Introduction

In the past few years, we have gained considerable evidence that it is an abnormal mucosal immune reactivity, against enteric [gut] bacteria, that is ***<u>the key event</u>*** *leading to intestinal injury in patients with IBD.*
~Lukas et al., 2006, emphasis added

Conventional treatments for UC [ulcerative colitis] usually involves suppression or modulation of the host inflammatory response using corticosteroids, aminosalicylates or immunomodulatory agents, depending on the severity and localization of the disease. However, some individuals cannot tolerate these treatments, and they have various debilitating side-effects. **~Macfarlane et al., 2005**

Here in the pages of this book, I have an opportunity to share with you a story. It is a story about a very complex disease called ulcerative colitis. But I'll make it simple! And in this simple story about a very complex disease, I will include the stories of individuals who have achieved and maintained remission by the use of alternative and complementary measures. Of course, I'm assuming you would like to learn from the success of others.

Perhaps you know the disease all too well, and your life is so vastly different from anything you had in mind. Perhaps you would like to better understand the disease that you have. And perhaps you would like a change in the circumstances you are in. Have I got a book for you!

I suppose you would like to know why I spent several years of my life writing this book. It might be because the word is out: You have a disease that you know so little about, one that is out to destroy. (Did I just hear your cry for help?) Perhaps it is because knowing what I know, carries

with it a certain degree of responsibility. It could be because I want you to keep your colon and not have it surgically taken away. And it might be that I think I'll scream the next time I hear someone say, "Ulcerative colitis is an autoimmune disease." (It is not.)

In any case, what I offer is a unique opportunity. I offer you the opportunity to learn what this disease is all about and how this disease can be managed differently—perhaps more effectively—than standard drug therapy (and little else).

So, automatically, I am a little at odds with conventional wisdom and medical practice. I don't mean to be. I don't want to be. But, whenever new ideas are discussed, and unconventional insights are shared, eyebrows are typically raised. Just keep that in mind. Also keep in mind, although I speak of alternative and complementary therapies, I am a big believer in the use of drugs. Being a Registered Nurse, I am certainly no stranger to the use and value of drug therapy. Drugs can be very skillfully and very effectively used in the battle against disease, ulcerative colitis included. Actually, I favor their use in the management of this disease. But so often they fail and so often they harm (and fail). Our physicians know this all too well. And most would agree: The use of drugs should be limited when there is a clear opportunity to do so. **I believe we should carve out opportunities to limit their use and perhaps achieve better outcomes, one motivated individual at a time.**

So, in my view, drugs are warranted if needed to quickly get on top of a situation, if they are safely succeeding, and particularly so if that's all the patient has an interest in. But drug therapy should not be the only game in town in the treatment of ulcerative colitis. I can safely say this, in as much as the medical literature offers many alternative and complementary therapies to manage this disease.

Here I will do most of the work, but you will need to pitch in. **First**, you will need to set aside any notion that, given a little help and with adequate motivation on your part, you cannot understand what the science is saying. Practically anything can be brought down to layperson

level. You can do this! You *can* understand what this disease is all about and the reasons why the use of alternative and commentary measures can be effective tools in the battle against ulcerative colitis. **Second**, a personal comment is required. You want your life back, right? Commitment implies persistence. You get others to listen to you. You get someone (a physician) to respond and guide you in your efforts. You develop a winning attitude. There is no quit left in you! You realize you are at war.

But before we get started, I must issue this **warning:** Ulcerative colitis is just too complex, and the risks are too great, for you to attempt to manage this disease without the guidance of a physician. **I really mean this!** And perhaps most physicians want their patients to learn all they can, consider new ideas, offer suggestions, and adopt favorable lifestyle changes. But it is doubtful that your physician will want you to go out on your own or go against his or her advice. This seems reasonable. Always discuss with your physician any option you have an interest in perusing. ***Always!*** You can make mistakes, even with so called "natural therapies," and cause harm. I can give you example after example. And I will. So, promise me you will run things by a physician before you act on your own behalf or on the behalf of others.

There is one more thing we need to discuss before we continue. **Very important!** Be aware that there are divergent views on what ulcerative colitis actually is. Not everyone is on the same page. What I am leading up to is this: **I want you to be aware, right from the start, I view this disease differently than do others.** Again, consider the first quotation at the beginning of this *Introduction*. I'll repeat it here for your convenience.

> *In the past few years, we have gained considerable evidence that it is an abnormal mucosal immune reactivity, against enteric [gut] bacteria, that is **the key event** leading to intestinal injury in patients with IBD.* (Lukas et al., 2006, emphasis added)

I do not believe this concept at all. Not at all. I believe something else. **I believe ulcerative colitis is war. *War!* And I believe <u>this war is a war of necessity</u>.** Furthermore, I believe if you remove the reason(s) why this war is necessary, rather than simply manipulating the inflammatory response, a better outcome may be achieved. Let me explain.

The prevailing view, represented in part by the above quotation, goes something like this: IBD, ulcerative colitis included, is a disease caused by an abnormal immune response to normal, usual bacteria, and a loss of tolerance to the microbes within ensues. Inflammation follows. And, in as much as inflammation itself persists due to a complicated series of events—a response maintained by certain signaling molecules (cytokines) and activated proinflammatory pathways—suppressing these cytokines and modulating these pathways seems warranted and appears to be the key to success. And this might work, actually does work, but not as well or as often as we would like to see. The suffering of many, many individuals continues even under the best of medical care. Oftentimes, this disease is *so* resistant to our efforts. Perhaps we could use a few fresh, new ideas. Perhaps we should make it easier for the drugs to succeed and, hopefully, limit their need.

So why do I view ulcerative colitis as war, indeed, a war of necessity? It is because of this:

> *Normally, luminal bacteria in the gut are withheld from contact with the epithelium by an adherent mucus layer, but **in UC the bacteria reside on the luminal surface where they probably induce and maintain the inflammatory process**.* (Schneider et al., 2010, emphasis added)

Bacteria should *not* be living and replicating on the surface of the bowel. *Never* should this occur! A layer of mucus normally prevents relevant contact between the luminal surface of the bowel and bacteria. But in ulcerative colitis, the unthinkable occurs. There is a catastrophic loss of the protective mucous layer. This turn of events requires a

deliberate inflammatory response. Bacteria, normally well tolerated, normally held at arm's length, are now a serious threat. They are now living and replicating on the surface of the rectum and likely the colon. And an invasion must be prevented.

It is signaling molecules (cytokines and others) and activated proinflammatory pathways, indeed it is inflammation itself that the body uses to deal with threats. **Bacteria living on the surface of the bowel is unquestionably a threat, one most serious, and an inflammatory reaction must follow and must continue.** The immune system—whether its response is normal, excessive, awkwardly expressed or impaired—is *compelled* to act. ***This* is the disease that you have.** The immune system is out to save your . . . well, you know.

Yet, inflammation is meant to be of short duration and to quickly solve a problem. When inflammation does not resolve in a timely, orderly fashion, for whatever reason, I see nothing but trouble ahead. Inflammation itself inflects damage to the very tissues it is trying to protect, so we do need to take measures, even by the use of potentially dangerous anti-inflammatory drugs, to control all the madness, dial things back, turn things around, and head the patient in the right direction. But we also need to address the underlying problem. Furthermore, we need to limit the use of potentially harmful drugs whenever possible. All would agree with this (I hope). And how this can be done, and done more effectively and safely, will be the focus of this presentation.

In *Chapter 1* you will learn a little more about the inflammatory response, what it is, what it does, why it persists, and why it seems to hate your guts. But before we continue, please read the following quotations very carefully:

> ***A disturbed mucosal barrier is thought to be an initiating factor of the disease*** *and subsequent attacks from colonic commensal [normal, typical] bacterial flora result in inflammation of the mucosa.* (Stremmel et al., 2010, emphasis added)

*Although loss of tolerance to the gut microbiota [microbes] is demonstrated in animal models of inflammatory bowel disease, there is only limited evidence for this finding in patients with Crohn's disease and **none** in those with ulcerative colitis.* (Danese and Fiocchi, 2011, emphasis added)

And, of course, one thing leads to another . . .

Once damaged, the barrier is unable to exclude highly immunogenic fecal bacterial antigens [immune stimulating bacterial components] from invading the normally sterile submucosa. (Pravda, 2005)

Samples from both CD [Crohn's Disease] and UC [ulcerative colitis] subjects contained significantly more bacteria when compared to normal control tissue, and a gradual increase was observed from noninflamed to inflamed biopsy material. (Sasaki and Klapproth, 2012)

So, in view of the quotation directly above, can you see why an aggressive inflammatory response is necessary? It is necessary to deal with all the bacteria that have breached the mucous layer of protection and have achieved relevant contact with the intestinal cells below. Bacteria, living where they should not be, is a recipe for disaster. Ulcerative colitis is a disaster.

Behold the gray box!

I love these gray boxes! Each one that I add to the end of a chapter gives me an additional opportunity to share with you other things that I believe may contribute significantly to the subject matter at hand. The gray box will become particularly useful should one want to study a particular subject in depth. But they also give me an opportunity to have a little more fun. We all know how boring medically related books

and papers can be, so I will change this, one gray box at a time. I *will* be famous for my gray boxes; I just know it. The gray boxes are part of the experience of *More to Consider in the Battle Against Ulcerative Colitis.* Don't miss out!

On finding papers and videos on the web

That's easy! Go to Google (by way of example). Then, in the search box, type in the last name of the lead author and the title of the paper you wish to read. A list of candidate papers will appear. Just click on the one of interest, and it should appear in the blink of an eye. For videos, you need to first click the Video button at the top of the Google home page. Then type in the title of the video in the search box. Presto! You have a video to watch. (While on Google Video, try not to be distracted by videos of cute little kittens. Stay on track! You have a disease to fight! Cute little kittens can wait. Warning: Puppy dogs can be quite distracting, too. … Now, where were we? Oh!) One other thing: Sometimes a paper or a video will be withdrawn from a particular website. But chances are someone else will have it, so keep searching. Finally, some sources charge a fee for their research papers, but if you keep looking you may be able to locate a website that will provide it free of charge. Here's a tip: Try clicking on "Related articles" or "All versions"—usually placed somewhere in the article listing—and you may find a source that will provide the paper free (while others want to charge you an arm and a leg).

Basic terms and concepts

Obviously, there are a few terms and concepts that you will need to become familiar with as we continue. For starters:

Inflammation—a cell or tissue response to a threat (e.g., injury or bacterial invasion), generally characterized by redness, pain,

swelling, and sometimes ugliness. It involves changes in metabolism and cellular behavior, as well as the production of specific molecules (particularly complex proteins called cytokines) used to orchestrate the inflammatory response, a response that should defeat the enemy and lead to resolution (healing).

Cytokine—a regulatory protein produced by a cell for the purpose of promoting or decreasing an inflammatory response or other cellular activity. For example, **TNF-α** and **IL-10** are cytokines that act to increase the inflammatory response or decrease the inflammatory response, respectively. A cytokine produced by one cell may act locally, regionally, systemically, or even act on the cell of origin. Recently, the term cytokine has been expanded to include various regulatory peptides and growth factors that exert an influence on tissues and cells (Sturm and Dignass, 2008).

Inflammatory pathway—a series of cellular mechanisms that coordinate with each other to initiate and sustain a particular aspect of the inflammatory response. The inflammatory response is highly regulated. This requires cellular mechanisms that both activate or restrain a particular series of events that will increase or decrease inflammatory activity. An example of a proinflammatory pathway is **NF-κB**. The NF-κB is intimately involved in the pathogenesis and perpetuation of ulcerative colitis.

Epithelium—a group of cells positioned at a tissue surface. The intestinal epithelial cell lines the intestinal tract and is the interface between the external environment and the internal cells, tissues, and structures. The surface of the epithelial cells that line the gut are covered by a layer of mucus, giving rise to another term, *intestinal mucosa*, referring to both as one.

~References ~

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