## <u>Chapter 1</u> Nonresolving inflammation

When a pathogen comes into contact with the host, a struggle [war] between the pathogen and the local innate host defense systems ensues. The resolution of this encounter is a critical determinant of whether the interaction leads to infection and overt disease. ~Lu and Walker, 2001

Inflammation is a normal and vital protective response to the harmful stimuli such as infectious agents, antigen-antibody reactions, thermal, chemical, physical agents, and ischemia [injury from low blood flow]. ~Kulkarni et al., 2006, emphasis added

The **usual result of inflammation is protection** from the spread of infection, followed by resolution—the restoration of affected tissues to their normal structural and functional state.

The problem with inflammation is not how often it starts, but how often it fails to subside. Perhaps no single phenomenon contributes more to the medical burden in industrialized societies than nonresolving inflammation. ~Nathan and Ding, 2010, emphasis added

It appears that a central factor in virtually all inflammatory modulatory genes is NF-κB. ~Neish, 2002

n the *Introduction* we learned that in ulcerative colitis, bacteria reside <u>directly</u> on the surface of the bowel, more specifically the colon and/or the rectum. And we learned that this situation should not be taking place. Actually, this should <u>never</u> be taking place. We also learned that inflammation occurs in response. Inflammation is directed at threats. It is purposeful. It is *war!* 

Normally, the physical layer of protection called the mucus layer prevents <u>any</u> contact between bacteria and the cellular lining of the gut. And, as you will later come to understand, it is one very sophisticated defensive barrier. But in ulcerative colitis this layer of protection is disturbed, compromised, progressively lost, and all hell breaks loose. The inflammation that follows fails to resolve . . . <u>because it is necessary</u>! Inflammation is occurring at a potential site for bacteria to enter (you), to advance (within you), and to destroy (you). And we just cannot let bacteria succeed in this effort. (We'd like to keep you around.) The immune system understands <u>exactly</u> what is going on, and inflammation is how it deals with the situation at hand. Inflammation stops bacteria in their tracks (or tries to), it controls their numbers, it deliberately tries to prevent their advance, but it's not a pretty sight and not always successful. If unresolved, a disease process takes hold and takes on a life of its own.

Inflammation, whether of short-term duration or whether it is persistent, is maintained by cellular mechanisms that become active in order to orchestrate the inflammatory response. One such mechanism, hidden deep with the cell—including both the intestinal epithelial cell and the immune cell—is a molecule called NF-κB. When unleased, NF-κB leads to the production of cytokines and other signaling molecules that compel other immune cells to act. Some immune cells produce toxic chemicals in response. Some immune cells become more aggressive killers in response. Some immune cells respond by sending out molecular signals that invite (compel) other immune cells to join in the battle. And some immune cells tell other forms, and play new roles. All the above is just a part of a bewilderingly complex network of actions that initiate, perpetuate, and control the inflammatory response, a response tailored to a particular threat. The immune system means business. Since I want to keep the initial chapters relatively short, I will not go in great detail now on all the proinflammatory pathways, cell types, and cytokines involved. I wouldn't get very far anyway—even the physician is barely hanging on here, as things are incredibly complex! I simply want to tell you a story, a simple story. But do not despair, you will learn more concepts and terms—even the names of more cytokines and pathways as we continue through the pages of this book, all brought down to earth so that even I can understand.

Let's wrap things up here and move on. I have so much to share.

In summary: I believe ulcerative colitis is war. It is a war of necessity, a campaign conducted for very good reasons. Ulcerative colitis develops as an attempt to resolve or at least to decisively deal with one very serious problem, the problem of bacteria living where they should not be (and constantly threating invasion). In ulcerative colitis, bacteria—even "normal" bacteria—are living and replicating directly on the surface of the rectum, and, if they are lucky and able to advance, they are living and replicating directly on the surface of the move. Territorial expansion, the objective. This situation is *so* unacceptable. We should do something about this and do so without delay. The immune system has already gone to work and is trying to deal with the situation. However, and for a variety of reasons, with ulcerative colitis the immune system is struggling. But do not despair. I have some good news to share:

The mucosa of the colon is more likely to heal in patients with ulcerative colitis than in those with Crohn's disease. (de Chambrun et al., 2010)

More good news:

The prognosis for patients with ulcerative colitis is generally good during the first decade after diagnosis, with a low rate of

colectomy; over time, remission occurs in most patients. (Danese and Fiocchi, 2011)

So you're in luck! (If you call ulcerative colitis luck.) But, wouldn't you know, I have some bad news to share:

As the medical professionals taking care of patients with UC [ulcerative colitis], we have to admit that our treatment concepts have not been very successful. Ongoing disease activity is present in  $\sim 50\%$  of all patients with UC, colectomy rates remain high, and impaired quality of life, sick leave and disability pensions are higher in patients with UC than in the general population. (Ochsenkühn and D'Haens, 2011)

More bad news:

The most potent anti-inflammatory agent currently available, infliximab [Remicade], brought only one out of three patients into remission, not taking into consideration that one third of these patients were still receiving steroids in addition.

In summary, the perception that UC is a benign disease is not justified. UC is a disease that leads to organ loss in **5–25%** of cases, is associated with increased mortality and has a negative impact on daily life. The drugs that we use and the way in which we use them do not bring the majority of affected patients into "remission," which is the most desirable outcome. UC is a potentially aggressive, most undertreated and sometimes lethal chronic disease. Only a minority of patients experience a disease course that can be called "benign." (Ochsenkühn and D'Haens, 2011, emphasis added)

Yes, you have a very tough disease to deal with, one that can be *so* resistant to our efforts. We could use some new ideas. Perhaps I can help.

## More on ulcerative colitis

To get you off to a good start, I have selected the following videos to help broaden your understanding of the disease in question. Please take a few minutes to watch the following:

—Ulcerative colitis – short animation from sixpartswater.org www.youtube.com/watch?v=FjUke8TMwhU

—What is Ulcerative Colitis? www.youtube.com/watch?v=JMApMBY0CfQ

## More on Crohn's disease

Some individuals are under the impression that ulcerative colitis and Crohn's disease are similar diseases or, perhaps, different forms of the same disease. So not the case! Although there are some similarities, there are many differences that set them apart. If you'd like, I can take you on a journey into the world of Crohn's disease. I have written a most informative book on the subject, entitled *More to Consider in the* **Battle Against Crohn's.** In the book I tell a different story than is typically being told. (Of course, you'd expect this.) I tell the story of the intense battle between pathogen and host over, of all things, iron. Iron! I also showcase alternative and complementary therapies that are suitable for use in the treatment of this disease. And you're in luck! The book includes a great deal of information relevant to the patient who suffers from ulcerative colitis—same immune system, different circumstances, different expression, different disease, but generally responsive to the same therapies. If interested, go to www.impactofvitamind.com to purchase a copy. And if you know an individual who suffers from Crohn's, promise me you will tell them about the book. And promise me you will do so without delay.

## ~ References ~

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