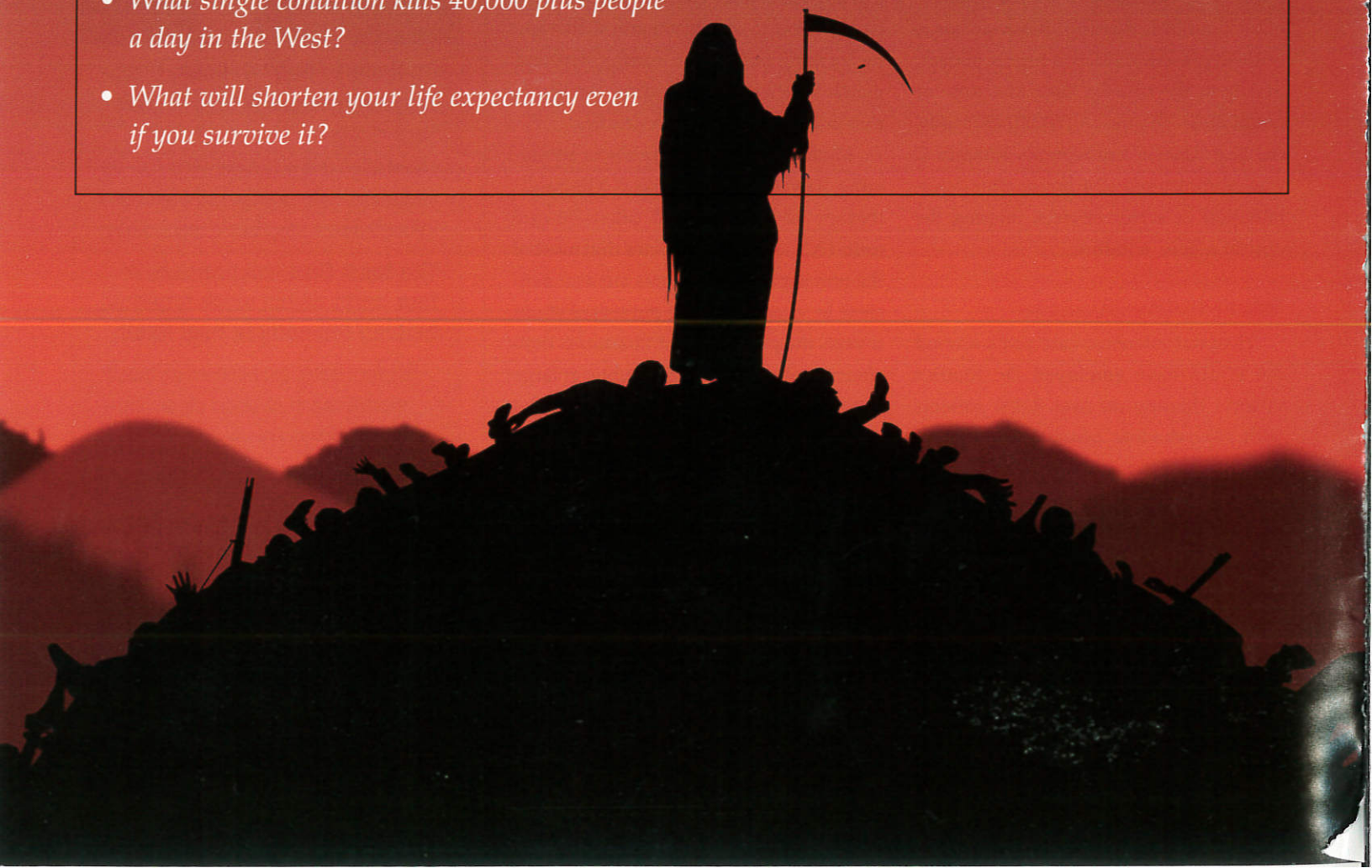
The Human Toll

- *What do the deaths of Pope John Paul II and Superman Christopher Reeve have in common?*
- *What is the 3rd leading killer in the West? [No, it is NOT COVID-19!] What seriously affects 30 million people worldwide each year, with over 8 million deaths?*
- *What is the leading cause of death in U.S. and European hospitals, accountable for nearly 50% of all clinical deaths?*
- *What kills the majority of cancer patients who die of infections? What kills more than 6 million Third World children each year, and is the largest killer of children and infants in the First World? What leads to frequent amputations?*
- *What causes over 75,000 maternal deaths worldwide each year?*
- *What single condition kills 40,000 plus people a day in the West?*
- *What will shorten your life expectancy even if you survive it?*
- *And make you 42% more likely to commit suicide?*
- *What causes death in antibiotic-resistant diseases, and is now a worldwide pandemic?*

The Answer is ... *Sepsis*

Sepsis is our real pandemic, long before SARS-CoV-2 / COVID-19 appeared on the scene. Yet, ironically, people who die of, or with COVID-19, are actually mostly dying of Sepsis.

The combined immune over-reaction and later immune depression of COVID-19, followed by organ failure, often with acute respiratory distress syndrome (ARDS), also constitute sepsis and septic shock.



COVID-19, COBALAMIN / B12, AND SEPSIS:

A Left-of-Field Solution

BY DR. CARMEN WHEATLEY

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In spite of all of the advances of modern medicine – vaccines, antibiotics, antivirals, antifungals, and intensive care support – nevertheless, worldwide, sepsis remains the primary cause of death from infections, whether bacterial, viral or parasitic. Moreover, **the incidence of sepsis is doubling every decade.** Infants, particularly premature infants, the elderly, cancer patients and the immune-compromised, blacks, and obese people are most at risk for sepsis. With the exception of infants, these are pretty much the very same groups of people currently dying of COVID-19.

Yet, sepsis is no respecter of persons. There is at times a seeming randomness in the victims it takes. Youth, privilege, and fitness are, at first sight, not necessarily a protection. Olympian athletes, Brazilian models, rock stars, young actors, and celebrities have died of sepsis, often suddenly and unexpectedly. Think of Socrates the soccer player, George Michael, Prince Rainier of Monaco, Amy Purdy, Patty Duke, Muhammad Ali, and Christopher Cazenove.

COVID-19 too has sometimes claimed the most unexpected victims.

Is there sense and a connecting thread behind the apparent occasional randomness of sepsis and of COVID-19 mortality amongst the seeming well?

To try and answer this leading question, we must first understand what sepsis entails.

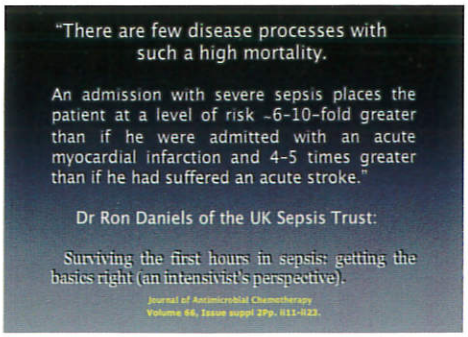
Causes

Sepsis, which includes septic and toxic shock (the latter being a more accelerated version of sepsis), may have multiple overt causes: trauma; surgery; kidney and other organ failure; burns; smoke inhalation; obvious immune vulnerability, as in HIV/AIDS, advanced cancers and tuberculosis; malaria, particularly cerebral malaria; ebola; meningitis; pneumonia; urinary tract infections; wounds, even pin pricks; implanted medical devices; cellulitis; poor dental health or dental procedures; tattoos and body piercings; animal bites; appendicitis; peritonitis, perforated bowel; pregnancy/childbirth; gallstones and kidney stones; spleen removal; molds or fungi; viruses, as in flu, and the known killer flus, avian and swine flu; many of the now notorious antibiotic-resistant bacteria, such as E. coli, staphylococcus aureus, klebsiella pneumoniae, clostridium difficile, pseudomonas, streptococci, listeria, salmonella, may all trigger sepsis. And, of course, more latterly, the SARS-CoV-2 virus/COVID-19.

You Need to Know the Symptoms

Unfortunately, the initial symptoms of sepsis are very general and non-specific. Nonetheless, sepsis should always be suspected when someone suddenly becomes confused, even perhaps mentally disturbed and hallucinating; if there is unexplained shivering, with notably cold extremities; together with enlarged lymph glands; an unusually low, or high, temperature; failure to urinate in a day; unusual and severe breathlessness, a feeling of doom, and discolored or mottled skin, with or without any distinctive rash.

Any of these symptoms, or any combination of these symptoms, in a child or adult, is a justifiable cause for an urgent visit to the Emergency Room. It is better to be safe than sorry when it comes to sepsis, *because time is never on your side.*



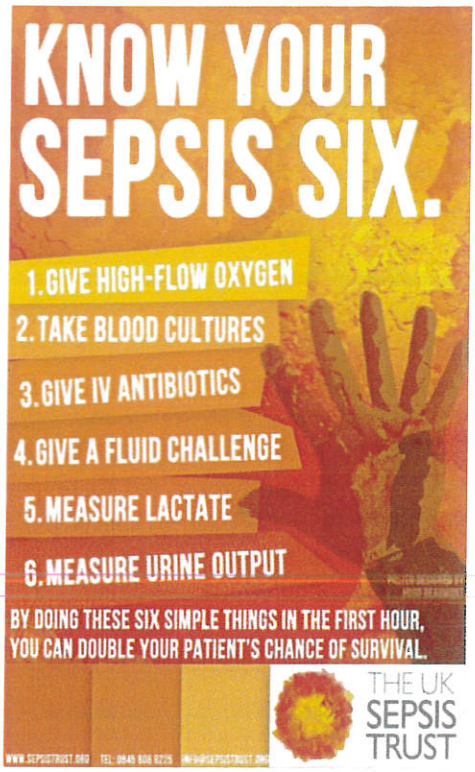
To Save a Life, Time Is of the Essence

Mortality from sepsis can range up to 50% or higher, depending on the hospital, and the chances of dying increase by 8%

for every hour that treatment is delayed. **As many as 80% of sepsis deaths could be prevented with rapid diagnosis and standard treatment.** Hospital staff need to be fully aware also, and implement, established protocols within a given time frame. Oxygen, fluids, total supportive care, and broad-spectrum antibiotics must be given within the hour of first suspicion or admission. Delay can be fatal.

In the United States, Rory's Regulations (standard sepsis treatment but tied to an early intervention time protocol, introduced into many hospitals by the parents of Rory Staunton, a young boy who died of sepsis as a result of fatal delays and diagnostic failure) have already saved 40% of children's lives that would otherwise have been lost.

Critical Information for Nurses and Doctors



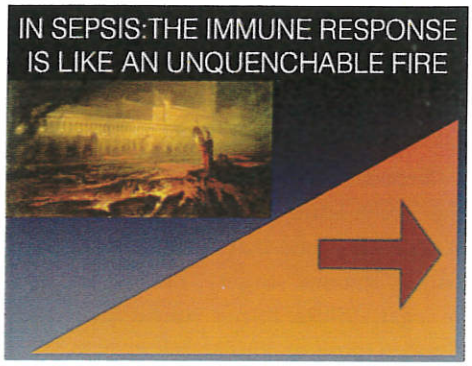
Repeat Hospitalizations: Post-Sepsis Syndrome

Sixty-two percent of people hospitalized with sepsis are re-hospitalized within 30 days. Patients who survive sepsis have double the risk of death in the following five years when compared with other hospitalized controls. They will also suffer the untold burden of ongoing physical, mental, cognitive, and emotional health problems.

What Happens in Sepsis?

Sepsis is the end result of a profound immune-system deregulation. A normal, healthy immune-system response to danger involves a necessary and useful degree of inflammation, which reaches a peak when the challenge is met or overcome, and then gives way to a predominantly anti-inflammatory state and resolution.

However, even as this useful inflammation reaches its peak, the immune system has already begun to produce anti-inflammatory agents, which shift the pro- and anti-inflammatory balance, ensuring inflammation does not get out of control.



A healthy immune system behaves like a lion awash with adrenaline and angry for a fight, but able to sleep peacefully like a baby immediately after the kill and feast. This kind of controlled inflammation is necessary to signal the immune cascade into action, to ward off or kill invaders.

However, in sepsis, the anti-inflammatory agents and hormones are either not produced, or not produced at sufficient levels, whilst the necessary pro-inflammatory hormones are over-produced. There is no resolution, and, as a result, the immune inflammatory response is continuously amplified and unceasing. What this leads to is popularly known as "a cytokine storm." In other words, a relentless production of predominantly inflammatory agents, stoking increasingly worse symptoms.

Veins and arteries become like spent elastic. Then they begin to leak, and you blow up like a balloon because the vital fluids go everywhere. You may look unrecognizable, like Elephant Man, one of the Northwick Park, Parexel, London drug-trial victims of more than a decade ago. Your blood pressure plummets and is unresponsive to adrenaline injections. Your organs are starved of oxygen, and one after another they fail. Biochemically, it is a very complex story indeed; yet, outwardly, this is what happens in sepsis and septic shock. This happens also in very sick COVID-19 patients whose immune systems, for whatever reason, cannot mount a normal response.

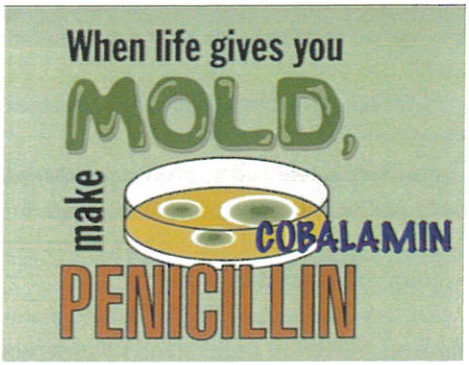
But it need not be like this. Nature does not intend it thus. Our immune systems are actually designed to avoid sepsis.

Sepsis & COVID-19 Treatment: The Solution Has Been with Us All Along

Sepsis has been called "a graveyard for clinical trials," with more than 60 failed clinical trials to date, and some drug trials even having to be stopped prematurely because they actually increased the death rate. The official available treatments – essentially antibiotics and optimal intensive-care measures – are clearly not enough. Moreover, antibiotics, antimalarials, and antivirals are now failing fast, which may soon lead to an even higher death toll.

The clinical drug trials have failed because they were based on the wrong paradigm of the real biochemical cause of sepsis. Attempts to suppress the immune system in sepsis are completely misguided. What is needed is something that will regulate a deregulated immune system and allow it to do its work. Nature has given us just such a central immune-system regulator: cobalamin/Vitamin B12, the product of a humble mold, just as penicillin is.

Two decades ago, I read the French medical case literature on the antidotal treatment of otherwise lethal cyanide (CN) poisoning cases with enormous doses of Vitamin B12 given intravenously, a standard CN antidote treatment in France for the last 70 years.



(The cobalt atom in B12 acts like a mag-

net for cyanide, which then becomes cyanocobalamin B12, and is safely excreted in urine.) What struck me the most in such cases, however, was that such high-dose, intravenous (IV) B12-treated, CN poisoning victims not only survived, but that they walked out of intensive care within days completely unscathed, when they should have been as sick as sepsis patients. The speed of recovery was nearly miraculous. The doctors who wrote the cases up noted that.

As there are many physiological parallels between sepsis/septic shock, and CN poisoning effects in the body, I realized that the hydroxocobalamin/B12 must be doing more than acting just as a magnet for the cyanide. Some years later I found some willing collaborators at the Biochemical Pharmacology lab of the William Harvey Research Institute, in London, a team with a special interest in natural and endogenous regulators of the immune response. They had read a theory paper I published in Medical Hypotheses in 2006 outlining why high-dose IV B12 should work for sepsis treatment, and together we made a key discovery. In a mouse model of sepsis we demonstrated repeatedly that high-dose IVB12 can regulate the entire immune response, because it regulates the supposed bad boy of sepsis, a potential double-edged sword but also the universal biochemical signal agent, the gas nitric oxide. Regulated by good levels of B12/cobalamin, nitric oxide in its turn exerts a central control of the vital immune response cascade of all the pro- and anti-inflammatory hormones that run amuck in sepsis, just as they do in CN poisoning, and other similar scenarios.

We observed that high-dose B12, ***particularly in its enzymatically active methylcobalamin form,*** lowers dangerously high levels of the leading pro-inflammatory immune hormones, Interleukin 1 (IL1) and tumor necrosis alpha (TNFa), as well as a late mediator of sepsis, high mobility group box 1 protein (HMGB1). We also discovered that B12 acts as a natural COX-2 inhibitor, and that all of these effects, which translated into significantly increased survival in the mice, were accompanied by a perfect, time-dependent, regulated rise and fall in levels of nitric oxide, and levels of the enzymes that synthesize it, although, importantly, there was never a complete inhibition, as that too would be dangerous.

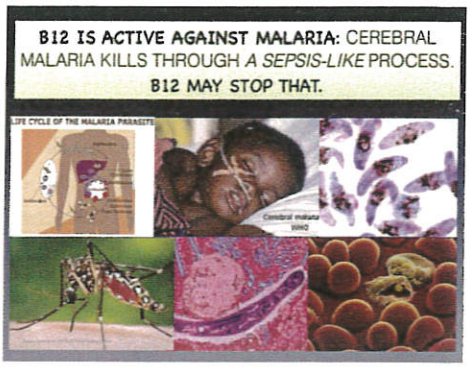
Thrillingly, the protocol that I advocated for sepsis back in 2006 has already been used to save lives for related conditions involving acute inflammation: three years ago it saved the life of a young woman, accidentally exposed, in a new operating theatre for 20 minutes to the anesthetic gas nitrous oxide – not the same as nitric oxide – from which she would have died. Yet, within 48 hours an initial 5-day treatment with high-dose IV B12 restored her from complete paralysis and voicelessness, and left her totally unscathed. Not long ago, cardiologists at the Mayo Clinic in the U.S. also used the 5-gram IV B12 dose to rescue a serious cardiac surgery patient with "vasoplegic syndrome." While still on the operating table, the patient's blood pressure plummeted dangerously, as his heart function deteriorated further. Both vasopressors (blood pressure supportive drugs) and repeated, standard, hazardous infusions of methylene blue were of no avail. Then, a B12 infusion was given, as a last resort. Recovery took place in a mere quarter of an hour.

Several other cases of high-dose IV B12 use for vasoplegic syndrome, including during liver surgery, confirm this dramatic and safe therapeutic response to mega high-dose IV B12. **Vasoplegic syndrome/ plummeting, unresponsive blood pressure, caused by a deregulation of nitric oxide supply in the circulation, is a key characteristic of sepsis** and is a frequent harbinger of death. High doses of B12 given IV are known to raise blood pressure, which in sepsis is just what is needed. *Yet, no one has ever tried treating this aspect of sepsis with high-dose IV Vitamin B12.*

Incredible Safety of High-Dose Injected B12

Safety is really not an issue here. High-dose IV Vitamin B12 has an enviable clinical and pharmacological safety record. (The entire medical safety literature references are in the draft protocol on my ResearchGate page.) Because of its safety and efficacy profile, the FDA long ago gave IV B12 "orphan drug" status for use as a treatment for CN-gas inhalation in smoke victims from fires and in suspected terrorist scenarios.

B12 is also very cheap, by comparison with the cost of drugs. In theory, even without a clinical trial, given its CN antidotal existing use in intensive-care medicine, B12 could also legally be used "off-label" in dying sepsis patients, in children with meningitis, in antibiotic-resistant patients, in flu and in other epidemics, not least for COVID-19 right now. It is a matter of political and medical will, and of having this information.



B12 Has Known Anti-COVID-19 Actions

I posted this basic information as an emergency treatment for COVID-19 on my ResearchGate page at the very beginning of March this year. Many doctors read it, but it seems that none decided to act upon it.

And yet, in June 2020, a small, controlled clinical study from Singapore General Hospital, which gave COVID-19 patients just an oral combination of Vitamin D, magnesium, and B12, found that in older COVID-19 patients this simple combination was associated with a significant reduction in the proportion of patients with clinical deterioration requiring oxygen support and/or intensive care. Another study from India performed molecular modelling with B12 and found that methylcobalamin had the potential to bind the SARS-CoV-2 viral RNA replication protein, nsp12 polymerase, and thus **prevent viral replication. The potential for direct binding of B12 to synthetic RNA receptors has been known since 1994. This fact inspired yet** another molecular screening study which found that niacin (Vitamin B3) and cyanocobalamin B12 could bind and interfere with the COVID-19 virus' main protease.

B12 Has a Historic Record as an Antiviral

I am now completing a review of the known effects of B12 on the immune response, which points out its significance for COVID-19 treatment. To give but one example, the fact that while COVID-19 depletes Natural Killer (NK cells), and other immune cells, B12 is known to boost them. The review covers much lost, forgotten, or overlooked B12 clinical data in multiple foreign-language journals dating back to 1949.

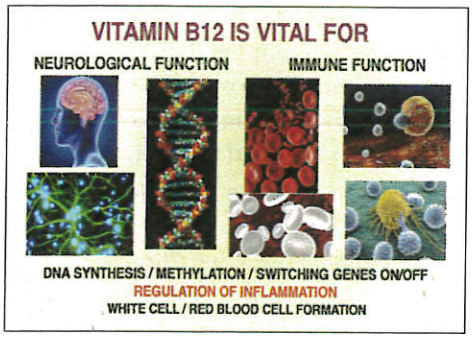
It presents considerable evidence of the multiple antiviral potential and clinical uses of B12 in the last 70 years, which are inexplicably being ignored: the research shows B12 has antiviral action against influenza A & B viruses, and human papillomavirus (HPV), with many – forgotten – early clinical studies showing cobalamin's effectiveness against viral hepatitis, neurotropic viruses, polio, herpes simplex, herpes zoster, and varicella (chickenpox). In HIV, in vitro, cobalamin significantly inhibits HIV integrase, the gp120 glycoprotein, thus preventing HIV infection, in a non-strain specific manner.

Luc Montagnier, the French virologist who discovered the HIV virus, and his associate Dr. Perez, recently demonstrated the unique existence in the SARS-CoV-2 genome of a seemingly exogenous/inserted region containing 16 exogenous "informative elements" (Env, Pol, and Integrase genes) derived from diverse specific HIV-1/2 and Simian immunodeficiency retrovirus genomes, and also from the malaria Plasmodium yoelii genome, which, in sum, give SARS-CoV-2 its virulence and pathogenicity.

These inserted HIV/malaria genome regions may perhaps account for SARS-CoV-2's response to HIV retroviral drugs and anti-malarial hydroxychloroquine, which, like cobalamin/B12, has pleiotropic anti-viral action. One might therefore expect therapeutic effects also from cobalamin against SARS-CoV-2 on this count alone, given its anti-HIV, and also its known, 2008 published, anti-malarial actions.

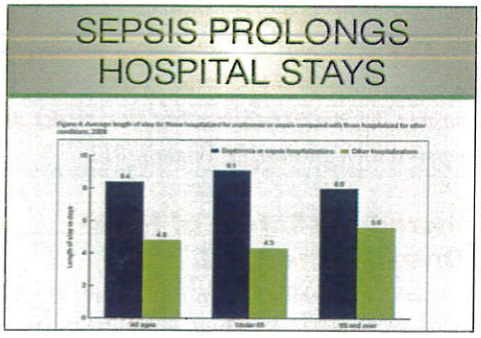
How High-Dose B12 May Be Deployed for COVID-19 and Sepsis: A Threefold Plan

Whilst much has been written about potential anti-COVID-19 drugs, nature's own antivirals are not getting much airtime. Yet, data has correlated poor outcomes in COVID-19 with poor Vitamin-D status. This means that summer sunshine should play a part also. Vitamin C is also known to have antiviral actions. So, taking these vitamins prophylactically, along with a liposomal form of B12 as methylcobalamin, and also a synergistic methylfolate supplement, is a first step for prevention, and early treatment.



In at-risk categories of patients with COVID-19, I would also advise using daily high-dose methylcobalamin B12 injections to prevent any deterioration to sepsis and ARDS. This would likely also shorten COVID-19 hospital stays, and has already been clinically tested at 50 mg parenteral daily doses, in a six-month Japanese ALS clinical trial. So, we know this is very safe.

Finally, for sepsis and COVID-19 sepsis/ARDS, doctors should go up to the full 5-gram IV dose, preferably of methylcobalamin. There are some cautions for certain patients at this dosage: anyone with poor kidney function could, according to the Merck Cyanokit studies, be susceptible to further kidney damage, even if this is potentially a very rare event, and these will be mitigated for in my forthcoming clinical trial protocol.



Sepsis Does Not Strike Randomly as at First It Appears

Varied genetic inheritance affecting B12 biochemical pathways means that some need more B12 than others. Blacks are probably more susceptible to COVID-19 because, genetically, they require much higher levels of B12 (and they tend to have lower Vitamin-D levels).

Further, people no longer eat abundant B12-rich foods such as liver, kidneys, eggs, and seafood. Antibiotics, junk food, and obesity have wiped out many people's natural immunity. Acid-blocking (B12-blocking) medication prescriptions are epidemic, even given to babies; and smoking rapidly depletes B12: Socrates (the soccer player) was a two-pack-a-day smoker.

Crippling Economic Costs of Sepsis

In the United States alone the annual cost of treating sepsis is over $24 billion, reaching $35 billion, if one includes all antibiotic-resistant infections. Across Europe, annual sepsis treatment costs are £17 billion and rising. Recently, an independent report from the UK Sepsis Trust found that sepsis-related treatment costs had been radically under-estimated and that it costs the UK £15.6 billion a year. No health economy can sustain such rising costs. Yet a lifesaving and cost-cutting solution is staring us in the face.

More than that. There is no guarantee that any of the SARS-CoV-2 vaccines in the pipeline will work. The Oxford frontrunner vaccine trial has already been halted because of adverse effects. Yet, if one has a safe and effective treatment now, as I believe we may, the World could go back to normal, and normality would not hinge on a distant hypothetical vaccine solution.

Luc Montagnier said that "Nature abhors disharmonies," and recently observed that the SARS-CoV-2 virus was already shedding the pathogenic inserts first, mutating into less-aggressive forms, and might well disappear. Just like SARS and MERS.

Yet, sepsis, the true pandemic, will remain. So, what are we waiting for?

The registered UK charity, Survive Cancer, is fundraising for formal clinical trials of high-dose B12 for sepsis, and working to find interested clinicians.

HELP OUR CLINICAL TRIAL FUNDRAISING EFFORT.
Get the cobalamin COVID-19/sepsis clinical trial protocol.

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