Prophylactic Use of Ivermectin
In Anticipation of a Highly Virulent SARS-CoV-2 Variant

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For more than three years, Dr. Geert Vanden Bossche has been warning that the COVID-19 mass vaccination campaign will inevitably lead to a SARS-CoV-2 variant that will be highly virulent when contracted by highly COVID-19-vaccinated individuals, particularly in highly and rapidly vaccinated countries, and this will result in catastrophic consequences.[1]

When highly vaccinated individuals---particularly the elderly and those with co-morbidities, especially those who did not develop productive SARS-CoV-2 prior to vaccination---contract this virulent variant, many will have very little immune defense against the virus. It is likely that many will quickly become life-threateningly ill, and there is great risk that anti-viral treatment (and other treatments) will inadequately control their infection/illness.[1-4] In contrast, healthy unvaccinated individuals are expected to handle this highly virulent variant well, primarily because of their well-preserved and well-trained innate immunity.

The most important way to try to help highly vaccinated individuals is to try to prevent them from becoming infected with the highly virulent variant in the first place.[3-5] The best way to prevent them from becoming infected is to encourage them to begin taking a prophylactic anti-viral medication well in advance of their exposure to the virulent variant.

The most affordable, safest, most studied, most practical, and, on balance, the most effective anti-viral medication for prophylactic use against COVID-19 is ivermectin (IVM).[6-9] This appears to be the case despite continued strong recommendations by the highest health authorities in the USA, Canada, and most western European nations to **not** use IVM to either treat acute COVID-19 or to prevent infection with SARS-CoV-2.

During the first 2-3 years of the COVID-19 pandemic many controlled trials of prophylactic IVM were conducted, and several government-sponsored community IVM mass distribution experiences were studied, to determine whether prophylactic use of IVM could substantially reduce the likelihood of becoming infected with SARS-CoV-2.[6-9] Most of these studies were conducted in countries outside of the USA and western Europe. Many of the studies were published in peer-reviewed journals. Many of the studies demonstrated a convincing reduction in the likelihood that a person on IVM prophylaxis will become infected with SARS-CoV-2.

Virtually all of the above-mentioned studies used relatively low and infrequent doses of IVM. Most studies used a dose/regime in the range of 0.2-0.3 mg/kg 2x/week.[6-10] One study used a dose of 12 mg (about 0.2 mg/kg for an average small woman) once per week for up to 10 weeks.

Based largely on the above studies, the current recommendation of the **FLCCC (Frontline COVID-19 Critical Care Alliance)** for prophylactic use of IVM against COVID-19 is:[7]

- 0.2 mg/kg 2x/week (to be taken with fat-containing food to aid absorption) OR
- Daily IVM just prior to and during periods of high possible exposure (e.g., travel, attendance at a wedding or conference)

The current recommendation of the **CCCA (Canadian COVID Care Alliance)** for prophylactic use of IVM is:[8]

- 0.2 mg/kg 2x/week (to be taken with food)

A problem with the above recommendations is that they are primarily based on studies done during the first 2-3 years of the COVID-19 pandemic. Most of those studies were conducted during 2020-2022. During those years, the dominant circulating SARS-CoV-2 variants were much less infectious than current extremely infectious variants. Furthermore, when the highly infectious and highly virulent variant (anticipated by Dr. Vanden Bossche) arrives on the scene, it will likely be ubiquitously present, such that it will be extremely difficult for individuals to avoid frequent exposure, even if they wear masks and adhere to "social distancing."

The point is that a dose/regimen of 0.2-0.3 mg/kg 2x/week may have worked well during the first three years of the pandemic, but this dose/regimen may not be sufficient to adequately protect individuals from becoming infected with the anticipated highly infectious, highly virulent, and highly ubiquitous variant. A higher and daily dose might be necessary, <u>now</u>, to optimally protect people from the anticipated highly virulent variant, and this prophylaxis will need to be started well in advance of exposure.

Furthermore, the less than 100% protection (even considerably less than 100% protection) provided by the prophylactic IVM dose of 0.2-0.3 mg/kg 2x/week was probably adequate from 2021 to late 2023, when compensatory mechanisms of the immune system of highly vaccinated individuals (e.g., production of virulence-inhibiting PNNAbs, production of SIR-created partly neutralizing antibodies, and activation of CTLs)** were able to protect those individuals from severe disease and death when they developed breakthrough infections.[11] However, once the highly infectious and highly virulent variant arrives on the scene, those compensatory immune

mechanisms will no longer be working for those highly vaccinated individuals. That is, instead of usually becoming only mild-moderately ill (or not ill at all) when they became infected in the past, they will be at great risk of becoming life-threateningly ill once they become infected with the anticipated highly virulent variant.[1-4, 11]

In other words, the stakes are much higher now. For example, a prophylactic dose of IVM that results in only a 73% reduction of infection will not be good enough, because the 27% of people who become infected despite taking that prophylactic dose will be at great risk of developing life-threatening infection. Whereas 100% protection was much less important during 2021-2023, 100% protection (if achievable) is far more important now.

[** Note:** PNNAbs = Polyreactive non-neutralizing antibodies. SIR = Steric Immune Refocusing. CTLs = Cytolytic T Cells (which kill virus-infected host cells). When the neutralizing capacity of vaccine-induced neutralizing antibodies markedly decreased (due to mis-match with new immune escape variants), the immune system of highly vaccinated individuals compensated for this situation by producing virulence-inhibiting PNNAbs and partially protective SIR-created antibodies, and by activating CTLs.**]**[11]

The problem is that we do not currently know what the most effective and, yet safe prophylactic dose/regimen of IVM might be, for the upcoming highly virulent variant(s). It is possible that a higher and daily dose will be needed. Making matters more complicated, we do not know how long people might need to take a higher daily dose or how safe it is to take a relatively high daily dose of IVM for many weeks. Although the anticipated highly virulent variant may threaten a given community (once it arrives in that community) only for a relatively brief period of time (several weeks or a few months?), the duration of the intense threat is uncertain, which means that the length of time people will most need to take prophylactic IVM is uncertain (several weeks or a few months?).

For example, it is possible that a prophylactic dose of 0.4-0.6 mg/kg/day will be necessary to protect people from becoming ill, and it is possible that individuals might need to take this daily dose for several weeks, even for a few months. But it is unknown whether that dose is sufficiently effective (particularly for the most vulnerable), nor is it known with certainty whether taking that daily dose for many consecutive weeks is adequately safe. It is important to take relative risks into consideration: if an individual's risk of dying from infection is extremely high, then a less serious side-effect risk associated with a high and prolonged daily dose of IVM might be the better risk to take.

Because of the above-mentioned concerns and uncertainties, it is unfortunate that we do not already have solid data regarding the safety, efficacy, or necessity of prolonged daily use of prophylactic IVM at doses in the range of 0.4-0.6 mg/kg or higher. I say "higher" because it is possible that a dose in the range of 1 mg/kg/day may be needed, and it would be good to know whether prolonged use at that dose is relatively safe---again, compared to what is at stake (potential death) if the prophylactic dose is too low or stopped too soon.

Some guidance regarding the safety of a relatively prolonged course of relatively high doses of daily prophylactic use of IVM is indirectly provided by the FLCCC and CCCA in their recommendations for the treatment of acute and severe COVID-19. For patients who become seriously ill with COVID, the FLCCC and the CCCA recommend a dose of 0.4-0.6 mg/kg daily for at least 5 days. If needed, that dose may be continued on a daily basis for an additional 5 days. That 10 day exposure appears to be safe.

Unfortunately, there is a dearth of data regarding continuation of a relatively high daily dose of IVM (e.g., 0.4-0.6 mg/kg) for a total duration longer than 10 days. An excellent and comprehensive review of the safety of IVM, published by Dr. Jacques Descortes in 2021, summarizes what is known about this issue, and is largely reassuring[10] Dr. Descortes points out the following:

"The safety of repeated daily oral administrations of up to 100 µg/kg [0.1 mg/kg] *ivermectin over 28 days is being evaluated by a randomized, controlled study in human volunteers. At near completion of this study, no safety concern emerged [MedinCell SA, unpublished results]."*

"Last but not least, the putative anticancer effects of ivermectin were tested for humane reasons in 3 children with unmanageable acute myelogenous leukemia at the daily dose of 1 mg/kg by continuous infusion for 15 days to 2 children aged 11 and 13 years, and for 6 months to another child aged 5 years. The authors concluded that ivermectin induced no serious adverse effects [Galvao de Castro, 2020]."

Unfortunately, there appear to be no other available data <u>in humans</u> regarding the safety of taking a daily dose of 0.4-0.6 (or higher) for several weeks or a few months. There is some information regarding prolonged daily use of relatively high doses of IVM <u>in animals</u>. (See APPENDIX.) Most of those studies in animals are reassuring. However, **there are two studies in beagle dogs that suggests that prolonged use of a 1.5-2 mg/kg daily dose (particularly the 2mg/kg/day dose) may be dangerous:**

"Beagle dogs treated with 0.1, 0.25, 0.5 or 1.5 mg/kg/day ivermectin by oral gavage for 14 weeks developed excessive salivation and decreased body weight <u>at the highest dose only</u>, and

no other significant adverse effects were noted. During another ***study in Beagle dogs treated orally with 0.5, 1 or 2 mg/kg/day for 14 weeks, 4 out of the 8 dogs from the high dose group had to be euthanized due to neurotoxicity and poor health condition.*** *In contrast, Beagle dogs administered 0.1, 0.5 or 1.5 mg/kg/day ivermectin orally for 39 weeks experienced neither mortality nor marked adverse effects."*

The above beagle studies argue against prolonged use of a daily dose in the range of 1.5-2 mg/kg/day (and higher).

As stated earlier, the highest health authorities in the USA and western Europe have strongly discouraged use of IVM for acute COVID-19 illness or for prophylaxis. Accordingly, they have made no recommendations regarding a prophylactic dose/regimen, other than to not recommend any use of IVM for COVID-19.

Finally, in addition to considering use of prophylactic IVM, people should be sure to optimize their Vitamin D levels, use other nutraceuticals, improve their overall physical, nutritional, and emotional health, and consider optimal use of mouth washes and nasal sprays, as explained on the FLCCC website.[7]

Conclusions:
Currently, there is a dearth of data regarding the most appropriate dose/regimen of IVM for prophylaxis against an anticipated highly infectious, highly virulent, and ubiquitous SARS-CoV-2 variant. It is possible that a dose of at least 0.6 mg/kg will be needed and that daily use of this dose may be necessary for at least a few weeks, possibly for several weeks. However, the safety of using a daily 0.6 mg/kg dose for more than 10 days is unknown, or at least insufficiently documented. It is also unknown whether a daily dose of 0.6 mg/kg is sufficiently high to adequately prevent infection with an anticipated highly virulent variant.

Proposal:
Because of the above-mentioned unknowns and uncertainties, it would be prudent to urgently conduct studies to determine the most appropriate dose and duration of IVM prophylaxis for an anticipated highly infectious, highly virulent, and ubiquitous SARS-CoV-2 variant (or variants).

We need to know if it is safe to take a dose of 0.6 mg/kg/day (or even higher) for several weeks (or even longer). We need to know what dose/regimen is needed to adequately prevent infection by an anticipated highly virulent variant.

We need to be prepared to study and learn from real world experience once the anticipated highly virulent variant arrives. For example, if this variant arrives in Community A and

prophylaxis with 0.6 mg/kg/day is started in that community (ideally) before the arrival, and the same prophylaxis is also started in a nearby Community B in which the virulent variant has not yet arrived, we need to know (for the sake of future communities that will experience arrival of the highly virulent variant) the extent to which that prophylactic dose (in Communities A and B) was safe and effective and whether continuation of that daily dose for several weeks was still safe and needed. Collection of such data will be needed in order to determine the most appropriate dose/regimen and needed duration of IVM prophylaxis. At the very least, we can study, learn, and adjust as we go.

It is vitally important to immediately ramp up production of IVM and provide it at an affordable price (or even for free) so that all people who need prophylactic IVM can easily obtain it. Unfortunately, the current global supply of IVM is most likely too small and is priced too high for many (even most) people.

Unfortunately, there has been no acknowledgement by health authorities that Dr. Vanden Bossche's warnings need to be taken seriously. His warnings have been ignored by health authorities in the USA and western Europe. These health authorities have continued to discourage use of IVM. They have shown no interest in encouraging prophylactic use of IVM, even at 0.2 mg/kg 2x/week. They have shown no interest in performing updated studies of the prophylactic use of IVM---to determine the most appropriate dose/regimen, the most appropriate duration of prophylaxis, and the safety of prolonged use of higher daily doses. As a result, we do not know, with certainty, how to optimally use IVM for prophylaxis against an anticipated highly virulent variant. This represents yet another failure of health authorities to honor and practice basic principles of science, preventive medicine, and public health.

DISCLAIMER:
This article is not intended to provide a recommended dose/regimen and duration of prophylactic use of IVM to protect against an anticipated highly virulent variant of SARS-CoV-2. If individuals wish to explore the possible prophylactic use of IVM for an anticipated highly virulent variant, they are encouraged to discuss this issue with their personal physicians or seek advice from their health authorities. Because IVM might interact with other medications a person may be taking, this issue should be discussed with one's personal physician before IVM is started.

This article is, in fact, intended to point out that **adequate scientific data are not currently available regarding the most appropriate dose/regimen and duration of prophylactic use of IVM for adequate population-level prevention of infection with an anticipated highly virulent**

variant. The purpose of the article is to document what is known, what is unknown, and how the most appropriate use of prophylactic IVM for a highly virulent variant could be determined.

The article is also intended to document that, despite Dr. Vanden Bossche's repeated warnings that a highly infectious, highly virulent SARS-CoV-2 variant will eventually arrive on the scene and cause catastrophic damage, no updated guidelines for prophylactic use of IVM to protect the population from such a variant have been provided by our health authorities. Whether there is still time for health authorities to determine and promote a wise recommendation for prophylactic use of IVM to protect against a highly virulent variant is unclear. Time is rapidly running out.

If health authorities do not provide a wisest-possible recommendation for prophylactic use of IVM to prevent infection with the anticipated highly virulent variant, prior to the arrival of that variant, an opportunity to save millions of lives will likely have been lost, and those who are fortunate enough to have an adequate supply of ivermectin will need to use their own intuition for its best use.

RELATED READINGS:

For further information about the statements made in this article, please see the following websites and articles, as well as the **APPENDIX** at the end of this article:

[1] Dr. Vanden Bossche's website: www.voiceforscienceandsolidarity.org

[2] Dr. Rennebohm's website (Notes on COVID-19): www.notesfromthesocialclinic.org

[3] Video-presentation: *Clinical Implications of Geert's Predictions: Vanden Bossche, McMillan, Chetty, and Rennebohm*
https://www.youtube.com/watch?v=UAblCGtVzVo

[4] In Anticipation of a Highly Virulent SARS-CoV-2 Variant: An ADDENDUM
https://notesfromthesocialclinic.org/in-anticipation-of-a-highly-virulent-sars-cov-2-variant-an-addendum/

[5] An Open Letter to Physicians and Physician Organizations
https://notesfromthesocialclinic.org/an-open-letter-to-physicians-and-physician-organizations/

[6] Ivermectin in the Prevention and Treatment of COVID-19—A Summary Statement
https://notesfromthesocialclinic.org/ivermectin-a-summary-statement/

[7] FLCCC website: https://covid19criticalcare.com/

[8] CCCA website: https://www.canadiancovidcarealliance.org/

[9] Turkia M. A Timeline of IVM-related Events in the COVID-19 Pandemic. https://www.researchgate.net/publication/350610718_A_Timeline_of_Ivermectin-Related_Events_in_the_COVID-19_Pandemic_April_3_2021

[10] Jacques Descortes. Expert Review Report: Medical Safety of Ivermectin https://cdn2.alaskawatchman.com/wp-content/uploads/2021/10/14132903/Clinical_Safety_of_Ivermectin-March_2021.pdf

[11] Do the COVID-19 Vaccines Protect Against Severe Disease and Death? https://notesfromthesocialclinic.org/do-the-covid-19-vaccines-protect-against-severe-disease-and-death/

APPENDIX:

The review article by Dr. Jacques Descortes[10] provides comprehensive information about the safety of IVM, as of 2021. Below are several particularly helpful quotations from that article:

For parasitic diseases: *"Typically, ivermectin is administered as a single dose of 150-200 µg/kg* [0.15-0.2 mg/kg] *for the treatment of a variety of parasitic diseases. Dosing can be repeated once or twice after a few days, or 3 to 6 months after the last oral dose."*

For crusted scabies: *"The Center for Disease Control (Atlanta, GA) recommend an oral dose of 150 µg/kg on days 1, 2, 8, 9, 15, 22 and 29 in patients with crusted scabies [CDC, 2019]."*

Regarding studies of prolonged use of daily IVM in animals: *"The repeated dose toxicity of ivermectin was assessed in a 3-month oral study in mice, a 4-week dermal study and 3- and 6-month oral studies in Sprague Dawley rats, in 3- and 9-month oral studies in Beagle dogs, a 2-week dermal study and a 2- week, 3- and 6-month dermal studies in minipigs, and finally a 2-week oral study in rhesus monkeys [Campbell, 1989; JECFA, 2016]."*

"In rats treated orally with 1, 3, 9 or 12 mg/kg/day ivermectin for 13 weeks, mortality was noted at a dose ≥ 9 mg/kg/day. In rats treated orally with 1, 3 or 12 mg/kg for 27 weeks, death preceded by neurotoxic manifestations was observed only in those animals given the highest daily dose. In both instances, mortality was mainly noted in females and during the first two

weeks of treatment. No toxicity was noted in rats treated dermally with 20 mg/kg/day ivermectin for 4 weeks."

"Beagle dogs treated with 0.1, 0.25, 0.5 or 1.5 mg/kg/day ivermectin by oral gavage for 14 weeks developed excessive salivation and decreased body weight at the highest dose only, and no other significant adverse effects were noted. During another study ***in Beagle dogs treated orally with 0.5, 1 or 2 mg/kg/day for 14 weeks, 4 out of the 8 dogs from the high dose group had to be euthanized due to neurotoxicity and poor health condition.*** *In contrast, Beagle dogs administered 0.1, 0.5 or 1.5 mg/kg/day ivermectin orally for 39 weeks experienced neither mortality nor marked adverse effects."*

"Rhesus monkeys did not experience adverse effects after 2 weeks of daily ivermectin administrations. The NOEL (No Observed Effect Level) was determined to be the highest dose level tested (1.2 mg/kg/day)."

"Finally, no remarkable toxic effects were noted in either mice or minipigs treated daily by the dermal route with up to 13 and 20 mg/kg/day ivermectin, respectively (for 13 weeks in mice and up to 39 weeks in minipigs)."

Regarding clinical trials of IVM for COVID: *"Let it be said that globally well above 10 000 human subjects have been enrolled in investigative studies or clinical trials. It is of note that neither deaths nor severe adverse events attributable to ivermectin have been reported."*

Regarding massive overdose of IVM: *"A suicidal intake of ivermectin was reported in a 19-year-old woman with severe Loa-Lao filariasis. She developed nausea and vomiting, and moderate neurological manifestations including ataxia, reactive mydriasis and hyperreflexia after possibly ingesting 100 times the recommended therapeutic dose (≈400 3-mg ivermectin tablets). She received conventional supportive treatment and could be discharged from hospital on day 4 post-ingestion [Djeunga et al., 2019]."* [The dose she took was approximately 20 mg/kg.]

In Summary: *"Taking into account all the above, the author of the present analysis of the available medical data concludes that the safety profile of ivermectin has so far been excellent in the majority of treated human patients so that ivermectin human toxicity cannot be claimed to be a serious cause for concern."* This represents Dr. Descortes' summary statement as of 2021.