

TRANSCRIPT

It's Up To You: Decisions & IBD Management
David Schwartz, MD
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Operator:

Hello, everyone, and welcome to *It's Up To You: Decisions & IBD Management*, a free telephone web education program. It is my pleasure to introduce your moderator Laura Wingate, Senior Director, Field and National Programs, of the Crohn's & Colitis Foundation of America.

Laura Wingate:

Hello, everyone. And on behalf of the Crohn's & Colitis Foundation of America, welcome. And thank you for attending today's program.

This activity is supported by educational grants from Elan and UCB, and a sponsorship from Shire.

Thanks to everyone who submitted questions in advance of the program. After the presentation, we will open up the program for your questions. We will take as many questions as time allows from both telephone and webcast participants. If we are not able to take your question, our Information Resource Center can be reached Monday through Friday, 9 AM to 5 PM Eastern, by calling 888-694-8872.

We encourage you to complete the online evaluation form after the program.

I now have the pleasure of introducing our speaker for today's program. David Schwartz, MD, is the Director of the Inflammatory Bowel Disease Center and Associate Professor of Medicine at Vanderbilt University Medical Center in Nashville, Tennessee. Dr. Schwartz completed his internship, residency and gastroenterology and hepatology fellowship at Mayo Clinic. His clinical and research interests include inflammatory bowel disease and endoscopic ultrasound. Dr. Schwartz, thank you for joining us today. It's now my pleasure to turn the program over to you.

Dr. David Schwartz:

Thank you, Laura. I first want to thank the CCFA for giving me the opportunity to speak to you all today and I want to also thank everyone for logging in online today for this educational webcast. I hope you'll find it entertaining and educational.

We're going to cover a lot of ground today. Mainly we want to discuss both the traditional and complementary and alternative medicine options for patients with inflammatory bowel disease. We'll spend some time discussing the risks and benefits of the different treatment options that are available for IBD. And then spend a lot of time really focusing on self-advocacy for optimizing care for people with IBD and how to build an effective healthcare team for your care.

We know that there are 1.4 million Americans today who are living with IBD and the number of patients being diagnosed is increasing every day. There's equal incidence of ulcerative colitis and Crohn's disease in this country, with the peak onset occurring anywhere between age 15 and age 25, right around the time of life when people are just starting to gain their independence and become productive, so it can have a tremendous impact on one's life.

The second peak incidence is somewhere between ages of 50 and 65 years of age. The symptoms really differ between individuals. The course of the disease and the prognosis really are quite individualized for each patient.

We now know that there are genetic factors that lead to a predisposition for developing inflammatory bowel disease. When one is born with this genetic predisposition, there have to be some environmental factors that then cause those genes to express themselves. There are a number of different possible environmental factors that then trigger those genes to become active, including infections, antibiotics, nonsteroidal anti-inflammatories, different dietary intake, smoking or stress have all been implicated in possible causes of this genetic disposition becoming active. Once this occurs, the body has an abnormal immune response to what we believe are normal bacteria within the GI tract, causing chronic inflammation.

Inflammatory bowel disease encompasses both Crohn's disease and ulcerative colitis. These are very similar diseases, but there are some really important differences which are highlighted here. For Crohn's disease, when we do biopsies to look at the degree of inflammation present within the intestine, we'll see inflammation that extends throughout the layer of the GI tract. Crohn's disease can affect anywhere in the GI tract, all the way from the mouth down to the rectum, but it is most commonly found in the distal ileum or right colon. There are a number of different features of Crohn's that are unique to Crohn's, including fistulizing disease, perianal disease, or strictures. With ulcerative colitis, the inflammation should be confined to the colon and tends to start in the rectum and be continuous throughout the colon.

It's not uncommon for us to see patients in the clinic who, when we ask them what they have, they'll say they have been diagnosed with both Crohn's and ulcerative colitis. Obviously this is a case where sometimes it can be hard for the doctor to figure out which of the two diseases that the patient actually has, and this usually occurs when patients have inflammation confined to the colon, but have some features of both ulcerative colitis and Crohn's disease present. We call this presentation indeterminate colitis and this occurs in anywhere from 10% to 15% of people with inflammatory bowel disease.

The treatment options for both Crohn's and ulcerative colitis have really largely become similar, although there are some key times where it's important to make this differentiation, in particular when one is contemplating surgery for inflammatory bowel disease.

When we approach patients with IBD, we really want to treat the whole patient and not just their GI tract, so this involves addressing a number of different facets of one's whole being that the disease affects, including the psychosocial realm, their nutritional status, and obviously the inflammation present within their GI tract. The goal of managing IBD is to treat the whole patient, control symptoms, control complications related to the disease, and improve one's quality of life.

We have a number of different traditional treatment options for IBD and we'll go through these one by one to review them before we move on to discuss complementary medicine.

The first category I'd like to talk about is over-the-counter medications. These are medicines that you can get at your pharmacy or grocery store, and these are largely focused on controlling the symptoms of IBD and not really addressing the underlying cause of those symptoms. So for instance, these would be antidiarrheal medications that slow down the bowel or pain relievers for situations where you may have joint pain or abdominal pain, to help relieve the discomfort of these manifestations of IBD.

Now it's important to realize that even though these medications are available over the counter, not all of them are safe for patients with IBD to take. Good examples are NSAIDs, medicines that are used for joint pain or abdominal pain. They can sometimes actually cause flares and it is important to really discuss what medicines you're considering taking with your GI physician, even over-the-counter medications, as some of these can prompt flares or worsen your symptoms.

The next category we'll be talking about is antibiotics. These are used in patients who

have pouchitis or perianal fistulizing disease, and we will occasionally use these for patients with Crohn's disease as well.

Now there are a lot of potential risks with antibiotics and I'm sure you've heard about them. Every day we hear stories about increasing bacterial resistance to the different antibiotics that are present, so the more often we use antibiotics for things, such as treating IBD, the more chance we have of developing resistant bacterial strains. We want to try to limit the use of antibiotics when possible.

Antibiotics are also associated with triggering flares. They change the bacteria flora of the intestine and sometimes this can lead to a flare in patients who have IBD. Some of the side effects of taking antibiotics for a period of time can mimic some of the symptoms of IBD, including abdominal cramping and diarrhea.

One of the key risks of taking antibiotics that is important to highlight is the risk of causing an infection called *Clostridium difficile*. This is an increasing cause of hospitalization for patients with inflammatory bowel disease. When we take antibiotics, we kill off some of the good bacteria in our colon and will allow some of these bad bacteria, such as *Clostridium difficile*, to become active and cause a serious infection.

Some of the typical antibiotics we'll use to treat IBD include ciprofloxacin, metronidazole, and rifaximin.

The next category of medications in our medicine cabinet includes aminosalicylates. These are used primarily for inducing and maintaining remission for patients who have ulcerative colitis. These are generally well tolerated and there are many different products available, and they're designed to release the medication by different mechanisms and to release it in different parts of the bowel, so one can think of these as sort of a "smart pill" to deliver the medication directly to where a patient has the active inflammation. These generally have few risks, although there are some very rare and important allergic reactions that can occur with aminosalicylates including increased abdominal pain and diarrhea and some potential affects on the kidney.

On the next slide you can see the various 5-ASA agents which are currently available in the U.S.

The next category of medications is corticosteroids. These are highly effective in inducing remission, both for Crohn's disease and ulcerative colitis. As anyone who's taken steroids knows, there are a number of side effects, unfortunately, that are associated with this medicine, including an increased risk of infection, problems with mood swings, and sleep disturbances. They can raise one's blood pressure or cause diabetes. They cause weight gain and fragile skin or easy bruising. And in children, they may lead to growth delay if given at a time when they are actively growing. They are also associated with increased bone loss and have been one of the main factors for causing osteopenia and osteoporosis in patients with inflammatory bowel disease.

We are also concerned that as we use more and more courses of steroids, one may become resistant to this medication and it may stop working. Examples of corticosteroids that are used for IBD include prednisone and budesonide.

The next category of medications is immunomodulators. These are used almost entirely to maintain remission because it takes about three to four months for them to become effective. So normally we'll start a medication such as prednisone, which works more quickly, along with these medications to get a patient better more quickly and then allow time for this to become effective and keep the patient in remission. When we're able to induce remission with steroids, these medications will allow a patient to stay well up to one year 42% of the time.

Any time we manipulate the immune system there are some potential side effects. And for this particular class of medication, this would include fever or myalgias and pancreatitis. As I

mentioned, they do suppress your immune system, so we need to monitor one's white blood cell count and also the liver enzymes, as they are metabolized in the liver.

Any time we manipulate the immune system there is also a risk of lymphoma and we'll get to the rate of that in an upcoming slide.

Some examples of immunomodulators which are currently available to treat IBD include azathioprine, 6-mercaptopurine, and methotrexate.

The last class of medications we'll talk about is biologics. These are designer drugs that were designed in the lab to block a signal that stimulates inflammation, or are antibodies that stimulate the anti-inflammatory process. Currently all the biologics that are available are given either via infusion or injection. These are often given to people who have not responded to standard therapy such as steroids and immunomodulator therapy, but as we have become increasingly aware of trying to prevent some of the complications associated with IBD, we're using some markers that identify patients with a more severe disease course, and using these earlier on in the disease course to prevent complications. These are highly effective and 60% of patients will respond within the first few doses of these medications.

The risks associated with these medicines are increased risk of infection, injection site reactions or infusion reactions, and an increased risk of lymphoma.

You can see here the list of biologics which are currently available for inflammatory bowel disease. The top three are anti-TNF antibodies (adalimumab, certolizumab pegol, and infliximab) and the other is a selective adhesion molecule called natalizumab. We'll talk about all of these in a little detail next.

When patients come to us and we get to discuss some of the risks and benefits of these medications, usually the patients have heard about potential increased risk of infections or lymphoma associated with immunomodulators and anti-TNFs. Generally what one has read is, their risk is elevated somewhere between four and six times. That's a very scary number. So it's important that we not deal in relative risk, but talk about absolute risk of these medications. This slide helps sort of put the risk of these agents in better context.

So if you look at everyone's baseline risk of non-Hodgkin's lymphoma, it's somewhere between one and two out of every 10,000 people per year will develop non-Hodgkin's lymphoma. When patients go on either immunomodulators or anti-TNF antibodies, that rate goes up to somewhere between four and nine out of every 10,000 people placed on the drug. There's one particular type of lymphoma which tends to be more aggressive, called hepatosplenic T cell lymphoma that seems to be primarily associated with young men who receive immunomodulators plus or minus anti-TNF agents. So now when we are considering starting anti-TNF agents, we'll usually try to not use concomitant immunomodulatory therapy in men in their twenties to help prevent or even reduce the risk of this particular type of lymphoma.

There is a slight increased risk of serious infection for patients on immunosuppressive agents. That risk is somewhere in the range of four out of every 1,000 patients placed on these medications. And for the anti-TNF agents there is an increased risk of tuberculosis, and that's why we do testing to look for any signs of latent TB before we start our anti-TNF agents.

Natalizumab is the selective adhesion molecule blocker that I discussed earlier. And there's one particular type of infection that is associated with this drug, called progressive multifocal leukoencephalopathy. I'm going to refer to this as PML in the next two slides, to make it a little easier for me.

PML is an infection of the brain caused by the JC virus. And it's a fairly aggressive infection that is either fatal or debilitating in most patients. In the past this has primarily been associated with people who had very compromised immune systems, such as those with hematologic malignancies, HIV, or patients who had undergone organ transplantation. But this

was seen in patients treated with natalizumab. Really because of this, we used very little of this medication earlier on when it was released about a decade ago. More recently we have been able to check for the antibody against the virus that your body makes if you've been exposed to the JC virus. This is a nice way to risk stratify patients against their risk of developing PML.

So we know that every patient tested so far who has developed PML has had an antibody against the JC virus. What I normally tell our patients, when we discuss the risk of natalizumab for treating Crohn's disease, is that if your JC antibody is positive, the risk of developing PML after one year of therapy is somewhere in the range of one in 500 and one in 1,000. If you are antibody-negative, that risk is probably higher than one in 60,000, so very low rate of potentially developing that infection. Once we start this medication in people who are JC virus antibody-negative, we will periodically recheck it to make sure that their antibody does not convert over time.

Before we move on to some of the surgical treatment options, I think it's important to briefly go through what clinical trials are and the different phases of drug development, as these are nice options for patients who have not responded to the available medical therapies for IBD.

When drugs are being developed, they go through a number of different phases of development. A Phase I study is a study looking primarily at the safety of a medication. If it looks safe, then it progresses on to the Phase II trial, where we look at different doses and the efficacy of the drug in a population, in a small population. Finally, if the drug appears to be effective, it moves on to a Phase III trial, where the drug is compared against either a control group or a reference standard to determine if it's going to be beneficial for treating in this case IBD.

Clinical trials are important because they give patients access to treatment options which are not available yet and they also advance science and help us to potentially find a cure for IBD.

Surgery is also a treatment option and historically a lot of patients with IBD have undergone surgery. When patients have surgery for ulcerative colitis, the goal is to treat and cure medically refractory disease or prevent cancer or pre-cancerous lesions from spreading. Surgeons generally will go and remove the colon and rectum, therefore remove the target for the immune system and cure the ulcerative colitis.

In Crohn's disease, the surgical philosophy is quite different. Cure is not possible except for in some cases of isolated Crohn's colitis, and therefore we're asking the surgeon to go in and fix a medically nonreversible manifestation of their disease, such as a stricture, that we cannot get better with medications. In a way, an operation sort of pushes the reset button and removes that nonreversible manifestation of IBD and lets us start over with medications.

There are a number of types of surgery for IBD. For ulcerative colitis, a surgeon is going to do a proctocolectomy, which means removal of the colon and rectum, and either create a permanent ileostomy or do what we call restorative procedure, which means creation of a J-pouch. The disease is considered cured once the colon is removed, although certainly patients can develop pouchitis, inflammation of the pouch post-resection.

For Crohn's disease, there are a number of different surgeries which are contemplated. Strictureplasty is a procedure where, when a patient has a stricture, the surgeon will make an incision in the stricture and sew it back together a different way to relieve that stricture and essentially create a little area of dilation in the bowel to improve the blockage that was present and also prevent loss of bowel in that location.

Resection of the small intestine is sort of self-explanatory.

If someone has inflammation of the colon, partial colectomy or proctocolectomy would be an option.

Crohn's patients who have perianal disease will undergo a number of different perianal surgeries, including seton placement or drainage of an abscess.

Much like the medical options, there are some risks with surgery. These would include just the general complications associated with anesthesia or surgery itself. There's a chance of developing adhesions at the time of surgery, so that can sometimes lead to small bowel obstruction. If someone has an ostomy, there are psychosocial implications related to the ostomy creation.

In Crohn's disease there is always a risk of recurrent disease, so we generally recommend being placed on or continuing on maintenance therapy after the surgery. With ulcerative colitis there is a risk of pouch failure of somewhere in the range of 8% to 10% of patients who undergo J-pouch formation. In women, because of the development of adhesions postoperatively, there is a little bit lower chance of being able to become pregnant without in vitro fertilization.

Now that we've reviewed the traditional medical and surgical options available for IBD, we'll spend some time talking about complementary and alternative medicine, which I'm going to refer to as "CAM" going forward.

This is a group of diverse medical and healthcare systems and practices and products not presently part of what we consider are conventional medical therapies. The National Center for Complementary and Alternative Medicine breaks CAM practices into four basic groups.

The first group is natural products and these would include supplements, vitamins, and probiotics. The second group is mind and body medicine, which would include meditation, acupuncture, and yoga. The third is manipulative or body-based practices including massage or spinal manipulation. And the last category is considered other CAM practices including movement therapy, energy medicine, or Chinese medicine.

We know from a number of different studies that the majority, up to 60% of our patients with IBD, will use at least one form of CAM therapy. The two most common reasons patients give for using CAM therapy is they want a greater sense of control of their IBD, and a lack of efficacy or side effects from conventional therapies. So for someone who's not completely in remission with standard therapy or having some side effects from traditional therapy, using complementary medicine or alternative medicine allows them to feel like they're more in control of their disease and are able to better control their inflammatory bowel disease.

When you look at what forms of CAM patients use, it's really widely spread out, with most patients using herbal supplements or using special dietary therapies to help control their IBD.

The most commonly used alternative medicine is probiotics. Probiotics are good bacteria that are used to restore balance to the enteric microbiota in the intestine. The idea is to give bacteria that have sort of an anti-inflammatory effect, and can crowd out the bad bacteria. They may be helpful in aiding recovery of the intestine and maintaining remission, and there are a number of different forms, as you can see, that are available on the market.

It's really important to discuss this with your physician before initiating therapy as sometimes you can take too much too quickly and you may actually cause more symptoms of gas and bloating. So it's important to discuss starting these with your physician before you start therapy.

Here are the three most common ones that I'm asked about in clinic. The first one is pig whipworm eggs. This is used to treat both ulcerative colitis and Crohn's. The data were presented about seven years ago, and it did show some promise in controlling and healing inflammation. The development of this treatment was placed on hold for a while, but now there's a multicenter clinical trial about to get started in Crohn's disease. We're looking forward to seeing what the results of that trial will yield.

Curcumin is an extract from turmeric. This spice is available in grocery stores. It has been looked at both for ulcerative colitis and Crohn's disease. Studies have shown that UC patients

who take this are able to reduce their 5-ASA dose, and there's been some symptom improvement for people on this who have Crohn's disease. The largest trial looked at patients who had quiescent ulcerative colitis to see if this would help maintain remission and in that study the group that was treated had two relapses, compared to eight relapses in those that were on 5-ASA only in a six-month trial. These are smaller studies. We need a larger scale prospective trial before we can recommend this more broadly.

Lastly, fish oil supplements are used commonly for the prevention of heart disease, but they have also been looked at for treating IBD. It's been shown potentially to reduce pain and inflammation when added to standard IBD therapy. The clinical trials are really inconsistent, so it's hard to make any clear recommendations. But in general we tell our patients that although this hasn't been proven yet to be effective, it has some other benefits beyond just treatment of IBD and we would not discourage our patients from going on this supplement if they wish.

It's really important to weigh the risks and benefits of complementary and alternative medicine. So as I mentioned before, these can provide some benefit when used as an adjuvant therapy. This is important to highlight. These are used as adjuvant to standard therapy and not instead of standard therapy. It allows the patient to restore some sense of control of the management of their IBD.

A con would be that all these agents do have some potential side effects. If you take these and do not discuss taking them with your physician, it may undermine that doctor-patient relationship, which is so important. These are expensive and are generally not covered by insurance, so you'll be paying for these out-of-pocket. We do not know the optimal dosing of a lot of these medicines, so we're sort of flying blindly a little bit when we recommend taking these and how much to take. Lastly, these agents are not FDA regulated.

So here are some important takeaways when considering complementary medicine. It's important to seek out the best possible data, to try to help minimize some potential risks. You want to really choose well-researched options, and consider the qualifications of the information resources that you're getting your information from. You want to look at ones that have references and not the ones that have anecdotal testimonials or ones that are on sites that are trying to sell a product. Alternative therapy should complement and not replace traditional therapy. And again, as I mentioned many times before, it's really important that you tell your doctor everything you're taking, so that we can help rule out interactions with some of the medicines you're on.

The last category we'll be talking about is self-advocacy for optimizing care. What this means is becoming your own best advocate. This is important because patients who are more involved in their healthcare have been shown to be more adherent with treatment and generally have better outcomes.

So what are the keys to becoming an empowered patient? You can see them listed here. These are really the five things that you need to work on to become the true empowered patient and achieve the best care possible. This includes choosing the right healthcare team for you, preparing for your doctor's visit, keeping track of your healthcare information, becoming educated about your disease and treatment options, and building a strong support network. We'll go through all these in a little more detail in the upcoming slides.

So the first category is how you choose your healthcare team. This is important. Not every doctor is a good match, so it's important that you find a doctor and healthcare provider that you're most comfortable with. There are a lot of different resources that will help you achieve this. You can certainly ask friends or patients, fellow patients, or other physicians. There are some reputable internet resources which you can see listed here. When you go to that first consultation, you should also treat that as an initial interview for that doctor and make sure that

you feel comfortable being under their care. These are some questions that you might want to ask your physician when you see them for the first time. They would include how many patients with IBD they treat. Someone who has only a couple of patients with inflammatory bowel disease in their practice may not be as familiar with a lot of the manifestations of inflammatory bowel disease as compared to someone who treats hundreds of patients with IBD. Does that doctor perform any research? Usually physicians who are participating in research in IBD will be up to date on the most current treatment options and also this allows you access to some of the newer treatment options, should you need them. You want to find out who is on that doctor's treatment team. As I mentioned in an earlier slide, IBD can affect many different parts of an individual's life, such as psychosocial and nutritional aspects. Besides the physician, who else is involved in the healthcare team? Do they have access to a dietician or a psychologist who can help address other factors in one's life that IBD affects? And then, what do you do when you actually get sick and flare? How do you get a hold of the healthcare team? How do you get the care you need to get well?

We know that the most satisfied patients are those who actually take part in the decision-making process about their healthcare. So talk to your doctor in an open and honest way. This can lead to better and safer healthcare decisions. If your doctor recommends one treatment option and you have some concerns, please share your concerns with the doctor and discuss them openly so that you can understand why the doctor is choosing that particular treatment option and what some of the risks and benefits might be.

Tell your doctor all the treatments you're on. This will help foster trust between you and the physician. It reduces the chance of any interaction and side effects between these medications and also will improve adherence with medical therapy.

Adherence is really one of the key things that keep you well. So C. Everett Koop famously said, "Drugs don't work in patients who don't take them." And you see in that graph on the right, this is a study from Susie Kane. She looked at patients who had ulcerative colitis and looked to see what happened to patients who were adherent with the doctor's recommendation for 5-ASA therapy and those who were not adherent. You can see a very striking difference with an increased risk of flaring in those patients who were not adherent with 5-ASA therapy.

So adherence is generally associated with improved outcomes, decreased risk of disease progression, reduced inflammation, and increased healing of the GI tract. Also, possibly a reduced risk of developing colorectal cancer. Those who stay on the recommended medications are less likely to experience flares.

One of the things that I like is when patients come with a list of questions or concerns to their appointment. A lot of times you go to your physician and you're not feeling well, there's lots of information that's given to you by the physician and sometimes you can forget some of the questions that you wanted to discuss with your doctor. So it's important to make a prioritized list of what you want to discuss with the physician. If you can, bring someone you trust to be another set of ears to listen to the information that physician is going to share with you.

On the right you can see a nice tool to help you prepare for your doctor's visits. This is from the website IBDetermined.org. It helps guide you through information and questions you might want to bring to the doctor's appointment. So write down your symptoms, write down any side effects that you may be having, any questions you really want answered during that visit. Take that list out and check them off one by one as you discuss them with the physician.

It's also really important to be your own advocate. So you need to keep track of your own medical history. Even though with the electronic medical records, we generally have access to your medical history, it's important you know in great detail what testing and manifestations and medications you've had in the past. So keep track of things. Know the health maintenance items

that you need. We are all guilty of focusing in on just the current manifestations of one's IBD during the doctor's visit. But there are a lot of other health maintenance things that need to be addressed to make sure that you stay well. You can see here another nice form that you can use as a tool to help keep track of the important health maintenance items that you all should be having on a regular basis. Ask questions. And of course, listen to the answers the physician is giving to you as well.

The next item to help you become an empowered patient is to be educated. Obviously, if you're on this call, you're on because you want to be educated about your disease and how you can become a better patient. So knowledge is powerful. Learn more about IBD and your medical options. Bring some of these options and questions about these options with you as one of the items you want to discuss with the physician. Ask your doctor questions and ask them to explain if you don't understand the answers, why do you recommend I take this medication, why do I need to have regular labs done. I think once you understand some of the recommendations the physician is giving you, it'll help you be more adherent. So ask what are my active health issues, what are the treatment options for those issues, and of course, what are the risks and benefits of the treatments you're recommending. Again, it's helpful to bring a family member or trusted friend to the appointment, so that they can be an extra set of ears for you. And attend a lot of the local education conferences put out by the CCFA and maybe some of the local healthcare providers, so you can learn more about your disease.

When you're getting educated, it's important to find reliable sources of information. So consider the source. Is this a reputable source of information or is this a website that's trying to sell you a product. And it's important that you use several different resources so that you can learn as much as possible. So questions to ask when you find that information source are, is what's being given an opinion or is this fact, are there references provided, who's the author of this particular article and when was it last updated. Thankfully, science is progressing quite rapidly and even websites that have information from six months ago may be outdated. And make sure there's no apparent bias, either commercial or otherwise, to the information being given. Use the CCFA or the Information Resource Center to help you identify some of the reputable information resources.

And then lastly, build a strong support network. It's really hard to do this alone, so ask friends for help, family for help, and fellow patients can be also a good source of help in building a support network. Attend the local support group meetings. Use the CCFA community site, CCFAcommunity.org, to interact with other patients online.

And lastly, most importantly, get involved with the different educational seminars and activities which are occurring locally.

So this will end my presentation and we'll move on to the question and answer session.

Laura Wingate:

Thank you very much, Dr. Schwartz, for your informative presentation.

Now it's time for the question and answer part of our program. For everyone's benefit, please keep your questions general, without many personal details, so Dr. Schwartz can provide an answer general in nature. In the interest of time, I also ask that you keep your questions related to the topics of treatment and decision-making. You are always welcomed to contact the Information Resource Center if you have other questions.

Operator, can you please give instructions to our telephone and webcast audience?

Operator:

To participate in the call by asking a question, please dial star-1 on your keypad. If you

are joining us by web, simply click on Ask a Question, type your question, and then hit Submit. We will take questions in the order they are received. We can only take one question per person. Once your question has been voiced, the operator will transfer you back into the audience line. Again to ask a question, please dial star-1 on your keypad, or click on Ask a Question, type your question and then hit Submit.

Laura Wingate:

Thank you. We'll take our first question from the webcast audience. Dr. Schwartz, the first question is from Patricia and the question is, my 16-year-old son is recently diagnosed with Crohn's disease and is on Pentasa[®]. He often has headaches, especially in the morning. Is this typical?

Dr. David Schwartz:

Thank you, Patricia. I guess the question I would have is if the headaches started after starting Pentasa. One of the side effects that can be associated with the use of this particular agent is headaches. So that would be something to discuss with the physician. Perhaps an alternative medication might help treat the Crohn's and also get rid of the headaches.

Laura Wingate:

Thank you. We'll take our next question from the web. This is from Shelley. What are the early markers of severe disease? This was mentioned on the biologics slide.

Dr. David Schwartz:

So this is really something in evolution. What we're trying to do is find things either in your history or blood work or genetics that help us try to figure out who is going to go on to have more aggressive disease before you actually have some of the complications of Crohn's disease. I think as we go forward over the next decade there are going to be a lot more things available to help us do this, but currently what we look at are different things in your history such as how did you first present. Were you sick enough where the doctor wanted to place you on steroids right off the bat? Did you have any perianal fistulas at presentation? What was the age that you developed Crohn's disease? If you're less than 40, that's one of the markers of more aggressive disease. There are also different serologic and genetic tests that we do that can help us sometimes determine the different antibodies. Genetic testing such as the NOD2 gene can help us identify patients who have more aggressive disease course. So we look at all these factors and hopefully make a correct determination that someone is either going to or not going to have more aggressive disease and then make a treatment decision based on that.

Laura Wingate:

Thank you. Our next question is from Lu Ann. What are the psychological implications of an ileostomy and how does one know the risks?

Dr. David Schwartz:

I think the biggest thing we see in patients after colectomy with ileostomy formation is the difficulty initially adjusting to this. I think one of the key things is to talk to other patients who have gone through a very similar process. They've had the surgery and have an ileostomy. Talk to them about how they adjusted to it and what to expect so you're not unprepared for it. Certainly the CCFA is one of those places where you can be matched up with someone who is in a very similar situation, so that you can ask the questions you need to, so you understand what's going

to happen after the surgery.

Laura Wingate:

Thank you. Operator, we'll take our next question from the telephone audience.

Operator:

The next question comes from Rita in Florida. Your line is now open.

Rita:

Thank you. There are so many different probiotics to be found. Is there a specific probiotic that you might suggest, either refrigerated versus a shelf-stable kind?

Dr. David Schwartz:

Yeah, it can be confusing. When you go to the pharmacy you see about 100 different ones on the shelf and it's hard to know which one is best. What I would do, without naming a particular brand, is look at some of the data, some of the studies that have been done. There are a couple ones that have been actually tested in patients with inflammatory bowel disease. I try to steer our patients towards those products, because we have some data suggesting that they work for patients with IBD.

Laura Wingate:

Thank you. Our next question comes from Warren. What do you think of fecal transplant as a CAM option?

Dr. David Schwartz:

This is really interesting. So the idea here is that you get stool from someone that doesn't have inflammatory bowel disease, to sort of repopulate the intestines with good bacteria, to help reduce inflammation. We have been doing this for a short period of time for patients who developed really refractory *Clostridium difficile* colitis, which is that infection one gets sometimes from taking antibiotics, to restore normal colon flora and help get rid of the bacteria. Some recent studies have looked at doing this in a very small group of patients with ulcerative colitis with some success. I think it's an interesting concept. It's a little too early yet to really recommend this universally, but I'm looking forward to future studies, looking at this in more detail.

Laura Wingate:

Operator, we'll take our next question from our telephone audience.

Operator:

The next question comes from Wendy in New York. Your line is now open.

Wendy:

Yes, hi. My 16-year-old daughter was diagnosed two years ago and she's just begun Remicade[®]. She's had Remicade three times. Initially, two weeks later, four weeks after that. And we're not seeing any kind of improvement. Do you have any idea how long it takes to build up or if we should be seeing an improvement soon?

Dr. David Schwartz:

In general, infliximab (Remicade) and some of the other biologics tend to work pretty

quickly. Usually we'll give patients some time to allow the medicine to work, but normally after the third infusion with Remicade we would have already seen a response in most people. Sometimes we'll see a patient have a partial response, they've gotten a little bit better, but they're not completely well. Then we may increase the dose of future infusions. But if your daughter has not had any response after three infusions, it would seem that it's unlikely that she will respond to that particular medicine. But there are other options available.

Laura Wingate:

Our next question is from Allison. What dose of curcumin was shown to help?

Dr. David Schwartz:

I would have to look that up. I'll have to get back to you on that actual exact amount that was used in the study. I'm sorry.

Laura Wingate:

Not a problem. We can always email afterwards. The next question is from Jill. Does Dr. Schwartz have any insight on becoming pregnant during a flare or using medications like Imuran[®] and Cimzia[®] and their safety during pregnancy?

Dr. David Schwartz:

That's a whole hour-long conversation in itself. But what we generally tell patients is that we would really advise not getting pregnant while you're flaring. In general, if you go into pregnancy flaring, you have a higher rate of continuing to have symptoms or getting worse during pregnancy. So we really want to get you well first before you try to get pregnant. Then ideally use medicines that we feel are safe in pregnancy, so you can stay on them during pregnancy and stay well. That's what's best for the baby as well. As far as the safety of different agents, that's really a more lengthy discussion you can have with your gastroenterologist, but the short summary is that Imuran or azathioprine and 6-mercaptopurine are considered Category D in pregnancy by the FDA. But we have a lot of data now that would suggest that they are safe in pregnancy, so we generally continue it in people who need that medication. The anti-TNF agents, which certolizumab or Cimzia is one of, are Category B in pregnancy and we feel that in general they are safe and we'll continue them throughout the course of the pregnancy so that the patient stays well.

Laura Wingate:

Thank you. Operator, we'll take our next question from the telephone audience.

Operator:

The next question comes from Elizabeth in Pennsylvania. Your line is now open.

Elizabeth:

I'm 78, I've had ulcerative colitis for more years than I can count, maybe about 18. I've been on and off of prednisone. I've also had a course of Remicade and other things that have not worked and it's been suggested I need a colectomy, which I've resisted. I think I may have reached the time when I need a low dose of prednisone all of the time to stay in remission. Seems if I get to about 5 milligrams or 2.5 and then go off of it, I start a flare. What is your opinion on maybe some people needing to stay on small doses of prednisone?

Dr. David Schwartz:

In general, we're taught that prednisone is bad and we would try to do really everything we can to get you off of steroids and keep you well. There are some times, very rarely, where we've sort of exhausted all our medical options and surgery is not an option, where we may use lower doses to help you stay well. I'm not a big advocate of that, but sometimes that's out of necessity. There are a lot of really negative things that having active inflammation will lead to, including heart disease and cancer. So I think you need to have a very frank discussion with your physician about why they're recommending colectomy and see if there are other medical options that may be of benefit, to help get your colon healed up and get you feeling better. You may not have used all the available options for ulcerative colitis. There are also other reasons why people sometimes need to stay on lower doses of prednisone. If someone's been on steroids for a long period of time, the adrenal gland makes cortisol and prednisone is cortisol. And sometimes if you've been on steroids for a long period of time, the adrenal gland stops working as effectively as it used to and so you need to stay on steroids to help sort of make up that deficit. So that's also something that may potentially need to be explored with your physician.

Laura Wingate:

Thank you. Our next question comes from David. What evidence exists for a special diet to positively affect IBD, i.e. GAPS?

Dr. David Schwartz:

Doing scientific studies with diet is very hard because it really requires people coming in and getting all their food from one source to control things. So a lot of the evidence we have with dietary therapy is largely anecdotal. There really hasn't been any particular diet that's been shown to treat inflammatory bowel disease. There are certainly diets that help with symptoms. In general when someone's flaring, we recommend a lower residue or lower fiber diet to help reduce some of the gas, bloating, pain, and bleeding that can sometimes be associated with active inflammation. Certainly if someone has stricture in Crohn's disease, for instance, higher fiber diet will cause more symptoms. Also another example would be a lot of patients with IBD are lactose intolerant and if you've taken a large amount of lactose (milk), you may get gas, bloating, and abdominal pain. So there are certain dietary measures we can do to reduce symptoms, but as of yet not really a dietary therapy that we can advocate for.

Laura Wingate:

Thank you. Operator, we'll take our next question from our telephone audience.

Operator:

Our next question comes from Roslyn from California. Your line's now open.

Roslyn:

Hello. I think you may have already answered this question about a recommended dose for curcumin. And possibly using it to help with IBD disorders.

Dr. David Schwartz:

We don't have that off the top of our heads, but we're going to have that and post it online for you all.

Roslyn:

Okay, thank you so much.

Laura Wingate:

Our next question comes from Elaine. Can anti-inflammatories like Voltaren® gel cause a flare in ulcerative colitis?

Dr. David Schwartz:

That's a good question. Nonsteroidal anti-inflammatories include medications that we use for pain relief over-the-counter, traditionally ibuprofen or naproxen. Usually the ones we worry about as triggering a flare are ones that you would take orally. Voltaren gel is a type of NSAID that's prepared in a gel form, you apply it, like, to joints when you have pain. It's absorbed in a small amount, but I'm not aware of any evidence that it actually would trigger a flare. So a lot of times when someone is having joint pain and we want to use an NSAID for one particular joint or a couple of joints, one way to get the benefit of an NSAID without increasing the risk of flares is to use something topical like a Voltaren gel. So it should be okay.

Lauren Wingate:

Thank you. Operator, we'll take our next question from the phone.

Operator:

The next question comes from Lisa in New York. Your line's now open.

Lisa:

Hi. My daughter's been on Remicade for two years now, she's 20. She developed the HPV virus, even though she was vaccinated. The doctors want to keep her on the Remicade, but it seems like the only way to get rid of it is through your own immune system. So I don't really know what the right thing to do is. They want to keep her on it but the immunologist wants to take her off of it.

Dr. David Schwartz:

Has she had an abnormal Pap smear?

Lisa:

She had a colposcopy. And it came back with precancerous cells. And I think the only way to get rid of that is through your immune system. So she's on the Remicade, which depresses her immune system. So I guess they want to watch it, but I guess at what point do you take her off of it?

Laura Wingate:

Dr. Schwartz, can you give some advice here?

Dr. David Schwartz:

We generally use medicines like Remicade only in people who need it because they have severe disease. So it probably wouldn't be advisable to stop the Remicade. But what we try to do is, for instance, if they're on another medicine that may also suppress their immune system, such as azathioprine or methotrexate, you may reduce or stop that particular medicine for a period of time to help your body deal with the HPV. The gynecologist would obviously need to continue to follow her Paps a little more closely to make sure that no other abnormal cells develop. But I

wouldn't recommend stopping the Remicade in this situation.

Laura Wingate:

Thank you. I just want to remind our audience to try to keep our questions as general as possible. So we're going to take our next question from Debra and her question is, if on Remicade for UC, what classes of antibiotics should be avoided when another infection is present, like a sinus infection?

Dr. David Schwartz:

That's a good question. Ideally you'd avoid all antibiotics, but that's sometimes not possible. So the general rule of thumb is, if you have an infection and you go to your physician and they prescribe an antibiotic, you want to ask them to make sure that it's as narrow of a spectrum as possible. Sometimes we'll write for a really broad spectrum antibiotic if someone has a severe infection, when a more focused antibiotic to target, let's say, strep, would be just as effective. So you want to make sure that the physician puts you on a very narrow spectrum as possible of antibiotic. And sometimes taking probiotics with it may help reduce a flare with it. But it's hard to say take one particular type of antibiotic or not. Ones that we know are really highly associated with, for instance, *C. difficile* colitis, which is one of the things that we talked about earlier, would be a medicine such as clindamycin. We try to avoid something such as clindamycin because that's been shown to really increase the risk of *C. difficile* colitis.

Laura Wingate:

Thank you. We have another follow-up question on antibiotics. This one's from Meryl. Given the risks associated with antibiotics, why are they so often chosen by GI physicians as the first course of treatment?

Dr. David Schwartz:

Well, there are a lot of reasons for that. One is that in certain situations they're really effective. So for treating pouchitis or for treating perianal involvement with Crohn's, they're one of the better medicines we have. They're also generally well tolerated. We talked about some of the potential side effects, but in general most people do really quite well on antibiotic therapy. And so there are some antibiotics that are a little bit safer. Metronidazole being one of them. So that's probably the most commonly used one for IBD. I think it has a lot to do with the relative safety of these medicines and the effectiveness and that's usually why they're chosen first. You know, a lot of the other options suppress your immune system and these are one of the few that have an effect without really suppressing the immune system.

Laura Wingate:

Thank you. We'll take our next question from the phone.

Operator:

The next question comes from Molly in Illinois. Your line is now open.

Molly:

My 16-year-old son has Crohn's disease. He's on Pentasa. You mentioned that one of the few potential side effects of that could be kidneys and he did have kidney stones earlier this year, which I thought was just a manifestation of the disease, not necessarily from the medication. I guess I'm just asking, if it's a medication issue you think, or just a disease issue?

Dr. David Schwartz:

I should have been a little more specific when I talked about the renal manifestations. The thing we worry about with the 5-ASA agents and kidneys is more of an allergic type of inflammation in the kidney that can cause kidney problems. It's not kidney stones. You're correct; kidney stones are one of the manifestations of Crohn's disease.

Laura Wingate:

Thank you, Dr. Schwartz. Our next question is from Christine. She says you talked about supplements, but didn't address the efficacy of other alternative treatments like acupuncture, massage, yoga. Is there anything known about these?

Dr. David Schwartz:

As I mentioned, there are a lot of different alternative therapies. I tried to focus in on the three or four that really we get asked about the most and our patients use the most. There's starting to be some evidence presented on some of these other alternative therapies in treating IBD, but as of yet not really large well-done studies to prove their benefit. I think most are very beneficial in some way, but I can't definitively tell you it has proven efficacy in either Crohn's or ulcerative colitis.

Laura Wingate:

Thank you. Our next question comes from Susi and she says hello from the UK, great webinar. I'm on steroids at the moment and I'm in the middle of a flare. I've noticed that I got a flare when I gave up smoking. Is it because of stress or because I stopped smoking?

Dr. David Schwartz:

Well, it may be a combination of the two. So it's one of the odd things. People who smoke don't get ulcerative colitis. It appears that smoking may be somewhat protective against the development of ulcerative colitis. We'll sometimes use that to our benefit by using nicotine patches to treat patients who have refractory ulcerative colitis. So she probably did develop ulcerative colitis when she stopped smoking. We do know that stress also is important for triggering flares, so if she's under stress, that may be one of the reasons why she's having more symptoms now.

Laura Wingate:

Thank you. We'll take our next question from our phone audience.

Operator:

The next question comes from Sharon in Ohio. Your line is now open.

Sharon:

Hi. My granddaughter was diagnosed with Crohn's at 3½. She's now 11. She'll be 12 in March and she's been on Remicade for the last three years. Just concerned with the long-term effects of the Remicade and the methotrexate and some of the heavier drugs that she's had to take.

Dr. David Schwartz:

She developed Crohn's very, very early in life. This is a common question. Usually when

we are starting these medications, one question we get asked is, will I have to be on this my whole life and is it safe to be on it for long periods of time. Remicade has been out for about 13 or 14 years for Crohn's disease, and so we have a decent duration of experience with this and I think we're fairly comfortable with the side effect profile of that medicine. We haven't seen any really new side effects come to light in the last five to ten years. And the other thing I would say is that even though your granddaughter has been on this for a while, there are a lot of things in development that likely in five to ten years from now, she'll be on something completely different. The main thing to focus on is, are the medicines working, are they keeping her well, and preventing the symptoms and complications related to Crohn's disease.

Laura Wingate:

Thank you. Our next question is from Allan. Fatigue with ulcerative colitis, how do I treat that?

Dr. David Schwartz:

Fatigue is one of the more difficult things to sort out. There are so many things that can cause fatigue that it's hard to give a general answer. It's important that your physicians rule out some of the obvious causes, such as are you anemic, do you have active disease. If you have active disease that can make you fatigued. Do you have problems with your thyroid or are you B12 deficient. So there are a lot of different things that need to be looked at first before I can really have a good explanation as to the etiology, the cause of your fatigue. But this is probably one of the more common symptoms we see in people who have IBD and sometimes it's obvious, such as some of the things I mentioned. Other times it's really hard to know what exactly is causing a patient's fatigue. It may just simply be the disease process.

Laura Wingate:

Thank you. We'll take our last question from the web. How unusual is depression with Crohn's disease? Is there a specific treatment for Crohn's-related depression? And this question is from Bryn.

Dr. David Schwartz:

Crohn's and depression are very commonly associated. Somewhere probably in the range of about 40% to 50% of patients will have some element of depression associated with this. Much like any chronic illness, it can be associated with both anxiety and depression. And as far as treatment, we treat Crohn's-related depression or IBD-related depression very similarly to how we treat regular depression. It needs to be addressed by your primary care provider or a qualified psychiatrist in picking the right medication or therapy to help treat the depression. We have found that treating the underlying depression sometimes actually may help the IBD as well. So it's really important to be addressed.

Before we go on, while we were talking I did look up the dose of curcumin and in the studies, at least one of the studies, it was 550 milligrams taken twice a day.

Laura Wingate:

Thank you very much. So we've answered the curcumin question. Thank you.

Thank you, Dr. Schwartz, for your insightful presentation and the answers to all of our questions. If your questions were not answered, you can call CCFA's Information Resource Center Monday through Friday, 9 AM to 5 PM Eastern Time, at 888-694-8872.

An archive of today's program will be posted on CCFA's website next month.

I encourage all of you to complete the post-program evaluation. Your feedback helps us shape future programs.

To help us further our understanding of IBD, we encourage you to join CCFA Partners, our national registry of patient-reported outcome. Visit www.CCFAPartners.org, to learn more and to participate.

Finally, we'd like to extend a special thank you to Elan, UCB, and Shire for their support of this event.

On behalf of the Crohn's and Colitis Foundation of America, thank you for joining us. Good-bye.

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