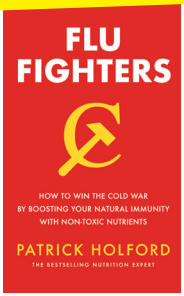


Chapter 9

Surviving Respiratory Distress

Every year in the UK there are over 17,000 flu-related deaths, with 84% being people over 65. The winter of 2017/18 was particularly bad – 26,408 died. Of course, our focus now is on the increasing death toll of COVID-19. But what is going on at the sharp end of flu, including COVID-19 and other 'killer' flus that have emerged in the last two decades? How can the survival rate be increased?

In most cases fatality is due to *Acute Respiratory Distress Syndrome (ARDS)*, which is apparently occurring at varying degrees in about four in ten patients suffering from COVID-19. This figure, however, may be skewed by focussing on hospitalised cases and not considering those 'at home' who have had minor symptoms, and got over a likely COVID-19 infection without severe symptoms. The primary cause of ARDS is the body's immune system producing a *cytokine storm* where our immune system overreacts producing a massive state of inflammation. This inflammation in the lungs, causing difficulty breathing, is the basis of a diagnosis of pneumonia. All this is what makes flu potentially fatal and why COVID-19 patients in ICU need ventilators to keep them breathing. The important point is that it is not the virus that is killing people, it is this state of inflammation.

How Vitamin C Reverses ARDS

During ARDS there is extreme inflammation and swelling in the *alveoli*, the balloon-like air pockets in the lungs, *haemolysis*, which is the rupturing of red blood cells and blood vessels, and

blood coagulation. You may have heard of *haemoglobin* (spelled *hemoglobin* in the US), which is the critical iron containing protein that carries oxygen in the blood, and gives blood its red colour. COVID-19 specifically attacks haemoglobin resulting in haemolysis. With haemolysis cell-free *heme*, unbound into this protein and no longer contained in the red blood cell, wreaks havoc triggering a cascade of highly damaging oxidative reactions.

Fortunately, we have a backup system, a protein called *haptoglobulin*, which binds to and hence mops up and disarms this dangerous cell-free heme, thus reducing inflammation and oxidation. However, it needs vitamin C to do this.

Heme contains iron. Normally the iron is held in a stable unreactive *ferrous* state (Fe2+). It is in this form that it can bind to oxygen and carry it around the body in haemoglobin. That's why you get tired when your iron levels are low – you're lacking oxygen. But if it changes to the oxidised *ferric* state (Fe3+) it becomes very dangerous. That is what's behind numerous reports of the dangers of having too much iron, especially later in life. This form of iron can damage arteries increasing cardiovascular risk.

Vitamin C, you may know, helps iron to work in the body and facilitates its incorporation into haemoglobin. Vitamin C also disarms this chain reaction of damage caused by cell-free heme. Researcher Doris Loh believes this is why, "the use of intravenous vitamin C in the treatment of COVID-19 has shown such remarkable success in speeding recovery and reducing mortality in critical COVID-19 patients," she says. "Erythrocytes (red blood cells) must have access to ascorbic acid in order to maintain hemoglobin in the ferrous redox state. Without adequate ascorbic acid, heme will rapidly oxidize and become cell-free heme. This is the reason why even young adults in good health and no underlying health conditions can develop ARDS quickly upon COVID-19 infection." Exactly how vitamin C does this was unravelled by scientist Dr Peilong Lu from Washington University, in 2014.

IV Vitamin C is Being Given to COVID-19 Patients in China, the US and Italy

You may have heard that many Chinese hospitals, some American and Italian hospitals are now giving intravenous vitamin C (IVC). This needs to happen everywhere and fast if we are to save lives. The Shanghai Medical Association describes the use of IVC as safe and effective adjunctive care of hospitalized COVID-19 patients. In the IVC treated patients, so far, there was no mortality, no reported side effects, and shorter hospital stays universally. They recommend their doctors use vitamin C for the treatment of COVID-19 infections.

Reports from the prestigious Ruijing Hospital in Shanghai, China, documented the treatment of 50 cases of moderate to severe COVID-19 cases with high dose intravenous vitamin C (IVC). Dr Mao stated that his group "treated ~50 cases of moderate to severe cases of COVID-19 infection with high dose IVC. The IVC dosing was in the range of 10,000 mg - 20,000 mg a day for 7-10 days, with 10,000 mg for moderate cases and 20,000 for more severe cases, determined by pulmonary status (mostly the oxygenation index) and coagulation status. All patients who received IVC improved and there was no mortality. Compared to the average of a 30-day hospital stay for all Covid-19 patients, those patients who received high dose IVC had a hospital stay about 3-5 days shorter than the overall patients." Dr. Mao discussed one severe case in particular who was deteriorating rapidly and expected to die. He gave 50g IVC over a period of four hours. The patient's pulmonary (oxygenation index) status stabilised and improved as the critical care team watched in real time. There were no side-effects reported from any of the cases treated with high dose IVC.

A registered trial of 140 patients treated with intravenous vitamin C has been under way since February in China. Another trial of 500 patients started in March in Palermo, Italy. Two more trials are happening in China but I have no details.

A Wisconsin state hospital and two New York state hospitals are now following suit. Dr Andrew Weber, a pulmonologist

and critical-care specialist affiliated with two Northwell Health facilities on Long Island, said his intensive-care patients with the coronavirus immediately receive intravenous vitamin C. "The patients who received vitamin C did significantly better than those who did not get vitamin C. It helps a tremendous amount, but it is not highlighted because it's not a sexy drug," he said in an article in the New York Post. They are also using the anti-malarial drug, hydroxychloroquine, which also binds to cell-free heme. This is why it's effective in treating malaria which emphasises why high dose vitamin C, also neutralising the cell-free heme, is the right approach.

Dr. Pierre Kory, the Medical Director of the Trauma and Life Support Center and Chief of the Critical Care Service at the University of Wisconsin in Madison says "If you can administer Vitamin C intravenously starting in the Emergency Room and every 6 hours thereafter, while in the hospital, the mortality rate of this disease and the need for mechanical ventilators will likely be *greatly* reduced," The big question, he says, is "Why aren't many more U.S. hospitals adopting this protocol? "The only reason I can give is that there is widespread, and often well-founded, bias amongst physicians against the use of vitamin therapy," says Dr. Kory. He adds, "The persistence of this bias is inexplicable given that the evidence is in plain sight." He points out that despite the publication of a major study of intravenous Vitamin C in ARDS (the syndrome that is killing patients with COVID-19), which reported dramatic reductions in mortality, days on the ventilator, and days in the ICU, only a minority of critical care doctors adopted the therapy as part of routine practice"

Vitamin C Reduces Time on Ventilators in ICUs

As these reports suggest vitamin C is highly likely to reduce time spent in Intensive Care Units (ICUs) which is so desperately needed. Twelve trials involving 1,766 patients show that vitamin C reduced the length of ICU stay on average by 7.8%. In six trials, oral vitamin C supplements in daily doses of 1–3 g/day reduced the length of ICU stay by 8.6%. That might not sound much but it would increase ICU

capacity by the same amount. In other words, instead of being able to help a thousand people these hospitals could help a further 80 people if they just gave vitamin C supplements.

In five trials in which patients needed mechanical ventilation for over 24 hours, 1 to 6g of oral vitamin C shortened the duration of mechanical ventilation by over 25%! That again would have a massive impact on the number of people who can be treated.

Why Oral Ascorbic Acid and IV Sodium Ascorbate Combined Might Work Better

As you learned in Chapter 3 the natural form of vitamin C, as produced by almost all animals, is ascorbic acid. It is, however, acidic and too acidic to inject directly into the blood stream. That is why an alkaline form of this vitamin, sodium ascorbate, is given intravenously.

During a cytokine storm, and the consequent massive increase in inflammation, ascorbic acid is being used up at an enormous rate because it has the ability to mop up oxidants. It then becomes oxidised (dehydroascrobic acid), but can then be recycled back to its 'reduced' or reloaded form, assisted by specific co-factors. We saw the kind of co-factor nutrients that help this in Chapter 6.

Doris Loh, however, thinks "It is possible that sodium ascorbate may not be utilized in the same manner as a result of its molecular structure" and is thus less able to be recycled than pure ascorbic acid. It would still perform vitamin C's other important functions but not, perhaps, be so rapid in calming down a cytokine storm as ascorbic acid. Also, while there is a general belief that intravenous vitamin C is so much better because it is thought to raise blood levels faster than oral supplementation an experiment by Steve Hickey (co-author of *Ascorbate: The Science of Vitamin C*) and Owen Fonorow (who runs the vitaminCfoundation.org) found something rather remarkable. First, they compared blood levels of vitamin C in a volunteer after ingesting 10g of ascorbic acid, compared to 11.3g of sodium ascorbate (to account for additional weight of sodium in the compound) taken by mouth.

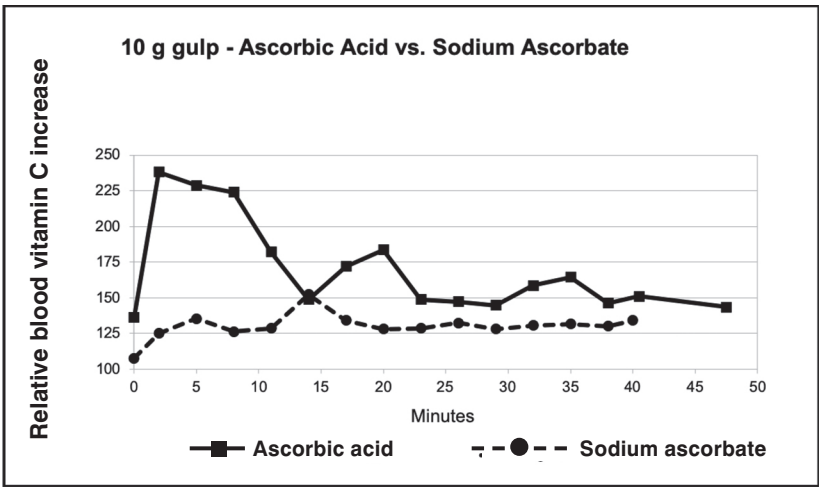


Figure 5 - Absorption of oral ascorbic acid vs oral sodium ascorbate. Credit: *Data from* O Fonorow, *Townsend Letter. March 13, 2020, prior to print publication. See reference 142. Reproduced with permission.*

As you can see ascorbic acid caused an immediate high level in the bloodstream, which tapers off quite rapidly, but then goes up again after 15 minutes, and again at around 30 minutes. In stark contrast, the sodium ascorbate creeps in more slowly and fails to get higher than ascorbic acid in the first 40 minutes.

But the real surprise was what happened when they compared the results of a single 10g oral dose of ascorbic acid (the solid line) given to three people… with the average increase produced by intravenous sodium ascorbate (the dotted line) over 50 minutes from ingestion or injection. (see overleaf).

What this graph overleaf shows is that oral ascorbic acid is extremely well absorbed and pushes blood levels much higher than intravenous sodium ascorbate for the first ten or so minutes. This of course contradicts the widely held myth that you can't absorb more than 200mg of vitamin C. But there's something even more interesting that is the unique 'recycling' hallmark of ascorbic acid.

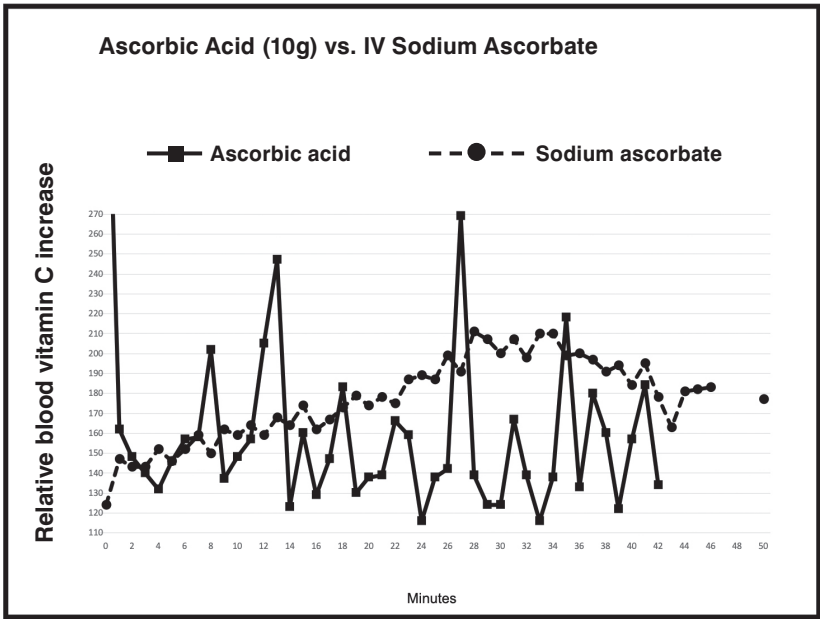


Figure 6 – Absorption of oral ascorbic acid vs mean intravenous sodium ascorbate.

Credit: *Data from* O Fonorow, *Townsend Letter. March 13, 2020, prior to print publication. See reference 142. Reproduced with permission.*

You will notice that, more or less every 12 minutes after the oral dose vitamin C levels dip then rise again. This is probably ascorbic acid being 'spent' disarming oxidants, then reloaded, then spent, then reloaded three times before petering out after an hour. This is the same cyclical effect seen in the first experiment comparing oral ascorbic acid with sodium ascorbate. This is another extremely good reason to take vitamin C (ascorbic acid) every hour when fighting an infection. The relatively flat line, with no peaks and troughs, might suggest that sodium ascorbate can't be recycled as efficiently as ascorbic acid can. There could be merit in having both ascorbic acid and sodium ascorbate, especially during an acute infection.

A similar kind of effect was seen in one of the first studies, by Katsu Takenouchi and Kazuo Aso in Japan way back in 1964. They measured blood plasma ascorbic acid levels after giving three 1g oral doses to two volunteers. In the graph below the arrows indicate when the 1g oral supplement was given. Again, you can see an initial increase in blood vitamin C levels after the first dose, but then, around 3.5 hours, before the second dose, vitamin C level goes up again. Could this be indicating the same recycling process kicking in? Also, you can see blood levels are maintained for at least 12 hours from three 1g doses.

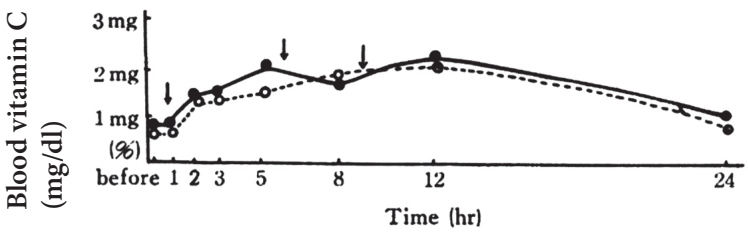


FIG. 7 *Blood Level of Total Ascorbic Acid after Oral Administration of 1,000 mg Ascorbic Acid Three Times Daily*
Arrows show administration of 1,000 mg ascorbic acid.

Figure 7 – Blood level of ascorbic acid over 24 hours after three 1g doses of ascorbic acid.

Credit: *Data from* K Takenouchi and K Aso, *J Vitaminol; 1964;10: 123-134. See reference 143.*

On the basis of this hypothesis, because it is a theory at this point, but one that makes alot of sense, Doris Loh recommends the following treatment strategy:

Initial onset of symptoms:
3g to 5g of ascorbic acid in one dose, followed by 1g every 30 to 60 mins for the following three hours. Repeat this cycle until symptoms subside.
Milder cases:
2g to 5g in one dose, followed by 1g every hour for the following four to six hours. Repeat this cycle until symptoms subside.

Severe/critical cases:
10g in one dose, followed by 2g every 15 to 30 mins for the following two hours. Repeat this cycle until symptoms improve.

This is not so far off what Linus Pauling told me back in the 1980s. "My recommendation is not 1 gram a day, or 2 grams a day of vitamin C but at the first sign of a cold, take a gram of vitamin C or 2 grams and then an hour later if the symptoms still exist - if you're still sneezing, or your nose is running or feel shivery - take another 1 or 2 grams of vitamin C. Keep doing that until you forget because the symptoms have gone away and this will stop a cold in almost every person who follows the regimen." Something more aggressive, along the lines of Loh's recommendations, may be needed for a serious flu such as COVID-19.

Combining oral ascorbic acid with intravenous sodium ascorbate may be the best of both worlds. Let's hope that this becomes standard treatment very quickly as COVID-19 spreads across humanity with devasting results.

Understanding and Controlling a Cytokine Storm

Normally, when under attack, the body produces small proteins called cytokines as part of its natural inflammatory reaction. We've come across these in numerous chapters where nutrients have been shown to have a positive effect on cytokine levels. Some cytokines switch on inflammation (pro-inflammatory) while others are anti-inflammatory, switching off the pro-inflammatory ones.

A *cytokine storm* happens when the immune system overreacts with too great a pro-inflammatory response. For example, when the COVID-19 virus enters the lungs, it triggers an immune response, attracting immune cells to attack the virus, resulting in localised inflammation in the lungs. This is a normal part of an immune response. It also increases body temperature, which helps fight off infection. But, if the immune system overreacts the massive over-inflammation, coupled with localised bleeding and coagulation, as well as too high a temperature, can seriously harm or even be fatal.

That is why it is very important to both reduce the viral load quickly, supply lots of antioxidants and especially vitamin C as oxidation goes through the roof, and bring inflammation back under control.

I had first-hand experience of this earlier this year when, out of the blue while travelling in Kenya, I started aching, shivering and shaking. Despite feeling really cold inside I was burning up with a fever. I thought I had malaria but it was sepsis, or septicaemia, brought on by a bacterial infection. I was experiencing, first hand, a cytokine storm.

Normally, one's *white blood cell count* (that's all those immune cells) should be between 3 and 10. Mine shot up to 24. *C-Reactive Protein (CRP)*, which is a measure of inflammation, and should be below 10. It shot up to 160. The treatment was intravenous antibiotics for 48 hours. I also took 1g vitamin C every two hours (I had limited supplies and slept a lot on day 1). Within 48 hours I felt absolutely fine. My raging temperature had returned to normal and my white cell count had returned to 9, the normal range.

Cytokines are mainly made in T-cells and macrophages. 'Cyto' means cell and 'kine' means 'moves towards'. So these cytokines are what our immune cells release when under attack. They have strange names – interleukin (IL), tumor necrosis factor (TNF) and interferon (IFN) – and different forms. For example, IL-1b and IL-6, as well as TNF-alpha, are pro-inflammatory and cause pain. That's why my body was aching during my sepsis.

Anti-inflammatory cytokines include *interleukin* (IL-1) receptor antagonist, IL-4, IL-10, IL-11, and IL-13. IL-10 is the most anti-inflammatory, along with *interferon*, often abbreviated to IFN.

Don't think of one as bad and the other as good because there's a complex dance that our immune system initiates and simply killing inflammation isn't the whole answer because it is part of the body's response to an invader.

The as yet unsubstantiated rumours that non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin and ibuprofen may

not be a good idea could be because they interfere with this process in a way that might not be so good. In an article in the Guardian Professor Ian Jones, a virologist at the University of Reading, said "There's good scientific evidence for ibuprofen aggravating the condition or prolonging it." Paul Little, a professor of primary care research at the University of Southampton, said: "There is now a sizeable literature from case control studies in several countries that prolonged illness or the complications of respiratory infections may be more common when non-steroidal anti-inflammatories are used." A study headed by Professor Little, published in the *British Medical Journal*, found patients with respiratory infections such as coughs, colds and sore throats, who were prescribed ibuprofen rather than paracetamol by their GP, were more likely to subsequently suffer severe illness or complications. Other researchers have linked NSAID use to worsening pneumonia. Professor Little thinks this is because inflammation is part of the body's natural response to infection. "If you're suppressing that natural response, you're likely inhibiting your body's ability to fight off infection," he said. Paracetamol, which can also reduce fever and pain, is used instead. That's what I was given, during my bout of septicaemia, not NSAIDs. NSAIDs also make the gut wall more permeable. In acute situations paracetamol is given four times in 24 hours, with at least four hours between doses. Too much is harmful to the liver.

What we have learnt is that the nutrients discussed in this book such as vitamin C, vitamin D, zinc, selenium, glutathione and so on, help the immune system to react appropriately. By rapidly cleaning up the oxidant chaos, carried out most effectively by ascorbic acid, especially if it can be rapidly recycled. This is where these other synergistic nutrients come in, as they help reduce inflammation, but in a natural way, while also being antiviral. There is certainly good logic to increase or optimise supply of the chain of antioxidants shown on p.58 which could most practically be done by taking an antioxidant formula containing all these four times a day, alongside vitamin C. It may also be a good idea to increase your vitamin D substantially during an infection, especially if your blood level is

below 50nmol/l, with at least 100nmol/l being optimal. See the studies below.

Nutrients that Help Pneumonia

Most flu-related deaths, and serious complications, are attributed to it causing respiratory distress, the hallmark of pneumonia. While it is too soon to have research results on COVID-19 there's plenty of evidence that lack of several nutrients covered in this book increase risk of respiratory distress and pneumonia. There is less good evidence due to a lack of trials, but not ineffective trials, that supplement nutrients help in the recovery from pneumonia. Those with clinical evidence of aiding recovery include vitamin C, D and E. Selenium has been studied for sepsis – a meta-analysis of thirteen trials concluded "selenium supplementation could not be suggested for routine use". A trial on 99 mechanically ventilated pneumonia patients comparing selenium with saline solution for 10 days found no significant difference in symptoms or death rate, although the levels of glutathione peroxidase, the selenium dependent enzyme, went up. Perhaps it was too little too late.

Vitamin C and Pneumonia

It is a well established fact that pneumonia is the usual cause of death in vitamin C deficiency (scurvy), but can high doses help recovery? An official statement from Xi'an Jiaotong University Second Hospital where they are trialling high dose intravenous vitamin C states: "On the afternoon of February 20, 2020, another 4 patients with severe new coronaviral pneumonia recovered from the C10 West Ward of Tongji Hospital. In the past 8 patients have been discharged from hospital…. High-dose vitamin C achieved good results in clinical applications. We believe that for patients with severe neonatal pneumonia and critically ill patients, vitamin C treatment should be initiated as soon as possible after admission". The research study will be completed in September and hopefully published shortly thereafter.

The first study of the effects of vitamin C on pneumonia dates

back to 1948 when Dr Fredrick Klenner published his results of 42 cases of viral pneumonia treated with vitamin C over a five-year period. He started with 1g of vitamin C intravenously and repeated this dosage every six to twelve hours. For infants and smaller children, he halved the dose. As with the other viral infections already examined, Klenner had excellent results.

The latest review of studies in 2017, by Professor Harri Hemilä states "Three controlled trials found that vitamin C prevented pneumonia. Two controlled trials found a treatment benefit of vitamin C for pneumonia patients." However, some of these studies are very low dose, under 1g.

A more recent study, in 2018, compared the results of 46 severe pneumonia patients given standard treatment with 56 patients treated with 6g of vitamin C daily. Those given vitamin C had 85% less mortality and double the rate of radiologic improvement in the lungs at day 7. The vitamin C protocol did not increase the rates of acute kidney injury or superinfection. However, I still urge caution especially in those with decreased kidney function.

Vitamin D and Pneumonia

Low levels of vitamin D are associated with increased risk of pneumonia but will high dose help recovery? I know of two studies that have investigated this.

In one trial involving 30 mechanically ventilated critically ill patients were given 1,250µg (500,000iu) of vitamin D3. Supplementation significantly increased haemoglobin concentrations, improving iron metabolism and the blood's ability to transport oxygen properly. Like vitamin C, this would rapidly reduce the cytokine storm.

Another high-dose study in Georgia US, gave ventilated intensive care unit patients with mean baseline vitamin D blood levels below 50nmol/l either 1,250µg (50,000iu) or 2,500µg (100,000iu) of vitamin D daily for five days. It reported that hospital length of stay was reduced from 36 days in the control group to 25 days in

the 250,000iu group and 18 days in the 500,000iu group . That's a halving of hospital stay, and costs, in the high vitamin D group. Those in the lower dose group had healthy blood levels of 112nmol/l by the end of their treatment while those on the higher dosage had blood levels of 137nmol/l. This illustrates how easy it is to rapidly increase vitamin D blood levels with short-term high dosages.

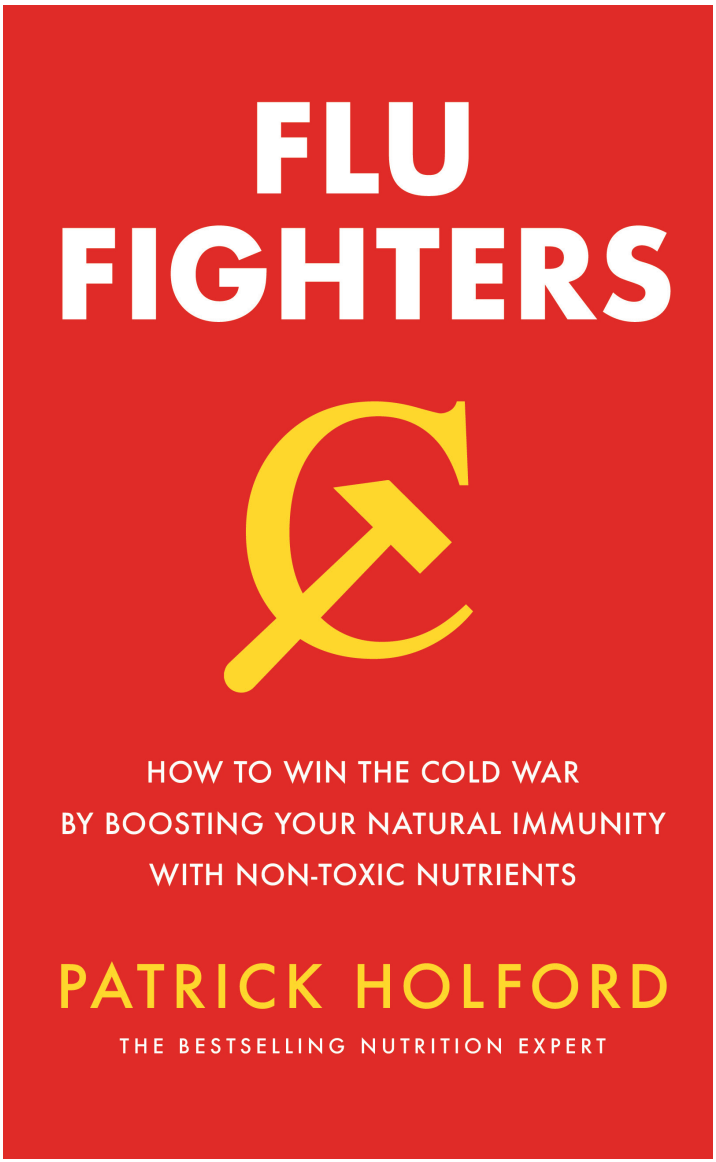
Vitamin E and Pneumonia

One study giving 50mg of vitamin E over 6 years to male smokers found 69% lower incidence of pneumonia in those smoking under 20 a day and exercising, and 14% lower in those smoking more than 20 a day and not exercising. This is not a treatment trial as such but does illustrate how optimum nutrition reduces pneumonia risk. Whether this translates into anything useful during a COVID-19 induced cytokine storm and consequent pneumonia is unknown.

In summary, the case for giving either high hourly oral doses of ascorbic acid, or IVC, or both, is compelling. So too is the rationale for upping vitamin D levels to above 100nmol/l with short-term high dose vitamin D. There is also very good logic in assisting vitamin C with concomitant antioxidant supplementation with a combination of as many of the following as possible – glutathione or NAC, selenium, alpha lipoic acid, anthocyanidins, vitamin E and CoQ10. We do badly need clinical trials of this kind of approach.

The good news is that none of these nutrients, even in the high amounts reported in trials, have resulted in any toxicity. However, once the emergency is over, it is important to reduce intake to the 'maintenance' levels given in the next Chapter 10.

Please note: *ARDS is a serious condition that requires immediate medical support. These nutritional suggestions are not in place of, nor any substitute for professional medical care. Please check with your primary care provider if there is any contraindication to adding in supplements during your medical care, if that is your wish.*



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