



Interview With an Expert:
**Answers to Key Questions in
Inflammatory Bowel Diseases**

May 7, 2009

Operator: Hello, everyone, and welcome to today's free educational teleconference and webcast, *Interview with an Expert: Answers to Key Questions in Inflammatory Bowel Diseases*. It is my pleasure to introduce your moderator Kimberly Frederick, vice president of Patient and Professional Programs at the Crohn's and Colitis Foundation of America.

Ms. Frederick: Hi, everybody. On behalf of the Crohn's and Colitis Foundation of America, I'd like to welcome and thank all of you for attending today's program, sponsored by Procter & Gamble.

The topic for today's program was chosen because we have received so many different questions from people living with Crohn's disease and ulcerative colitis on a variety of topics throughout the year. We have heard your requests for answers and information and are honored to have Dr. Stephen Hanauer, one of the leading IBD experts in the world, to answer some of these questions tonight.

We also want to thank all of you who submitted questions in advance of the program. After the interview, we will start taking questions from both the telephone and webcast participants, answering as many questions as time allows. If we are not able to take your question during the program, please feel free to call our Information Resource Center at 888-694-8872, which will be open for one hour directly after this program concludes. We also have regular hours from Monday through Friday, 9 to 5 PM Eastern Time.

We'd like to remind you all to fill out the program evaluation form, which is available online or in your registration packet. For registered nurses who wish to receive credit, please complete the CNE Evaluation form and return it to the address at the bottom.

Beginning tomorrow, you'll be able to view tonight's presentation with synchronized slides and audio on www.ccfa.org. The program will be available for one year. Registered nurses who did not participate in today's live teleconference will be eligible to receive continuing education credit for participation in the archived program.

And now I have the pleasure of introducing today's speaker, Dr. Stephen Hanauer. Dr. Hanauer is professor of medicine and clinical pharmacology at the University of Chicago Pritzker School of Medicine and chief of Gastroenterology, Hepatology and Nutrition at the University of Chicago Medical Center. Dr. Hanauer is one of the leading international clinical researchers in IBD and has participated in breakthroughs in epidemiology and the genetic links, effects of smoking, dysplasia risks, postoperative occurrence of Crohn's disease, and has led

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Ms. Frederick: many trials surrounding the efficacy of several current treatment medications and been instrumental in the development of guidelines for the development of drug approval for the FDA, as well as the development of national and international clinical guidelines for treatment of inflammatory bowel disease.

Welcome, Dr. Hanauer.

Dr. Hanauer: Thank you, Kim. You forgot to mention that I did that all at a young age of 32.

Ms. Frederick: Right, because you're only 35 right now.

Dr. Hanauer: You got it.

Thank you. And before we begin I'd like to acknowledge the disclosures that you'll see on slide 3 of the presentation, that recognize some of the work that I've done with industry that may or may not impact on discussions tonight.

On the next slide, I'd like to introduce the goals of tonight's discussion, which are to identify lifestyle factors that impact on the quality of life for patients with IBD, to identify current and emergent treatment strategies, and review some of the latest research direction. And finally, as you heard, we'll try to answer as many questions as we can tonight.

So to begin I'm going to hand it back to Kim to introduce the first question.

Ms. Frederick: Okay, thank you. Dr. Hanauer, as we all know, Crohn's disease and ulcerative colitis can be very unpredictable. What recommendations do you have for preventing flares and to helping improve quality of life?

Dr. Hanauer: Let's begin by remembering the two parts of the treatment for either ulcerative colitis or Crohn's disease. The first part is getting the disease under control, and the second part is keeping it under control or maintaining remission. So when we talk about flare-ups, we're talking about either the initial attacks of IBD, but mostly what happens during maintenance therapy, why there may be flare-ups of symptoms even though patients are taking their medication.

So the first reason that patients tend to flare up is that many patients forget to take their medicine or stop taking it or lower the doses. We know that 80% of patients who continue on their maintenance therapy will continue in remission. Only 20% of patients who stop or alter their therapy will maintain their remission. So it's most important to continue taking your maintenance medicine and at the correct dose.

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Dr. Hanauer: We've also recognized that a number of factors can interrupt the course. And the first that I like to consider are medicines called NSAIDs, nonsteroidal anti-inflammatory drugs. These are aspirin-like medicines. Aspirin, Advil®, Motrin®, ibuprofen, Aleve®, Vioxx®. These are medicines that, while they treat pain and fever, also disrupt the lining of the intestine and can cause ulcers and aggravate either ulcerative colitis or Crohn's disease. Sometimes changes in bacteria due to antibiotic therapy for other conditions, such as for sinus infections or tooth abscesses, some antibiotics can trigger flare-ups of the disease.

Diet factors usually do not cause flare-ups, but certainly there are factors in the diet that can cause symptoms. The simplest example, if someone eats a lot of prunes, they're going to get diarrhea. That's not necessarily a flare-up, but it's certainly a symptom.

Stress has been associated with flare-ups for a long period of time. But similar to diet, we have to consider the effect of stress on symptoms versus inflammation. It's really pretty uncommon that stress can affect inflammation, except possibly very severe stresses, such as deaths or divorces. Day-to-day stresses, while they can affect symptoms, usually do not affect inflammation.

And finally, cigarette smoking has opposite effects on two types of IBD. Smoking tends to protect against ulcerative colitis, but makes Crohn's disease worse. So starting and stopping smoking can actually lead to flare-ups.

So how do we affect this? On the next slide. What can we do? Well, first and foremost there are a few things that patients can do. Number 1, 2 and 3 is take medicines as directed. If you want to change, please discuss it with your doctor, so you know the impact. Avoid aspirin-like anti-inflammatory medicines that can trigger true flare-ups. Don't smoke cigarettes. And understand your diet, understand that there are some foods that may trigger symptoms and keep track of them.

What's next?

Ms. Frederick: Okay, that's really helpful, thank you. This next question is one of the most commonly asked questions that we hear. Would you tell us if there is a role of diet and nutrition in IBD and if there is one, what is it?

Dr. Hanauer: Well, of course, there's a role. And sometimes this gets confusing because, as I said just a minute ago, we are not aware of any dietary factors that trigger inflammation. But certainly there are many aspects of the diet that can trigger symptoms, and I gave the example of prunes.

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Dr. Hanauer: Many people have different food intolerances, such as an intolerance to the lactose in milk or other intolerances, often to different types of sugars. And some people just don't tolerate individual items.

What we talk about diet is actually the food that people are taking in. Nutrition is much more comprehensive and really applies to whether or not we're able to absorb the foods that we're eating in our diet. So it's important to recognize that diet does not cause or cure IBD to our knowledge. We can change our diet to minimize symptoms and that's often important, but the key, on the next slide, is really individualization because the diet that will help with symptoms is really going to depend on where the inflammation is and what the patient's symptoms are when they're presenting. So if patients tend to have diarrhea, we reduce the fruits and vegetables that can aggravate diarrhea. If patients are constipated, the opposite is the case. We'll add in fiber and fruits and vegetables.

It's most important for all patients with IBD to understand that adequate nutrition and a balanced nutrition is important for healing of any condition and just maintaining growth and our general well-being. Everybody does not need a vitamin or mineral supplement, but some individuals, particularly those who have extensive small intestinal disease, may benefit just from taking a routine vitamin. But the specifics to the diet should be discussed with your physician and/or a dietician because it's so individualized that it's impossible for me to say one diet fits for everybody.

Ms. Frederick: That clarifies a lot, thank you. You mentioned stress earlier, and a common misconception is that stress causes IBD. Can you set the record straight on that and if there is a role in stress and IBD?

Dr. Hanauer: Certainly. As I just mentioned, we do not believe that stress actually causes inflammation. You can stress animals until they die and they don't develop inflammatory bowel disease. But we all know that when we stress an animal, they can have symptoms, and it's come into our vernacular, to our common speech. We say that performers get butterflies in their stomach. When we scare an animal, they will defecate. So we often say that we are scared "*blank-less*." So we know that stress can affect symptoms. When we're under stress, our bowels are more active, we tend to have more acid production, more motility in the intestine, and the tendency towards looser bowel movements when we're stressed. But that doesn't mean that stress causes the inflammation of IBD.

Yet, there are some individuals who clearly have developed symptoms after a major stress, such as a death or divorce or loss of a job. Whether or not that truly triggered the IBD or it was a coincidence remains to be determined, and certainly we are doing a lot of research to look at the impact of stress on bowel function and possibly on inflammation.

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Ms. Frederick: That's good to know, and I think that relieves a lot of pressure that people may put on themselves, on whether they caused the disease.

Dr. Hanauer: We don't want people to stress over stress.

Ms. Frederick: Exactly. What about smoking cigarettes? What kind of impact does that play, if any, on IBD?

Dr. Hanauer: Well, there's a fascinating message to smoking and IBD that we actually haven't quite learned yet. But it turns out that there are opposite effects of smoking on the two types of IBD, on ulcerative colitis and Crohn's disease.

Smoking tends to protect against the development of ulcerative colitis. But interestingly, when patients stop smoking, and it may be many years later, there's an increased tendency to develop ulcerative colitis. And it turns out that ex-smokers who have ulcerative colitis are the most difficult to treat. Ex-smokers tend to have more refractory disease, require steroids or immunosuppressives or even surgery more often than patients who have never smoked. And even after surgery and pouches, patients who are ex-smokers tend to have more inflammation in the pouch. So smoking has actually a somewhat positive effect, it benefits or protects against ulcerative colitis.

The opposite is true in Crohn's disease. Smoking makes Crohn's disease more difficult to treat. Patients who smoke cigarettes with Crohn's have less response to any of our medical therapies, and after surgery for Crohn's disease, smokers have a recurrence of the Crohn's disease much sooner and more dramatic than patients who are nonsmokers.

So as smoking increases the risk for many other diseases including cancers, lung disease and heart disease, it's usually not recommended as a treatment for IBD. And even though, as I mentioned, it has a protective effect against ulcerative colitis, it's not a reason for people to continue smoking.

Ms. Frederick: Okay, so the take-home message is smoking is not good for anyone.

Dr. Hanauer: Smoking is usually not good for anyone. There are very rare patients who may benefit from low doses of smoking to control ulcerative colitis, but that is a rare exception.

Ms. Frederick: Okay, let's spend some time talking about treatment. We're hearing a lot about top-down and bottom-up therapy. Tell us what this is and what the difference is.

Dr. Hanauer: As you can see on the slide that says Current Standard Approach, which is bottom-up, at the present time we usually say that the punishment has to fit the crime. We assess how severe a patient's symptoms are when they present to us, and we determine the therapy based on that severity. So at the present time, patients who have mild symptoms may be treated with what are called the aminosaliclates. These are the mesalamine compounds.

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Dr. Hanauer: Or if they have Crohn's disease, sometimes antibiotics.

If patients present with more severe symptoms or if they don't respond to the first-line therapies, we kick it up to corticosteroid therapy, this therapy with prednisone, or in Crohn's disease with budesonide. Then if patients don't respond to steroids, we would add an immunosuppressive or a biologic agent or occasionally in Crohn's disease, put the patient on bowel rest. And if nothing else works, then we take the patient to surgery.

But we've learned now over the past several years that, similar to rheumatoid arthritis, if we treat Crohn's disease—and there's more data for this with Crohn's than in ulcerative colitis—that if we treat Crohn's disease aggressively early on, with combination therapy, to induce a remission and then maintain remission, that it appears to have a better effect than if we wait and treat patients with one drug than another.

So early aggressive therapy seems to be more beneficial in a large group of patients with Crohn's disease.

But the problem is picking out the patient who's going to benefit most from an early aggressive approach. It turns out that outside of the major medical centers or referral centers for inflammatory bowel disease, half of the patients with Crohn's or ulcerative colitis never even need steroid therapy. They can be treated successfully with the milder medicines. So we are now learning that patients who have a bad prognosis—these tend to be patients who present very early at a young age, patients who have extensive Crohn's disease involving large amounts of the intestine, patients who at presentation have fistulas or strictures or what we call extraintestinal manifestations like joint symptoms or skin rashes or fevers associated with IBD—these are patients who appear to benefit most from this early aggressive or what's called top-down therapy with combination treatment, with aggressive drugs, at the onset.

Ms. Frederick: Thank you. You explained that a lot, and I think basically people need to have open dialogue with their doctor about anything they learn tonight that may be different from how they're being treated. Is that correct?

Dr. Hanauer: Absolutely. I'm not making recommendations for any specific patient, but talking in generalities of how the field is approaching inflammatory bowel disease.

Ms. Frederick: Okay. So with some of these aggressive treatments, should we be concerned about long-term side effects of medications for IBD?

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Dr. Hanauer:

Well, it's important to remember that IBD is essentially a disease of a lifetime. And we are learning more and more that therapy is often long-term or lifetime therapy to control the disease. So certainly, as you imply, we must be observant for side effects regarding any medication in inflammatory bowel disease, since patients are going to be on it both short- and long-term.

Now usually we're willing to accept some short-term side effects to get patients under control, but that's really limiting it to short-term side effects. In maintenance therapy we are looking for drugs that do not have significant side effects, that can be taken safely.

The biggest issue at the present time in therapy for ulcerative colitis and Crohn's disease are steroids. Steroids are the best and the worst. They're very effective at bringing the disease under control, but since steroids affect every organ in our body, they really are associated with the largest number of side effects—and many of these are cosmetic, including a moon-shaped face, the development of acne, the development of increased body fat, thinning of the skin, as well as noncosmetic side effects that can be more serious. These include osteoporosis, elevation of the blood pressure, elevation of blood sugars and a tendency towards diabetes. And these side effects are only present when patients are taking steroids and are dose-related, but they can have long-term consequences.

With the immunosuppressives or immunomodulators, the main issue of these is a small, but recognized, increased risk of infection—particularly viral infections like skin warts or even some small skin tumors that may be related to viruses.

Also, because immunomodulators can lower blood counts—and we usually use a blood count to monitor therapy—it is important for patients on Imuran® or 6-MP to have blood counts every three months, even though they're perfectly well, to make sure that the blood counts are not dropping and making them more susceptible to infections.

With the biologic therapy, the TNF drugs, the anti-TNF drugs, these also have a small, but recognized, increased risk of infection. And that's the main consequence, although some patients can develop allergies to these.

There's been a big concern, as everyone in the audience knows, about the potential risk of cancer, particularly lymphomas, with medical therapy and with inflammatory bowel disease. Indeed, there is a very small but recognized increased risk with azathioprine and 6-mercaptopurine for lymphoma that may be increased in patients on anti-TNF therapy. But we have to recognize how small that risk is. We can't even tell you whether it's a 1% or 2% risk. It looks like the risk is something in the range of 1 in 400 patients, so it's extremely rare. And since these medicines are so effective short and long-term, it's a risk that we usually don't even pay attention to.

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Dr. Hanauer: So, in the next slide we talk about how to prevent the complications from inflammatory bowel disease. Since one of the major risks is infection, it's very important for patients at diagnosis of IBD to make sure that all of the immunizations are up to date before we start treating with any kind of potent therapy. Although patients respond to vaccines, there are some vaccines that you can't take when patients are on immunosuppression, so it is important to discuss this with your doctor and be sure all the vaccines are updated before we treat you at all.

In patients who are taking steroids, it's important that you supplement with calcium and vitamin D. As I mentioned, in patients on azathioprine or mercaptopurine, we need monitoring of blood counts every three months, and usually we'll check liver enzymes and kidney function tests once or twice a year.

Ms. Frederick: Okay, that was really thorough. I'd like to continue along the lines of medications and side effects and get more specific. What is the impact of drug therapy for IBD on pregnancy in women and fertility in men?

Dr. Hanauer: Well, we've become very aware of this because obviously patients who get IBD are patients who are in their childbearing years. And there's been a lot of observation regarding the impact of medicines on both males and females.

Males tend to be pretty easy in this. The only drug that seems to affect male fertility is the drug sulfasalazine or Azulfidine®. Azulfidine does impact on sperm counts and sperm's ability to be mobile. It's not a birth control. Many, many men are able to get their wives pregnant while taking Azulfidine, but sometimes if men are having difficulty while they're on the drug they should discuss that with the doctor.

As far as women are concerned, the news is also quite good. We are very comfortable with most of the medicines that we use for women during pregnancy. But we have to be aware that there are effects of pregnancy on women with IBD, and there are effects of the IBD on pregnancy.

It turns out that about a third of women will actually go into a remission when they get pregnant, so pregnancy can actually have a beneficial effect on the course of the inflammatory bowel disease. Unfortunately, about another third of women may have worsening of their disease, and that's usually in the first trimester of pregnancy. And then in the last third there's really no impact. We believe and we've found that women who are healthy going into pregnancy are likely to have the best outcomes.

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Dr. Hanauer: There is no increased risk of birth defects for women who are having children with IBD. It's important to remember. And the drugs that we use do not increase the risk of birth defects. Women who are sick during their pregnancy are more likely to have premature or low birth weight babies, but in general the outcomes of pregnancy in IBD are similar to the general population.

So when we get specific on the next slide, the salicylates, these aminosaliclates, the mesalamine drugs and steroids, appear to be safe. There are a number, although the slide says that antibiotics are dangerous, there are many antibiotics that can be safely taken during pregnancy. The only two drugs that we absolutely exclude for women anticipating pregnancy are methotrexate and thalidomide. These are drugs that have been known to induce abortion or birth defects.

As far as men are concerned, I already mentioned sulfasalazine. The fact that methotrexate, 6-mercaptopurine and azathioprine are listed there, I have to tell you are quite controversial, and the majority of us in the field feel that there is no impact of those three drugs on male fertility. In my practice, I do not have men stop those medications in pregnancy. And it just shows you we don't have all the data in the world, but we certainly have a lot of experience with it.

Ms. Frederick: Okay, and would you recommend for men or women who are wanting to start a family to talk to their doctor first before doing so?

Dr. Hanauer: I always do that. I tell my female patients who are anticipating pregnancy to give me a year before they want to get pregnant, so we can identify what's the optimal drug regimen for them and make certain they're in good shape when they want to get pregnant.

Ms. Frederick: Okay, great.

Similar to nutrition, another really hot topic is complementary and alternative therapy. We hear about probiotics, we hear about fish oil. Where does the research stand on this?

Dr. Hanauer: Well, that's a great question, Kim, and we're asked this all the time. And it turns out that about 50% or half of our patients with IBD are taking alternative medicines.

Now it's important for us to understand what makes a medicine alternative versus a prescription medicine? And the answer to that question is that prescription drugs have been demonstrated in controlled clinical studies to have a benefit. Complementary or alternative medicines are called alternative because they have not been looked at with the scientific method, have not been evaluated in controlled experiments, and hence we can't assess how good or bad they are. They just haven't been studied in the same way that prescription medicines have been studied for patients.

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Dr. Hanauer: And as you mentioned, these include vitamins, probiotics, fish oil supplements, different teas, different herbal therapies. And the problem is that we just don't have evidence or data that they help or harm one way or another.

But it is very important for everyone in the audience to understand that these medicines, even though we don't know whether they help or not, may or may not interfere with prescription drugs. So it's incredibly important for you to tell your doctor when you are taking these medicines, just to make certain that there's no interaction with the therapeutic drugs for IBD.

Ms. Frederick: Thank you. And again, we want to encourage people to talk to their physicians before trying any of these kinds of therapies, correct?

Dr. Hanauer: Absolutely. Communication with the doctor and back and forth is extremely important. It's a long-term relationship.

Ms. Frederick: Great. The topic of surgery still raises some concerns in people, and I'd like you to share with us your thoughts on when should surgery be considered as the next treatment option for IBD patients.

Dr. Hanauer: Well, often surgery is considered as a, quote, last resort. But we need to remember that surgery can very rapidly reestablish well-being and quality of life and even cure some types of inflammatory bowel disease.

With that respect, ulcerative colitis is an inflammation that is limited to the colon, hence removing the colon actually cures ulcerative colitis. We recommend surgery to cure ulcerative colitis in patients who, number one, have disease that's so severe that we cannot control it. Number two, have bleeding that's so severe that it can't be controlled. If patients develop toxicity, what's called a toxic megacolon, and this is something that occurs uncommonly, happily, now in patients with severe disease in the hospital, if that's not rapidly controlled it's an indication for surgery. And patients who have pre-cancer or cancer in the setting of ulcerative colitis need to be cured and have their colon removed.

Now the last indication for surgery is actually the most common, and that's patients who have chronic disease and are just not well despite medication or have side effects from medicine. If they're chronically sick, then that's another indication for surgery in ulcerative colitis.

In contrast, surgery for Crohn's disease does not cure Crohn's disease. So our indications for surgery in Crohn's disease is related to complications and we only remove the piece of Crohn's disease that is severely affected. And we can then reattach healthy portions of intestine together.

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Dr. Hanauer: So the indications for surgery in Crohn's disease are pretty much the same as in ulcerative colitis. If the disease is unable to be managed, if there are too many side effects from the therapy, and rarely patients can develop pre-cancer or cancer with Crohn's disease, but usually surgery for Crohn's disease is done for obstruction due to narrowing or due to perforation of the bowel, where the bowel actually leaks.

So what we do for these patients is demonstrated on the next slide. For Crohn's disease, we just remove the segment that is severely inflamed and usually reattach the two ends of the intestine. If there is a very short narrowing, we can actually just open that up with what's called strictureplasty. In patients with Crohn's disease who have their entire colon inflamed, removing the colon can actually also cure Crohn's disease if the small intestine was never involved.

In ulcerative colitis, the two options for surgery are to either remove the entire colon and bring the small intestine out to the side, which is called a stoma—or since it's a stoma of the ileum, it's called an ileostomy—or we can now remove the colon and create a pouch out of the small intestine, which is known as an ileoanal or J-pouch procedure.

Ms. Frederick: Okay then, surgery is curative in ulcerative colitis, but not in Crohn's disease.

Dr. Hanauer: The only time that surgery can be curative in Crohn's disease is that if the patient has Crohn's disease limited to the colon and the entire colon is removed.

Ms. Frederick: Got it. Okay, two common complications that we hear about in IBD are fistulas and abscesses. Tell us what causes them and how they're best treated.

Dr. Hanauer: First of all, the difference between ulcerative colitis and Crohn's disease relates to the type of inflammation. In ulcerative colitis, the inflammation only involves the innermost layer of the intestine, so it's a very superficial inflammation and doesn't affect all of the layers of the wall of the intestine. In contrast, in Crohn's disease, we call this inflammation transmural or through the wall.

The other difference is that ulcerative colitis is a continuous form of inflammation. So any part of the colon that's affected with ulcerative colitis, downstream the colon is affected in the same way. It's as if someone rubbed the colon with sandpaper. Crohn's disease is a more focal or patchy inflammation, so it would look more like someone took a pickaxe or a rake and scratched the lining of the bowel. But it's a much deeper inflammation. That deeper inflammation has two consequences. One is, when it heals, it heals with scarring, which causes a narrowing of the diameter of the bowel. The second consequence of the transmural inflammation is that the inflammation goes deeper and can lead to accumulation of pus or actually attach to another organ, another piece of intestine or the urinary—or actually the bladder, or in women, from the bowel into the vagina. Those abnormal connections are called fistula. The pocket of pus is called an abscess.

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Dr. Hanauer: And those are the complications that are seen much more frequently in Crohn's disease and often are indications for surgery, since the pocket of pus needs to be drained, the stricture or narrowing can lead to blockages, and the fistulas can lead to essentially short-circuiting of intestinal contents, or very uncomfortable drainage, either outside the butt or as I mentioned, through the vagina.

Ms. Frederick: Okay. More specifically in relationship to Crohn's disease, in your opinion does the disease change over time or get worse?

Dr. Hanauer: That's actually one of the reasons that we're considering the early aggressive or top-down therapy. When we follow a group of patients with Crohn's disease over a 20-year period of time, at the onset most of the patients present with mainly symptoms of inflammation. But over time, over 20 years, up to 80% of patients with Crohn's disease will develop strictures that lead to blockages or fistula complications. So we do believe that the transmural or through-the-wall nature of Crohn's disease is progressive and leads to these complications over time, and one of the concepts of early intervention is to prevent these longstanding complications of Crohn's disease.

We don't know that we can do it yet, but we have some evidence in rheumatoid arthritis that treating early can prevent some of these structural changes.

Ms. Frederick: Okay, I'd like to switch gears and talk a little bit about the cost of IBD. Can you give us some insight into that?

Dr. Hanauer: Well, I can give you some general insights, I think. We need to certainly divide cost into various different types. There's obviously a cost to society, which we've estimated to be about \$1.5 billion a year just in the United States. We can talk about cost to patients, which, of course, includes the out-of-pocket costs for medications or for nutritional therapies. Many patients with IBD get rated in insurance and may actually have increased insurance costs because of the IBD.

And then there's another type of cost that's very important, and these are known as the indirect costs. For instance, when a patient is sick with IBD they can't go to work or they can't go to school. If someone has to go in for a procedure or is hospitalized, the family members have to take time off from work or from school to visit. These indirect costs probably are double the total direct costs of medical therapy.

It's also important to remember that the biggest cost of treatment for IBD are actually costs of hospitalizations and surgery. So if we can prevent putting people in the hospital and we can prevent surgery, even if the medicines appear to be more expensive, that will reduce the overall cost of these illnesses.

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Ms. Frederick: Okay, so staying on your medication is really important in order to help reduce costs of possibly long-term stays in the hospital.

Dr. Hanauer: Well, we certainly understand that some people tend to reduce medicines because they can't afford it, but that's actually just going to increase the overall cost of care.

Ms. Frederick: Okay, we have a few more questions. I wanted to just ask you, is there any way that you know of to prevent IBD from occurring, especially in children?

Dr. Hanauer: Well, let's clear up a couple of things. Number one, genetics. Although there clearly is an increased risk of IBD in family members and we are recognizing genes that are associated with IBD, we're not recommending any genetic studies at the present time because they are not specific for inflammatory bowel disease. They are not good predictors of whether an individual is going to get IBD.

Because we do not yet know the exact cause of IBD, it's impossible to say how to prevent it in children. But in general we recognize that IBD is actually a disease of cleanliness. We don't see IBD in third-world countries. We don't see IBD until people from third-world countries move into first-world nations, and then it's usually their children who get it. So it turns out that bad sanitation, poor hygiene probably protects against IBD, and this is similar for other autoimmune diseases like asthma, arthritis, multiple sclerosis, are actually diseases of cleanliness rather than diseases of poor hygiene.

Since we know that anti-inflammatory medicines can sometimes trigger IBD, I tell my parents to avoid the use of aspirin and Advil and Motrin in their kids. Usually Tylenol® products are okay. Minimize the amount of antibiotics that children get. Most of the time kids get antibiotics because they have colds, they don't really need it. So be certain that the child actually needs the antibiotic before allowing the pediatrician to give it to them.

So I also actually tell my patients don't focus so much on cleanliness. If the pacifier falls on the ground, you can put it back in their mouth. You don't need to worry about being super-clean. It's not cleanliness that's causing the diseases, it's probably allowing them to occur.

Ms. Frederick: Okay. Finally, we know that a lot of new treatments have come out, just even in the last decade, and looking into your crystal ball, so to speak, what can we expect in research over the next year or so?

Dr. Hanauer: Well, as many in the audience know, and as you mentioned, Kim, we've actually over the past 10 years introduced probably five to six new medicines for inflammatory bowel disease, and there are several that are going to be coming out, probably within the next couple of years, and many, many drugs in the pipeline.

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Dr. Hanauer: What we are doing with our therapy for IBD is becoming much more targeted. We are now taking medicines that have tons of side effects because they affect all aspects of the body, such as steroids and cortisone therapy, and beginning to direct now smart weapons that only affect one chemical—and that would be an example of the biologic agents that target, for instance, tumor necrosis factor, a single chemical. So we are learning to be much more specific.

But what we need is additional research. Our research is identifying the genetics that lead to these diseases and what we're learning from the genetics is what the gene products are actually doing and how they contribute to this uncontrolled inflammation that we call ulcerative colitis and Crohn's disease. And as we dissect the inflammatory cascades and all the different chemicals related to this inflammation, we're developing specific targeted therapies that will actually impact on important pivot points within inflammation, and at the same time improve the effectiveness while minimizing the side effects. That's where we're heading right now.

When we do identify the cause of these diseases, then we're going to be even more specific. But I have to mention there are a number of diseases where we know the genetics and we know the causes, that we do not yet have cures for. But we are continuing to get better with more potent and safer medications every year.

Ms. Frederick: Thank you, Dr. Hanauer, you really covered a lot of ground and hit on some of the major questions.

We're now going to begin the question-and-answer session with our audience. And we know that many of you have questions and we're going to try to address as many questions as possible.

Operator: Our first caller is Sandra from Florida.

Ms. Frederick: Hi, Sandra.

Sandra: Good afternoon. Question I was going to ask, he actually answered it, but I'm going to ask another one now. And that is I got ulcerative colitis when I was 70, and I'm understanding that usually you get it when you're at a very young age. I'm trying to figure out, how did this happen? And also, does that mean that my case won't be that bad or what?

Ms. Frederick: Thank you. Dr. Hanauer?

Dr. Hanauer: Well, you're right, Sandy, most people who develop ulcerative colitis or Crohn's disease tend to be younger, in their teens or 20s or 30s. But we recognize that there is a second group of individuals who get their disease in the middle ages, in their middle ages.

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- Dr. Hanauer: Now what's most interesting about patients with ulcerative colitis who get the disease after the age of 40 is that we've found almost all of those patients are patients who had previously smoked cigarettes. So, far and away, the people who get the second—in the second peak—are patients who have been previous smokers with ulcerative colitis.
- As far as the severity of the disease in the older population, it usually is about the same as younger individuals, but we run into problems because of other illnesses. Seventy-year-olds are more likely to have other conditions, such as high blood pressure, arthritis, heart disease as well, so we need to be able to treat the IBD now within the context of having other illnesses and other medicines.
- Ms. Frederick: Thank you. We're going to take a web question from Jenny, and the question is, "Besides the colon and small intestine, what other organs might IBD affect? I continue to have inflammation in my eyes, for instance."
- Dr. Hanauer: That's a great question. And indeed, IBD is really a disease of the entire body. The primary inflammation may be in the intestines, but it can set up inflammation, as you mention, in the eyes, in the joints or in the skin, sometimes in the liver.
- It turns out that there are different patterns of IBD and usually patients who have inflammation of the eyes have a genetic—a different genetic type called HLA-B27—that can be associated with this eye inflammation with or without IBD. And the same with the joints. Patients who have inflammation of the spine, called ankylosing spondylitis or sacroiliitis, tend to have that same genetic background, and when they get the IBD, the joint or the eye symptoms may be more prominent. And sometimes they're even worse than the IBD itself.
- Ms. Frederick: Okay, thank you. We'll take a phone question now.
- Operator: Your next question comes from Brad from California.
- Brad: Yes, hello. I know that you talked a little bit about probiotics, and I know that that's a very hot topic now. For Crohn's disease specifically, what probiotics seem to work the best, and are there ones that you can take—can you take multiple ones simultaneously? And they're very expensive, so are there generics for those?
- Dr. Hanauer: Brad, to answer your question simply, we don't know. There are no data that show any—that we do not have any evidence thus far that any specific probiotic is helpful in Crohn's disease. There's no study that shows probiotic A, B, C or D is helpful.
- Now all the probiotics haven't been studied, so we don't have data on everything. That's why our answer is so neutral to this.

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- Dr. Hanauer: What probiotics are, are bacteria or sometimes yeast that do not cause disease in humans and may help with health. But thus far in IBD, we do not know of any specific probiotic that will help either ulcerative colitis or Crohn's disease. I can't tell you that they harm, but I also can't tell you that they help.
- Ms. Frederick: Thanks, Dr. Hanauer. I'm going to ask you a web question. This is from Jack. "I have Crohn's disease and take five or six Imodium® tablets daily to control diarrhea. Is this an acceptable method to control diarrhea, and is there any long-term impact to taking the Imodium?"
- Dr. Hanauer: That medicine is generally safe, and the main side effect is constipation or gas or bloating with it. I would say that it is okay to take it, but it's also important to remember that the diarrhea can either be due to inflammation or something else. If the diarrhea is due to inflammation, Imodium will not help that. It'll just reduce the symptoms. And our goal would be to control the inflammation. But for instance, many patients who've had a surgical resection for Crohn's disease may have diarrhea just because they've lost a segment of intestine with no inflammation. In that situation, the Imodium or Lomotil® or something like that can be very helpful to control the symptoms and will only benefit the quality of life.
- Ms. Frederick: Okay, great. Can we have a phone question?
- Operator: Your next question comes from the line of Sadi from California.
- Ms. Frederick: Hi, Sadi.
- Sadi: Hi. My 9-year-old daughter had something that they were not sure whether it's Crohn's disease or ulcerative colitis. The disease was limited to her colon, however, the pattern of the disease was more like Crohn's and the pathology came back as ulcerative colitis. And they left—she did the surgery, and they removed part of the colon that was diseased and she's doing fine now, but I'm concerned one way or the other, whether we should remove the rest of the colon and make a J-pouch, or just wait and see if the disease will occur. What do you do in cases like that?
- Ms. Frederick: Okay, so Dr. Hanauer will answer that in a general way.
- Dr. Hanauer: Absolutely, and it's a great question because people are often concerned about the diagnosis between ulcerative colitis and Crohn's disease.

Let me start by saying when something is inflamed, we add the term "itis." So if our skin is inflamed, it's a dermatitis. If our joints are inflamed it's arthritis. If our colon is inflamed it's colitis, and if the ileum is inflamed it's ileitis.

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Dr. Hanauer: Just as there are different types of arthritis and dermatitis—there's rheumatoid arthritis and degenerative arthritis, there's psoriasis, eczema, poison ivy or skin inflammation, there are different types of inflammation of the colon. And they may overlap dramatically, particularly in young children. Children can present with inflammation of the colon that may not fit perfectly into one pattern of ulcerative colitis or Crohn's disease at any time. The same can actually be said for adults as well.

Often treatment and time will help to identify which pattern this is going to evolve into. So I would say that if the child has had surgery and is doing well, there's nothing you need to do specifically at the present time as far as further surgery, unless the inflammation can't be controlled. And over that period of time, it's likely to become more clear.

As far as the diagnosis of ulcerative colitis and Crohn's disease is concerned, we don't have a perfectly specific marker. There's no blood test that tells you that this is ulcerative colitis or this is Crohn's disease. We have some blood tests that may or may not be helpful in individuals, but for the most part, it's the clinical pattern that we see based on the patient's symptoms and the way the intestines look, either when we scope them or do X-rays or scans, or do biopsies that help us. But still about 10% to 20% of patients, more often in children, with disease limited to the colon, we can't classify them right up front, and we say that they have an indeterminate colitis.

Ms. Frederick: Next question I'm going to read to you from the web, it's from Chuck. "How safe is Humira® in the treatment of pediatric Crohn's?"

Dr. Hanauer: Humira is one of the biologic therapies that targets the chemical of inflammation called TNF. And these other medicines that are of the same class include infliximab, which is Remicade®, adalimumab, which is Humira, and certolizumab, which is Cimzia®. These three medicines are all approved for Crohn's disease, and thus far, infliximab or Remicade has been shown to be effective in ulcerative colitis. Although the drugs are administered differently, infliximab or Remicade is given intravenously, and the other two are administered subcutaneously as an injection, they share almost all of the same benefits and side effects. The major difference is how we administer these over time.

Ms. Frederick: Okay, let's take a phone question.

Operator: Your next question comes from the line of Jane from Ohio.

Jane: Hi, Doctor. My son has Crohn's disease. He's had it about ten years, and now he is on Remicade. When he had his colonoscopy three or four months ago, he did have an abscess and he had some narrowings in his intestine. And since he's been on the Remicade, he's doing much better. How successful is this treatment of Remicade with the intestine, the narrowing of the intestines, and can he stay on this for a period of time?

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Dr. Hanauer: First of all, to the last part. All of these are meant to be long-term therapies. As long as the patients are responding, they should continue on them.

As far as the effectiveness, they've been highly effective, even in patients who've not responded to steroids or even Imuran or 6-MP, patients tend to respond to these biologics.

Now, you mentioned that your son has strictures. Strictures are due to scar tissue. We do not expect that these anti-inflammatory therapies are going to get rid of the strictures. That won't happen. There's still going to be some scarring, but it can minimize the inflammation. So we see some patients who have been successfully treated with these agents, who end up still needing surgery because of blockages from the stricture, even though we've cleared up the rest of the inflammation. These patients actually have a very good prognosis after surgery, so I think that you should be very optimistic for him.

Ms. Frederick: I'm going to ask you a web question, and it's from Arnold. "What do you think of MRI enterography to evaluate the small bowel for Crohn's disease? Is this one of the best ways to examine the extent of the disease and complications?"

Dr. Hanauer: A very sophisticated question. There are a number of ways that we can look at the small intestine. As you obviously consider, we know that colonoscopy can be used to directly scope and visualize the large intestine, but we don't do that—we're not able to do that routinely for the small intestine. So we have a number of different ways that we can image the small intestine.

One would be with the new capsule, the wireless capsules that we swallow, what are known as the PillCam®. In patients who do not have narrowing of the intestine, we can use a PillCam to examine the small intestine. But if there's narrowing, those pills can get stuck and mean the need for surgery.

As far as other ways to image, traditionally we've had patients do x-rays where they swallow barium, and the radiologist follows that barium through the small intestine and looks at the wall of the small intestine, compared to other areas.

Those tests require a lot of the radiologist's time. And to minimize that, we have over the past several years used CT scans—CAT scans—or most recently, MRI scans, as the technology has gotten more sensitive, to look at the small intestine.

Now MRIs can be used, they have to have the newest MRI because the sensitivity needs to be good enough to look at the small intestine. The advantage of the MRI is that there's no radiation, compared to x-rays or CT scans.

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- Dr. Hanauer: The disadvantage is that it's sometimes not as sensitive as the other techniques. But as the technology is improving, we are using these more and more.
- Ms. Frederick: Okay, I'm going to take another web question because there seems to be a theme going on here. So the question is, "How does an individual with UC control fecal incontinence, does it ever stop, or is it because remission has not been achieved? What's the best way to treat this?"
- Dr. Hanauer: Oh, what a challenging and great question. So the issue is how do we control incontinence, how do we maintain control in the setting of ulcerative colitis?
- Well, the ability to maintain control depends on really two factors. It depends on the anal sphincter, the muscle that leads to control. And it also relates to whether the bowel is inflamed and the liquidity of the stool. So it's pretty rare that anyone loses control of a full bowel movement. It's usually when there's liquid stool that we can't control. And this is due to inflammation in the rectum, in the lowest part of the colon.
- Under normal situations, the rectum, when a piece of stool comes into it, it stretches or complies, and that signals the need to have a bowel movement. In which case we go to the toilet, we actually relax the sphincter and bear down and push out the poop.
- In patients who have an inflamed rectum, the rectum doesn't stretch and anything that comes into that rectum causes the rectum to spasm, and we can't control the anal sphincter forever, we just can't voluntarily think to control it, and that's what leads to the occasional loss of control or incontinence.
- It should be fixable by fixing the inflammation in the rectum. That is unless—and it's a rare situation—that the sphincter has been so weakened, for whatever reason, that it no longer has strength. Far and away, the majority of patients who lose control—it's because they have active inflammation, the rectum goes into spasm with liquid stool that can't be contained.
- Ms. Frederick: Okay, great. We'll take a phone question now.
- Operator: Your next question comes from Brenda from New Hampshire.
- Brenda: Hello. Could additives or metals found in foods possibly be the trigger or the onset of Crohn's disease?
- Dr. Hanauer: Thus far we've not identified any additive or metal. I know that there have been some individuals who thought that silver fillings or such can lead to various types of inflammation. That has just never been found to be associated with IBD.

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- Ms. Frederick: Okay, we'll take another phone question.
- Operator: Your next question comes from Camilla from North Carolina.
- Camilla: Good evening. I've had ulcerative colitis for over 30 years and four generations of family with this kind of problem, so listening tonight, not a whole lot different from what I learned 30 years ago.
- Dr. Hanauer: Thanks a lot!
- Camilla: Well, you know, I do a lot of studying. But what I'd like to know, you were mentioning the aspirin, I have atrial fibrillation and have to take a baby aspirin every day. Is that a potential—baby aspirin, doing it that often, could be causing inflammation?
- Dr. Hanauer: No, it's a great question. A baby aspirin is not a sufficient dose to cause intestinal inflammation. So that's perfectly safe and you can take it for your atrial fibrillation. So cardiac doses of aspirin, which is "baby doses" or 81 milligrams, as you mentioned, are safe to take. It's the higher doses and it's probably the more you take, the greater the risk.
- Ms. Frederick: Okay, I'm going to ask you a web question from Sean. And the question is, "Since smoking seems to relieve UC, would a nicotine patch have any effect?"
- Dr. Hanauer: Another great question. I didn't say that smoking relieves ulcerative colitis. I said it protects against it or prevents ulcerative colitis. So we have actually looked for what ingredients it might be, and thus far, nicotine, which has been tried in clinical studies, has not led to remission. It may reduce symptoms in some patients who were ex-smokers, but it's not good enough to totally control the disease thus far.
- Ms. Frederick: Okay, and we'll take a phone question.
- Operator: Your next question comes from Pauline from Michigan.
- Pauline: Hi. I have a problem with oral mouth sores. I haven't had them biopsied to be conclusive of Crohn's, but I'm going to because I've been living with it for four months continuously. Please, is there anything for pain or for that particular syndrome that's used?
- Ms. Frederick: For oral mouth sores?
- Pauline: Well, possibly they could be Crohn's.
- Ms. Frederick: Okay, thank you.

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Dr. Hanauer: So let's remember, mouth sores or these ulcers can come with or without Crohn's disease. So it's the fact that—I will tell you that millions of people have mouth sores who do not have Crohn's disease. It's known as aphthous stomatitis. And these aphthae, which are cold sores, can be treated. The first thing is to make sure that they're not viruses, so they should be cultured if people have recurrent attacks. If they are associated with a herpesvirus, there are medicines that can prevent it. If they're not associated with viruses, then either—then they are very responsive to cortisone therapy. That cortisone can be given topically into the mouth, or even a very short course of prednisone or cortisone by mouth can actually get rid of them pretty quickly. If they keep coming back despite—you look for triggers and sometimes foods could be triggers for these, such as sometimes strawberries or citrus fruits can bring them out. But if there's no food trigger and if they come out frequently, sometimes we actually use immunosuppressant medicines like Imuran to control them.

But yes, they can be treated.

Ms. Frederick: Thank you. The question I'm going to ask you is from the web. And it is, "What is ischemic colitis and what are the causes?" Did I say that right, ischemic?

Dr. Hanauer: You're pretty close. It's called ischemic colitis.

So I said that there are several different types of inflammation of the colon or colitis. Crohn's disease can affect the colon, ulcerative colitis can affect the colon, infections can affect the colon, diverticulitis can affect the colon.

The other type of colitis, another type I should say, is when the colon loses its blood supply. The colon has a number of blood vessels that supply the lining, and when those blood vessels get clogged, just as if a blood vessel to the heart gets clogged, that piece that it supplies can die, and that is called ischemia. It's a loss of the blood supply to the part of the colon. There are a number of reasons why this can happen. It can happen because of atherosclerosis, it can happen because of a blood clot, or it can happen actually because of very low blood pressure. But those are all different types—causes—of low blood supply to the bowel, which is called ischemia.

Ms. Frederick: Okay, thank you. We'll take a phone question now.

Operator: Your next question comes from the line of John from Georgia.

John: Hello. Doctor, I just have a question about immunosuppression therapy. With regard to TNF blockers such as adalimumab and infliximab, is there a difference in immunosuppression between the two? And as far as comparing those with immunomodulators and steroids, just how far do they suppress the immune system as far as the overall functioning of the immune system?

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Dr. Hanauer: A very good question. All of the different drugs you mentioned, steroids, the Imuran and 6-MP and then the anti-TNF agents, do suppress the body's immune system, but in slightly different ways. So they are actually associated with slightly different risks of infection.

So for instance, with steroid therapy, the most common infection are yeast infections. With Imuran and 6-MP, the most common tend to be viruses like herpesviruses or papillomavirus that can lead to cervical dysplasia or cervical cancer in women. Sometimes herpes zoster. The anti-TNF biologics tend to make people more susceptible to certain bacterial infections like tuberculosis and other fungal infections, such as histoplasmosis, coccidiomycosis, and less commonly, viral infections.

So the drugs, while they suppress the immune system, do it in different ways that make one susceptible to slightly different infections.

Ms. Frederick: Okay, thank you for that question, and thank you to everyone, and thank you, Dr. Hanauer, for your time and expertise. We truly appreciate you being here with us today, and you are just a wealth of information, and all the work that you've done for patients. So thank you.

I'd also like to thank Procter & Gamble for making today's program possible.

And most importantly, on behalf of the Crohn's and Colitis Foundation of America, thank you to all of you who participated in tonight's program. We hope you enjoyed it.

And please remember to fill out and return your Evaluation form. You can visit www.RMEI.com/CCFAevaluation to complete the evaluation online. And for those on the telephone audience who received a confirmation packet, you can send that back in the self-addressed envelope.

For more information on how you can join the fight against IBD and get involved in our Take Steps Walks that are going on all around the country this spring, get involved, get out there, help raise money for research and other important programs, you can visit our Web site to get that information. It's www.ccfa.org. And again, our Information Resource Center is open for one hour tonight after this program. And we're also open 9 to 5 Monday through Friday Eastern Time, and our number is 888-694-8872.

Thank you and that concludes today's program.

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