Cytokine Storms, Elderberry, Ibuprofen, and Tylenol, Oh My!

Editorial by: David M. Brady, ND, DC, CCN, DACBN, IFMCP, FACN

OK, I can't take it anymore! Sometimes I would love to just pull the plug on the internet, honestly. Amazing how things are taken out of context, go viral, and then doctors like me get hundreds of emails and texts in a panic about things like "Elderberry causing cytokine storms"!

Cytokine Storm Issue: OK, this whole thing started from an isolated report about potential cytokine storm, a relatively rare occurrence and not completely understood phenomenon, with two patients in China, one who survived and one who didn't. Since then it appears that the older a patient is, and the more mature their immune response is, they may be more prone to a cytokine storm late in the sequela of a COVID-19 infection which may result in significant lung infiltration and life-threatening pneumonia. That being said, this morphed into a cockeyed theory being propagated across the internet that anything that is immune simulating, such as the herb Elderberry, could be dangerous because it "could cause a cytokine storm". Firstly, this is totally unsupported, as there is zero data that I am aware of showing this. Elderberry's main anti-viral actions do not even involve cytokine responses at all, and rather involves its neuraminidase enzyme inhibition, similar to the drug Tamiflu. The neuraminidase enzyme is expressed on the viral surface and promotes release of the virus from infected cells and facilitates viral movement within the respiratory tract. Elderberry also has an amphoteric effect (not in the strict acid-base definition, but in that it can correct from both sides of a metabolic process), including on cytokines, meaning it upregulates then when necessary, and downregulates them when necessary.

The Elderberry and cytokine storm issue was commented on, most eloquently, by my brilliant friend and colleague, *Dr. Peter D'Adamo*, as follows:

"Should I worry about my supplements triggering a cytokine storm? No. We need to stop worrying about an herb or vitamin triggering a cytokine storm (CS), a massive immunologic overreaction that is seen at the end stage of certain viral infections. Most of the time CS is not triggered by the virus but rather another end-stage consequence, septic shock, and with it, multiple organ failure. Septic shock is triggered by molecules known as TLRs (toll-like receptors) that are usually activated in response to bacterial toxins known as lipopolysaccharides (LPS). Activation of TLR leads to the production of 'inflamasomes' (principally one known as NLRP3), which then trigger the release of cytokines. NLRP3 is inhibited by nitric oxide (NO), a small signaling molecule produced by virtually every cell in the body. As a matter of fact, you may benefit from Elderberry in this regard, since it has been shown to enhance NO blockage of inflammasome activity and actually suppress TLR4. Dark pigmented fruits have been known to block LPS activation of inflammasomes for decades. So let's get things straight. This is "man-bites-dog" stuff. If you're headed for this type of consequence, a cytokine storm preceded by septic shock, I can

assure you they we need not worry about the Elderberry you've taken. In fact, PubMed shows zero studies when 'Elderberry' and 'cytokine storm' are entered as search terms. Zero. It's the equivalent of waiting for a commuter train, seeing a brown bag lunch on the track and worrying that it might potentially derail your ride. I'll put it in even simpler terms, virtually all rational natural therapies for Covid-19 are simply not potent enough to do this level of harm. If they did, that would be bad, but then again we'd have some really great new drugs for a slew of other human ailments, like cancer. As it turns out Elderberry, is directly lethal to coronavirus. In all fairness, it was studied in chickens, and the type of coronavirus was the gamma form (Covid-19 is the beta form). But in reading the entire article I could find no evidence that a single chicken went into cytokine storm after being administered Elderberry."
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3899428/

See this link *https://lindseyelmore.com/cytokine-storm-what-causes-immune-system-overdrive/* , which intelligently addresses the Elderberry issue and cytokine storm. Again, there is zero evidence that Elderberry induces such an event, and in-fact, it has an adaptogenic and amphoteric balancing effect on cytokines per need, and other anti-viral mechanisms.

The "Don't Take Ibuprofen and NSAID Medication" Issue:

This is on the internet and may have some truth behind it, although the issue is based on limited anecdotal reports, mainly from the UK. Some have equated this to the Elderberry issue above, but they are actually quite opposite. Those who have been given Ibuprofen, or similar NSAID compounds, have been seemingly recovering less well. This is not terribly surprising, as these drugs' main mechanism of action is the suppression on the innate immune response, or in other words, "inflammation". That is what they do! Others have pointed out that ibuprofen blocks the COX enzymes, which in turn affect the renin-angiotensin system, which ultimately lends to increased ACE2. Because COVID-19 attaches to ACE2 receptors as a means to enter into cells, this may be a reason why ibuprofen may be associated with negative outcomes. So, with the exception of someone actually entering the pre-mentioned "cytokine storm", for the majority of us, do you want a key element of your immune response dampened when you are trying to recover from a serious infection, even if it may alleviate some of your symptomatic discomfort? So instead they advise us to use Tylenol, but is this wise?

The "Use Tylenol (Acetaminophen) Instead" Issue:

This is an entire subject that makes my blood boil (*No pun intended*). I strongly feel that Western medicine has fallen into a very lazy reactive situation when it comes to fever, and this flies in the face of our understanding of physiology, common sense, and certainly naturopathic medicinal principles. The minute a person spikes a fever we should not be advising them to immediately reach for a bottle of Tylenol (acetaminophen)! Yes, it is an analgesic (pain reliever) and anti-pyretic (fever reducer), and may make you feel a bit less symptomatic. However, your body is spiking a fever for a reason! Your immune system is working hard to produce that elevated body temperature with a plan in mind, which is to make it too hot for the pathogen infecting you to want to stay around, or for it to survive in you. Why would you want to immediately sabotage your own immune response like that? We all understand that an uncontrolled and excessive fever can be deadly, but that does not mean we should immediately attempt to suppress any level of fever. We need to "control" a fever, not eliminate it. The magic number here is 103 degrees, as anything above that can become life-threatening. Keeping a fever in control by the use of hydrotherapy, such as a tepid bath with sponging or immersion in water lower than the temperature of the body (85–90 degrees Fahrenheit, or 29.4–32.2 degrees Celsius is about right). This

works just fine in most situations. Resort to fever-lowering medications and seek medical attention only when there is difficulty in keeping the beneficial fever in a safe range.

My Take Aways:

If you want to believe the unsupported rumor mill on the internet than just immediately stop taking anything that may enhance your immune response and body's ability to fight infection, including viruses. Good luck with that. Is Elderberry, or other herbs such as Andrographis, dangerous in viral infections? Not that we know of, and we have plenty of scientific evidence and hundreds, if not thousands, of years of traditional use to back up their value in such circumstances. If you are still not comfortable with the use of botanicals/herbals, then I would at least advocate that you consider taking some key vitamins and nutrients that support healthy immune function, such as quercetin and vitamins C, D, and A, and zinc. At least until we know more, I would not use Ibuprofen or other NSAIDS if you think you may be suffering from COVID-19 infection. However, I would also not immediately use fever-suppressing therapies, such as Tylenol (acetaminophen), but instead manage the fever with tepid baths and only resort to medical suppression of a fever if it becomes necessary. Finally, I would really advocate that everyone relax and take a few deep breaths!