Amie Skilton, ND, BHSc: Inflammation in the Gut Drives Systemic Inflammation

Interview by Craig Gustafson

Facilitated by InnoVision Professional Media's upcoming conference—Inflammation: Cooling the Heat—to be held September 30 through October 1, 2016, at the Scottsdale Hilton Hotel in Scottsdale, Arizona.

***Amie Skilton,** ND, DBM, BHSc, will address the topic of battling chronic inflammation at Inflammation: Cooling the Heat, a conference presented September 30 through October 1, 2016, at the Scottsdale Hilton Hotel in Scottsdale, Arizona, sponsored by InnoVision Professional Media. Dr Skilton graduated in 2001 with a diploma in botanical medicine, an advanced diploma in naturopathy, and a BHSc in complementary medicine. She has been in clinical practice for more than 14 years and worked concurrently for the BioCeuticals technical team for almost 11 years as a presenter, educator, and writer. She is also involved in corporate health, lecturing at numerous companies as part of their occupational health and safety programs. She specializes in several areas of integrative medicine, including women's health and hormones, natural fertility, healthy pregnancy, and healthy baby and child development.*

***Integrative Medicine: A Clinician's Journal* (*IMCJ*):** Inflammation is coming to be understood as a significant trigger for chronic disease. It is also understood by many integrative practitioners that immunity begins in the gut. What typically comes first: inflammation that triggers leaky gut, or leaky gut that triggers inflammation?

Dr Skilton: Inflammation can be triggered by an endless number of endogenous or exogenous insults, and that question is much like asking what came first: the chicken or the egg! Acute or chronic inflammation, of any cause, will have an impact on the gastrointestinal tract and can initiate or amplify leaky gut. Leaky gut then can perpetuate further inflammation to continue to affect both the gastrointestinal system, as well as the rest of the body. And, of course, anything that triggers inflammation in the gut—and increases its leakiness—can trigger a local inflammatory response that can then escalate to systemic inflammation. In many cases, a good case history will expose the likely chain of events. But irrespective of primary and secondary inflammatory sources, an approach that tackles systemic inflammation as well as modifying inflammation in the gut will have a timely and powerful impact.

***IMCJ*:** What are the mechanisms that drive leaky gut and how is that related to inflammation?

Dr Skilton: Inflammatory mediators may be triggered as a result of infection, injury, or some other source of inflammation—which may be physiologically or psychologically generated. And, local inflammation triggers immunological responses that ultimately compromise the integrity of the gut. Some major factors that drive leaky gut are as follows: First, poor habits, such as eating on the run or standing up and not chewing food enough—to a paste—which also affects the digestive system, resulting in a less than ideal result. Second, certain dietary components can irritate and inflame the gut either directly, or indirectly, such as by affecting the microbiome. Alcohol, sugar, and artificial flavors, sweeteners, and colors can all be an issue. In excess, tea and coffee can also be a problem. Third, stress is also a really important factor to address. The impact of sympathetic nervous system activation robs the gastrointestinal system of a large portion of its circulation, which dramatically reduces digestive secretions and increases the antigenic potential of food consumed. Fourth, many medications take their toll on the gut, with antibiotics being one of the single biggest culprits. Proton pump inhibitors and the oral contraceptive pill also affect gastrointestinal pH and, thus, the microbiome and gastrointestinal homoeostasis.

***IMCJ*:** The editor in chief of this journal has reviewed the role of zonulin in the past,[1] but are there other pathways that affect the ability of the gut to withstand pathogens?

Dr Skilton: Anything that causes inflammation in the gut can compromise the integrity of the gastrointestinal tract, and the upregulation of zonulin is one such outcome that drives leaky gut and unbalances the immune system. All of the factors listed above also affect the natural barriers the digestive system has to withstand pathogenic activity. If there are insufficient commensal microflora present and/or insufficient production of secretory IgA, or sIgA, this will also render our immune system more vulnerable to the impact of pathogenic microorganisms.

***IMCJ*:** How are these related to inflammation?

Dr Skilton: Inflammation can erode the innate defenses we have and anything that compromises our innate defense systems will trigger inflammation.

***IMCJ*:** Is there a mediating presence in the gut that acts to provoke or soothe the immune system response?

Dr Skilton: There are a number of checks and balances that attempt to keep immunological tolerance as the status quo. Three important ones are as follows: First, in addition to keeping pathogenic microorganisms in check, commensal microflora induce, via T-reg cells, the production of anti-inflammatory compounds like interleukin 10. They also affect dendritic cell maturation and, thus, T-cell maturation, driving T_{reg} cell production—and, in turn, keeping inflammation in check. Second, the production of sIgA is a key component of maintaining immunological tolerance; it exerts its anti-inflammatory effects in a number of ways, including by reducing bacteria-induced proinflammatory circuits, and it can mediate a potent anti-inflammatory function following the sugar-dependent interaction with SIGNR1 on dendritic cells, which induces an immune tolerance via regulatory T-cell expansion. Third, ensuring appropriate gastrointestinal permeability also reduces immunological provocation by reducing the passage of lipopolysaccharide, or LPS, and macromolecular translocation.

***IMCJ*:** How does a leaky gut drive inflammation in other parts of the body, such as the arterial network, brain, joints, skin, and nerve tissue?

Dr Skilton: The local shifts in T-cell maturation results in a cascade of inflammatory mediators produced locally that are also ultimately distributed systemically. One such example of this is that upon antigen presentation, the production of T_h1 cells, and in turn interleukin 2, IFN-γ, and TNF-α, results in inflammation that can quickly reach every cell in the body. In the context of a finite and self-limiting response, this is not a bad thing, as these chemical messengers marshal immune cells to attend the site of infection and mount a defense. However, when this is allowed to continue unchecked, chronic inflammation can ensue.

An extreme example of the systemic impact of cytokines can be seen when looking at influenza. Although the "flu" is a respiratory infection, the vigorous immunological response is so powerful the inflammatory cytokines cause systemic symptoms. The circulating inflammatory cytokines are responsible for the profound body aches that typically accompany influenza—and they provide a point of difference to the common cold. These cytokines can cross the blood-brain barrier and affect mood. In some cases, the impact is so severe, the depression experienced increases the risk of suicide. In extreme cases, in what is known as a cytokine storm, the flu can be fatal—demonstrating just how powerful these cytokines are.

***IMCJ*:** Is it possible to restore immunological tolerance once the disease process is set in motion?

Dr Skilton: Absolutely, the only question being to what degree and what kind of ongoing support is going to be necessary to sustain results. In addition to restoring immunological tolerance, you must also turn attention to the repair and regeneration of affected organs and tissues. In the case of cardiovascular disease, for example, aberrant blood pressure and lipid profile may need further attention, as well addressing any existing atherosclerosis.

***IMCJ*:** What steps can be taken to strengthen the gastrointestinal barrier?

Dr Skilton: There are 3 key parts to successfully restoring gastrointestinal integrity and immunological homoeostasis. First, restoring gastrointestinal tract integrity—addressing hyperpermeability. Second, replenishing mucosal secretions—mucosal biofilm and sIgA. And third, replacing microflora—providing commensal microflora.

Let's talk about restoring gastrointestinal tract integrity, first. Addressing gastrointestinal hyperpermeability can be addressed in a number of ways but should include glutamine, which is a preferred fuel source for enterocytes. Colostrum is also worth considering given its effect on reducing gastrointestinal permeability, as well as being a source of sIgA and antimicrobial substances.

Traditional carminative mucilages, such as *Aloe vera* inner leaf gel, marshmallow, and slippery elm, are valuable, as are water-soluble fibers like apple pectin. They go a long way to soothing the mucosa as well as providing nourishment for commensal bacterial colonies. Anything that reduces inflammation, including antioxidants, like curcumin, also helps to short-circuit the ongoing stimulation of the inflammatory cycle that can set in as a result of an overzealous immune response.

The problem with mucosal secretions comes when the/an inflamed gastrointestinal tract struggles to produce sufficient levels of our innate mucosal biofilm, including sIgA. This not only leaves the delicate mucosa vulnerable to luminal contents, but it means the very substrate required by our microflora for adherence and colonization is eroded. Thus, a healthy commensal population is unable to be maintained.

The gentle and consistent stimulation of the gut-associated lymphoid tissue, or GALT, to return sIgA and biofilm levels to sustainable therapeutic levels is critical not only to produce immediate results, but to ensure long-term maintenance of immunological homoeostasis—in part as this is the very foundation upon which our commensal flora rely on for their survival.

Lastly, the administration of probiotic microorganisms is essential to replace commensal bacteria that may have been lost due to any number of factors including medications like antibiotics, proton pump inhibitors, and the oral contraceptive pill.

Given the depth and breadth of our innate microbiome, a probiotic blend would ideally be broad spectrum and high potency. This would mean using doses of hundreds of billions of CFU—colony-forming units—per day and would need to include species for both the small and large intestine—that is, lactobacilli and bifidobacteria. Particular attention should be paid to the strain selection criteria and key things to look for include bile and acid resistance, as well as strain compatibility.

***IMCJ*:** By the same token, what steps can be taken to tame the inflammatory processes?

Dr Skilton: In addition to the strategies outlined above, key opportunities to influence the inflammatory load lies in 2 parts: first, removing, as much as is practical, any and all dietary and lifestyle inflammatory drivers; and second, providing anti-inflammatory and antioxidant compounds to support the body's efforts to reduce inflammation.

The first strategy is to remove dietary and lifestyle inflammatory drivers. As such, removing dietary antigens, such as gluten and casein, is critical. There are a number of ways to identify dietary triggers and each patient should be assessed for their own personal sensitivities. Gluten and casein are the most commonly identified culprits; however, almost any foodstuff has the potential to be antigenic. Additionally, compounds that can irritate or inflame gastrointestinal mucosa—that is, sugar, coffee, alcohol, and artificial colors/flavors/sweeteners—should be removed from the diet.

Another key is improving digestion. This includes supporting the cephalic phase of digestion as well as performing adequate chewing. Stress management will undoubtedly be a key element for most patients.

Another driver of inflammation can be removed by supporting appropriate detoxification through carefully selected nutrients and herbs. Normal healthy detoxification is heavily nutrient dependent and an insufficiency of any key nutrient in these processes will only see inflammation rise. B vitamins and antioxidants are some of the big players here, but each patient should be assessed individually for their own unique requirements. One intervention that everyone can benefit from is glutathione, as this plays a role in all 3 phases of detoxification.

Increasing anti-inflammatory and antioxidant compounds is another effective strategy for combating inflammation. Raising intake of dietary antioxidants will go a long way to boosting the body's ability to manage inflammation, and supplements can also be used for therapeutic effect—that is, curcumin, green tea, resveratrol, omega-3 fatty acids, and glutathione.

***IMCJ*:** How much do these goals depend upon strengthening the microbiome?

Dr Skilton: As you can see, strengthening the microbiome is considered a critical part of gut repair and the restoration of immunological tolerance via the GALT. Without strengthening the microbiome, it is unlikely that a powerful and sustained result can be achieved.

This is because our commensal microflora are responsible for many key roles in the health of our gut, and thus our entire system. These include the following: First, our microflora aid digestion and, as a result, help to normalize bowel function and habits, reducing diarrhea, constipation, and gas. Second, simply by being in our gastrointestinal tract, they offer competitive inhibition of pathogenic organisms and in many cases offer aggregation of these organisms as well. Third, they are responsible for short-chain fatty acid, or SCFA, synthesis. SCFAs are an important energy source for epithelial cell proliferation and, as such, are the key to maintaining intestinal integrity. As the name suggests, SCFAs are acidic—by virtue of their acidity, they help to maintain an acidic environment in the gastrointestinal tract, which is not conducive to pathogenic growth and, therefore, limits the potential for infection. A low—acidic—pH is also necessary for mineral uptake—for example, calcium. Fourth, the presence of commensal microorganisms and their metabolic byproducts help protect intestinal lining from stress-induced injury. Fifth, microorganisms also help reduce the passage of undesirable compounds—that is, LPS and potentially antigenic dietary compounds. Sixth, our microflora also synthesize nutrients, such as vitamins K_2 and B_{12}, and antibacterial compounds, such as bacteriocins and fatty acids. Seventh, these microbes also stimulate the synthesis of brush border enzymes including lactase, as well as sIgA.

Learn more about Dr Skilton's approach to inflammation at the conference. For more information, visit http://innovisionhm.com/inflammation/.

Reference

1. Pizzorno J. Zonulin! The wheat conundrum solved (well, mostly …). *Integr Med Clin J.* 2013;12(4):8-14.