norbert Perrimon. Downregulation of the tyrosine degradation pathway extends *Drosophila* lifespan. *eLife*, 9:e58053, dec 2020. URL: <https://doi.org/10.7554/eLife.58053>, doi:10.7554/eLife.58053.
- [20] Bindu D. Paul, Marian D. Lemle, Anthony L. Komaroff, and Solomon H. Snyder. Redox imbalance links covid-19 and myalgic encephalomyelitis/chronic fatigue syndrome. *Proceedings of the National Academy of Sciences*, 118(34), 2021. URL: <https://www.pnas.org/content/118/34/e2024358118>, arXiv:<https://www.pnas.org/content/118/34/e2024358118>, full.pdf, doi:10.1073/pnas.2024358118.

- [21] Chris A. Rees, Christina A. Rostad, Grace Mantus, Evan J. Anderson, Ann Chahroudi, Preeti Jaggi, Jens Wrammert, Juan B. Ochoa, Augusto Ochoa, Rajit K. Basu, Stacy Heilman, Frank Harris, Stacey A. Lapp, Laila Hus-saini, Miriam B. Vos, Lou Ann Brown, and Claudia R. Morris. Altered amino acid profile in patients with SARS-CoV-2 infection. *Proceedings of the National Academy of Sciences*, 118(25):e2101708118, jun 2021. URL: <https://doi.org/10.1073%2Fpnas.2101708118>, doi:10.1073/pnas.2101708118.
- [22] ukasz Szarpak, Micha Pruc, Aleksandra Gasecka, Milosz Jaguszewski, Tomasz Michalski, William Peacock, Jacek Smereka, Katarzyna Pytkowska, and Krzysztof Filipiak. Should we supplement zinc in covid-19 patients? evidence from meta-analysis. *Polish Archives of Internal Medicine*, 06 2021. URL: https://www.researchgate.net/profile/Michal-Pruc/publication/352809109_Should_we_supplement_zinc_in_COVID-19_patients_Evidence_from_meta-analysis/links/60dc3a9ca6fdccb745f48add/Should-we-supplement-zinc-in-COVID-19-patients-Evidence-from-meta-analysis.pdf, doi:10.20452/pamw.16048.
- [23] S S Tate and A Meister. Regulation of rat liver glutamine synthetase: activation by alpha-ketoglutarate and inhibition by glycine, alanine, and carbamyl phosphate. *Proceedings of the National Academy of Sciences of the United States of America*, pages 781–5, Apr 1971. URL: <https://pubmed.ncbi.nlm.nih.gov/5279520/>, doi:10.1073/pnas.68.4.781.
- [24] Suma Thomas, Divyang Patel, Barbara Bittel, Kathy Wolski, Qiuqing Wang, Anirudh Kumar, Zachary J. Il’Giovine, Reena Mehra, Carla McWilliams, Steve E. Nissen, and Milind Y. Desai. Effect of high-dose zinc and ascorbic acid supplementation vs usual care on symptom length and reduction among ambulatory patients with SARS-CoV-2 infection. *JAMA Network Open*, 4(2):e210369, feb 2021. URL: <https://doi.org/10.1001%2Fjamanetworkopen.2021.0369>, doi:10.1001/jamanetworkopen.2021.0369.
- [25] Jasper Seth Yao, Joseph Alexander Paguio, Edward Christopher Dee, Hanna Clementine Tan, Achintya Moulick, Carmelo Milazzo, Jerry Jurado, Nicolás Della Penna, and Leo Anthony Celi. The minimal effect of zinc on the survival of hospitalized patients with COVID-19. *Chest*, 159(1):108–111, jan 2021. URL: <https://doi.org/10.1016%2Fj.chest.2020.06.082>, doi:10.1016/j.chest.2020.06.082.