

OPERATOR:

Hello, everyone, and welcome to *Understanding Crohn's Disease*, a free telephone/web education program. It is my pleasure to introduce your moderator James Testaverde, Senior Director of Patient Services at the Crohn's & Colitis Foundation of America.

JAMES TESTAVERDE:

Hello, everyone. On behalf of the Crohn's & Colitis Foundation of America, welcome, and thank you for attending tonight's program.

This activity is presented by the Crohn's & Colitis Foundation of America and is cosponsored by the American Gastroenterological Association Institute. The program is supported by educational grants from Abbvie and Janssen Biotech, Inc., administered by Janssen Scientific Affairs, and it is also supported by a sponsorship from Takeda.

Before we begin, I would like to address a few housekeeping items. To allow full participation in today's program via the web, please be sure to disable any popup blockers on your browser or computer. Please note that this program will include interactive polling questions, which you will be prompted to answer throughout the program. Please respond when these questions appear on your screen and please note that your responses are anonymous.

For the participants listening via telephone, you will be unable to respond to the polling questions, but you will hear the questions and the answers.

Thank you to everyone who submitted questions in advance of the program. After the presentation, we will open up the program for your questions. We will review as many questions as we can from both telephone and webcast participants. If we are not able to answer your question on tonight's program, please contact CCFA's Help Center, which can be reached Monday through Friday, 9 AM to 5 PM Eastern Standard Time, by calling 888-694-8872.

Upon exiting today's program, you will be prompted to complete a brief program survey. We ask that you please take a moment to provide your responses, as your feedback is extremely important to us as we plan future educational activities.

I now have the pleasure of introducing our speaker for tonight's program. Dr. Raymond Cross is an Associate Professor of Medicine and the Director of the Inflammatory Bowel Disease Program at the University of Maryland School of Medicine. He is also the Co-Director of the Digestive Health Center at the University of Maryland Medical Center in Baltimore.

Dr. Cross, thank you so much for joining us, and I will now turn the program over to you.

DR. RAYMOND CROSS:

Thank you, James, and thanks, everyone, for attending.

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Over the next 40 or 45 minutes, I'm going to try to help you understand about Crohn's and the effects of Crohn's, review current treatment categories including medications and surgery, hopefully provide you some helpful tips to manage your disease, and James is going to share some resources with you to help answer questions and provide support.

And we're going to start with a polling question right away. "Which best describes you? A, I'm a patient with Crohn's disease. B, I am a family member of a patient with Crohn's disease. C, I am a friend of a patient with Crohn's disease. D, I'm unsure if I have Crohn's disease. Or E, no connection, just want more information." So which one of these choices best describes you?

Alright, so for most of you, 74%, have Crohn's disease. Okay, so let's go to the next. About 23% are a family member of a patient with Crohn's. Let's move to the next slide.

So what is Crohn's disease? So Crohn's is one of a group of conditions known as inflammatory bowel disease. So inflammatory bowel disease is comprised of Crohn's, ulcerative colitis, and what we call IBD, undetermined type or indeterminate colitis.

Crohn's is a chronic inflammatory condition that affects the gastrointestinal tract. So when we say chronic, that usually means for most patients life-long. And it's characterized typically by intermittent flares or relapses of the disease, followed by periods of symptom-free times, which is called remission.

And when we talk about medical therapy, our goal of medical therapy is to even out those peaks and valleys and prolong the amount of time that patients are in remission.

Crohn's, as opposed to ulcerative colitis, is a patchy disease. So typically inflammation is discontinuous and when the disease is severe, it can involve the full thickness of the intestinal wall, whereas ulcerative colitis only involves a superficial layer of the intestine.

Patients with Crohn's can have inflammation anywhere throughout the digestive tract, from the mouth to the anus or otherwise known as the back passage. But typically most patients have involvement of the small intestine and the colon.

It's estimated that Crohn's affects 700,000 Americans. There's a new study that's going to be presented this weekend that estimates that about 900,000 Americans are now affected with Crohn's disease. And as Crohn's is a very heterogenous condition, there are a few different types of Crohn's that are present, so the symptoms and prognosis and can be really – can differ for each individual person with the disease.

As I mentioned, since there are different types of Crohn's, the symptoms can vary, but most patients will have diarrhea, about a third of patients will have bloody diarrhea, abdominal pain is one of the most common symptoms, typically crampy pain in the right lower quadrant or right lower side of the abdomen. It's very common for patients to lose their appetite. And when the disease becomes more severe, weight loss can be seen. And often patients who suffer from Crohn's will have fatigue.

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Some patients can experience complications of their illness and we'll talk about this in a few slides. But strictures or blockages that can occur in the intestines, which can cause obstruction. Symptoms of obstruction could be worsening abdominal pain, bloating, loud bowel sounds, and in late stages nausea and vomiting. Fistulas are a tunnel or a connection between a loop of bowel to either another loop of bowel to the abdominal wall to the back passage or anus or the skin around the anus, or to another organ such as the bladder or vagina. Patients with fistulas often can be very ill with severe pain, fever, and sometimes a pocket of infection in the abdomen called an abscess. Fistulas can also occur around the back passage or anus and those are called perianal fistulas, and in some cases those can become infected, and a patient will have a collection of infection called an abscess.

About 7 or 8% of patients with Crohn's or ulcerative colitis will develop colon cancer in their lifetime. And patients with more severe disease, malnutrition can occur. And in pediatric and adolescent patients who are affected by Crohn's disease, growth and development can be delayed or decreased.

So Crohn's disease can cause symptoms outside of the bowel and that's called extraintestinal manifestations. And basically it can affect the eyes, the mouth, causing so-called canker sores in the mouth or aphthous ulcers. There are several types of arthritis that can occur in patients with Crohn's. There are at least two skin conditions that can affect patients with Crohn's, called erythema nodosum and pyoderma gangrenosum. The bones can be affected, either through the disease itself or through some of the medications used to treat the disease, such as prednisone, which can cause thinning of the bones or osteoporosis. Patients with Crohn's can develop malabsorption and thus can have kidney stones. And there are at least two types of liver disease that can occur in patients with Crohn's, both primary sclerosing cholangitis, as well as autoimmune hepatitis.

Unfortunately we don't know a precise cause of Crohn's disease. It's thought that a genetically susceptible host, so a patient with the right traits or genes inherited from their mother and father, will have an inappropriate immune response to bacteria in their intestines.

As I mentioned, genetics are important. Twenty to 25% of patients will have a close relative with Crohn's disease. And there have been over 150 genes identified that are potentially – play an important role in developing Crohn's.

Unfortunately, there's not one specific gene that's critical. It's thought to be that there are multiple genes or traits that are important for someone to develop Crohn's disease.

We know that the immune system itself acts inappropriately. In the very early stages of Crohn's, the innate immune system or the more primitive immune system does not respond appropriately to some injury, whether that's an infection or some damage to the intestinal lining. And therefore the acquired immune system kicks in and when it kicks in it will not shut itself off. That's why many of the medications that we use to treat Crohn's disease are designed to dampen or lessen the immune response.

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We mentioned already bacteria in the intestines are critically important. We have more bacteria in our intestines than we have cells in our entire body. And increasingly, there's research being done to look at those populations in patients that are healthy and those that have illnesses like Crohn's and colitis.

Also infections can be a trigger both for onset of Crohn's as well as a flare. Use of antibiotics, especially early in life, can trigger IBD. Nonsteroidal anti-inflammatory drugs such as aspirin, ibuprofen and Naprosyn®, can trigger onset of the illness as well as a flare. Stress can be an important factor.

And I think we should spend at least a few seconds and talk about smoking. Smoking is associated with a higher risk of Crohn's disease. In addition, smokers are more likely to have severe Crohn's and to undergo surgery. And in fact, patients that continue to smoke after surgery are more likely to require a second surgery and have a more rapid recurrence and need for surgery. So smoking is critically important in patients with Crohn's disease.

Location of Crohn's, we mentioned this briefly, most patients, 45%, will have involvement of the end of the small bowel or what's called terminal ileum, as well as the colon. That's the classic pattern. But about a third of patients will have involvement of the ileum or end of the small bowel alone. About 20% of patients will have involvement of only the colon. And if you're paying attention, that's not going to add up 100%. Less than 5% of patients are going to have involvement of the more proximal small bowel, the jejunum, duodenum, or even the stomach or esophagus.

I also mentioned that there's different patterns of disease. So typically when patients are first diagnosed, especially in young pediatric or adolescent patients, typically they have inflammatory disease. And that means that they haven't developed a complication yet, so they haven't developed a stricture or blockage, or they haven't developed an internal fistula or abscess.

Over time, if you're not treated appropriately, up to 90% of patients can develop a stricturing or perforating complication. Depending on the study, about 25% of patients can develop perianal fistulas or perianal abscesses over time.

So the treatment goals are essentially two-fold. In this slide there's three arrows, but I'll talk about the third arrow in a minute.

The first goal of treatment is to induce remission. To help you feel well. So if you're having symptoms, we're going to make the symptoms go away and the goal of treatment is for you to feel completely normal again. So the complete absence of symptoms.

In doing so, we also should see normalization of your blood work, we should be able to restore normal growth and development in children and adolescents, we should improve your nutrition, and in doing so your quality of life will almost assuredly improve.

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The next phase of treatment, once we get you there, is to keep you there. So the goal is for you to never have a flare again or at least to minimize flares. And we almost always achieve that with maintenance medical therapy.

In addition, our goal in 2014 is a maintenance of remission without steroids. So keeping patients on a dose of steroids to keep them well is no longer really a goal of treatment.

We also want to prevent relapses, as I've mentioned, and we think that through more aggressive early treatment we may be able to prevent some of these complications that I mentioned, such as strictures and these internal fistulas, and thus we might be able to decrease the need for surgery over time.

Now in the third arrow in this slide we talk about disease monitoring and prevention as being separate. Well, we're really monitoring your disease throughout both phases of treatment, both during induction of remission, and maintenance. Once you're in remission we're looking for signs of early relapse, which could be symptoms or abnormal blood work. We're also monitoring your maintenance therapies to make sure that they're safe, that you're not having any adverse sequelae from treatment such as low white cell counts or abnormal liver enzymes. We're also doing preventative strategies to try to prevent any infections that could be associated with the disease or the treatments. And then once you've had disease for a period of time, typically we start talking about cancer prevention, and most specifically for Crohn's and colitis is prevention of colon cancer.

So there are a number of medications that we can use to both provide symptom relief, to induce remission and to maintain remission. And we'll start with over-the-counter medications.

Before we do that, we're going to go to our second poll question. So before I talk to you about over-the-counter treatments, let's talk about what treatments you're on currently.

So "Your current treatment regimen includes A, steroids; B, aminosaliclates or 5-ASAs; C, immunomodulators or immune suppressants; D, biologics; E, antibiotics; or F, two or more of the above."

Alright, so not so much surprisingly I guess, 59% of patients on two or more medications, 20% of patients are on biologics, and 13% of patients are on immune suppressants. So the majority of patients attending tonight are on two or more agents, biologics, or immune suppressants.

So as promised, we're going to talk about over-the-counter medications. So the important point about over-the-counter medications is they can be very helpful in reducing symptoms. But importantly, it's highly unlikely that over-the-counter medications are going to decrease inflammation and induce remission and maintain remission. They're primarily used as supportive measures while our IBD-specific therapies are being used to get you well.

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Typically typical agents are anti-diarrheal agents like Imodium. Occasionally laxatives are used, things like MiraLAX® or Milk of Magnesia®. Pain relievers such as acetaminophen or Tylenol®. We mentioned nonsteroidals and I said that that can be associated with both the onset of disease as well as worsening or relapses of disease. So aspirin, ibuprofen, Naprosyn®, can be very dangerous to take if you're a patient with Crohn's disease.

We haven't mentioned yet, but I'm going to mention it for the first time, complementary and alternative medicine, and this can include things like vitamins and minerals as supplements and probiotics. It's estimated that about 50% of patients with Crohn's can use these type of medications. So I would encourage you when you're using these over-the-counter agents to discuss them with your provider before you start taking them because some of them, such as nonsteroidals, may actually make your Crohn's worse.

And next we're going to talk about antibiotics. So antibiotics are a frequently used therapy. Usually a supplement or adjunctive therapy. But there's a couple indications in which they can be particularly helpful.

In patients with ulcerative colitis who've undergone a removal of the colon or colectomy, they often are offered a restorative procedure where the ileostomy can be reversed and that's called the J-pouch. A J-pouch typically works well, but about a half of patients can develop inflammation of the pouch and antibiotics work very, very well to treat that inflammatory condition.

We talked about perianal fistulas. Antibiotics can be useful when fistulas are active, to decrease drainage and pain. And in some cases they can result in resolution of the fistulas. Abscesses associated with either the perianal type fistulas or internal fistulas, antibiotics are helpful at decreasing the size of those and helping to speed resolution.

They also can be used in patients who have involvement of the colon alone. And for whatever reason, patients with isolated colonic Crohn's may do well with antibiotics.

Typical antibiotics that we use are metronidazole or Flagyl®, ciprofloxacin or Cipro®, and a newer antibiotic called rifaximin or Xifaxan®.

The problem with antibiotic use, of course, can be resistance to bacteria. So if we use antibiotics prolonged or repeatedly, bacteria in our bodies can become resistant to them and thus the antibiotics would be not effective.

Also I mentioned that antibiotics are associated with flares in some patients. And antibiotics can cause an infection in the colon called *Clostridium difficile*. If this infection occurs in patients with Crohn's disease, it's associated with worse outcomes, including a higher need for hospitalization as well as a higher rate of surgery.

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The next class of medications we're going to talk about is aminosaliclates or 5-ASAs. This is a very – generally very safe class of medication that's used frequently because it's very safe. Unfortunately, aminosaliclates don't work very well for Crohn's disease. They're probably most effective for patients with milder Crohn's and they may be effective for a subset of patients, again, who have disease predominantly in the colon.

The different 5-ASA formulations that we've listed here are sulfasalazine, the salamine products, olsalazine, balsalazide, are all essentially the same as far as effectiveness. The differences between them are where the active component or the 5-ASA is released. And these formulations have slightly different variations on them, so the drug is released in different parts of the intestines.

Many of you may have been treated with steroids. Steroids are very effective drugs at making you feel better in the short-term and thus inducing remission. So steroids will often be used in combination with an immune suppressant, whereas the immune suppressant will remain your remission and steroids will induce remission. Unfortunately, steroids have so many side effects that there's actually been a book written about all the side effects from steroids. These include, but aren't limited to, infection, trouble sleeping, mood swings, other neurologic changes such as irritability, changes in your physical appearance such as rounding of the face, weight gain, abnormal fat deposition and stretch marks. And they can have a very negative effect on the bone, causing osteoporosis.

But there are some newer steroids available that have less side effects and those include the budesonide products such as Entocort® and Uceris®. So these may be safer steroids that can be used to help get patients into remission.

Also the topical steroids, those given in the enema form, may have less side effects.

Steroids can also be given through the vein or intravenously if you're very sick, and they work more rapidly if given through the IV as compared to giving it orally or by mouth.

The next class of medications is immune suppressants and specifically we're going to talk about the thiopurines, which are azathioprine and 6-MP.

So these are drugs that are used to help patients come off of steroids and maintain remission. And they can be very effective in up to 50 to 60% of patients. Unfortunately, azathioprine and 6-MP don't work rapidly. They take a few months to really kick in and have a peak effect. So often, especially if you're having significant symptoms, you'll need another agent like steroids to induce remission while this medication is started.

There are some risks of therapy. They include infection, including unusual infections. We worry about certain types of cancer such as blood cell cancers or lymphoma. There's also an increased risk of non-melanoma skin cancer in patients who take these agents. Early on, patients can develop a flu-like syndrome, which is basically an allergy to the medication. Also about 3% of patients can experience

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inflammation of the pancreas or pancreatitis. Over time, patients need to be monitored closely with labs taken anywhere from every one to three months to make sure that their white blood cell count doesn't drop or that their liver function tests don't elevate.

The next immune suppressant is called methotrexate. This can be given either orally or by mouth or through an injection under the skin. It's often recommended again to help facilitate coming off of steroids. It's also used in patients who are not tolerant of azathioprine or 6-MP or those that experience side effects. It also may be particularly helpful in improving fistulas. To minimize some of the side effects of methotrexate, we recommend that patients take a daily folic acid supplement.

The most common side effects of methotrexate are more nuisance side effects such as nausea, fatigue and headache. Importantly in women of child-bearing age, you cannot take methotrexate because it can either cause abortion or it can cause birth defects. So it cannot be used in women of child-bearing age that intend to conceive.

The next class of agents we're going to talk about is the biologic agents. The analogy I use with these drugs is compared to steroids, which would be a nuclear bomb or atomic bomb, these are more smart bombs to block specific aspects of the immune system to decrease inflammation and improve symptoms.

They are typically used in patients who don't respond to standard therapy or who are no longer responding to standard therapies. However, increasingly as we – in the polling we did here – they're being used more often earlier in treatment.

Risks of all biologic therapies include an increased risk of infection as well as infusion or injection site reactions. Patients using anti-TNF agents have a higher risk of melanoma as well as other autoimmune type reactions such as drug-induced lupus, a multiple sclerosis-like reaction, and a psoriasis-like eruption on the hands, feet and scalp.

When we talk about biologic, there's three classes of – or two classes of biologics. One are the anti-TNF agents which include adalimumab or Humira®, certolizumab pegol, which is also called Cimzia®. Both adalimumab and certolizumab are injections given under the skin. Infliximab is another anti-TNF, also called Remicade®. It's given as an intravenous infusion.

The next class of biologics are anti-adhesion molecules and they basically work by blocking white cell entry into the intestine. So if you imagine that your white cells are boats, they need to be able to dock somewhere and they're trying to dock in the inflamed intestine. So drugs like natalizumab or Tysabri® or vedolizumab or Entyvio™, which is the most newly approved drug for treatment of Crohn's and colitis, block the entry of white cells into the intestine and thereby decrease inflammation.

Some special things to consider in patients is the benefits and risks of therapy. So when you sit down with your provider to consider a new medication, it's very important that you go over the benefits of

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the medication specific to your case, as well as the specific risks to you. In general, the risks of treatment almost always greatly outweigh any risks associated with them. But that's important that your provider go over them with you before you make changes.

Children also require special consideration. It's estimated that 10% of patients or more are affected by Crohn's and colitis under the age of 18 years of age. And they may require individualized treatment, especially in those patients that have experienced growth delay and developmental delay. It's very important that we get them back on the growth curve quickly, so that they can attain their maximal height and growth and development.

In addition, we tend to extrapolate our treatment from adult trials to children and that's a problem. So we need more trials addressed specifically in children, to make sure that we have effective treatments and, importantly, effective doses of medications.

And when we're talking about women, women who are thinking of conceiving or those that are pregnant, it's very important to go over the medications because there are some, like methotrexate, that are inappropriate in a woman of child-bearing age who intends to conceive, and in a woman that's pregnant. So ideally I tell my patients the best time to talk about that is before you're pregnant, not coming back to clinic when you're already in the first or second trimester.

So a couple of questions we're going to go over, such as judging response of treatment. How do you know if your treatment's working? We're going to talk about timing, but in general you know your treatment is working is if you feel better. And I set the bar high, is your expectation should be to feel normal. So if you start a new drug and you feel normal, your treatment's probably working.

If you're in remission, what do you do next? The first thing you should do is you should pat yourself on the back because you've achieved remission, that's very important. Many patients want to know once they feel well, is when they can stop meds. Unfortunately, most of the time when patients stop medications, the symptoms recur. So it's important at least for a period of time, and I usually tell my patients that we're going to keep you well for four to five years and then we can talk about whether it's okay to withdraw medication. So once you get there, it's very important, for at least a period of time, that you stay on your medications, and you should never stop before consulting with your medical provider.

The next question is also important. How much time should you allow before determining if the medicine's effective? And that depends on the medication. Typically medications like steroids and anti-TNFs tend to work very quickly. Usually within 30 days or so, you'll know – you should have some improvement in your symptoms. For drugs like methotrexate, azathioprine, Tysabri®, Entyvio™, those may take a couple months to really know if they're effective for you.

What about surgery? So I think many people mistakenly associate surgery with some kind of failure of your treatment and I think surgery is just one option to get you feeling better and restoring quality of

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life. Especially when combined with medication. The primary goals of surgery in patients who develop complication are to alleviate those. Also when you do that you should improve symptoms. And patients who have disease that's not responding to medical therapy, surgery can alleviate your symptoms as well. And typically this will restore quality of life.

Whenever you're talking to a surgeon about treatment, it's very important that you pay a very close eye to bowel conservation so that you don't develop short bowel. So we want to reduce the minimum of bowel possible to alleviate your symptoms, reduce your complications, restore quality of life, without compromising your long-term function.

The most common surgery in patients with Crohn's is a resection, so that's a removal of the damaged or diseased segment of bowel with a reconnection then of the two non-diseased end of bowel. That's called a resection and a primary anastomosis.

A strictureplasty basically is a repair of a diseased segment. So especially in patients who have multiple narrowings or strictures or blockages, strictureplasty can be performed so that you don't reduce the length of the bowel, but you do relieve the obstruction.

When you resect part of the colon, either total colon or part of the colon, that's called a colectomy. And when you remove the entire colon and rectum, that's called a proctocolectomy.

Some patients that have disease of the colon or the perianal area can have what's called a diverting colostomy or diverting ileostomy. This can be done to allow healing of the segment of intestine that's below the diverting stoma. So it's typically a temporary surgery until the inflammation or infection is controlled.

Now for Crohn's disease, surgery is not curative, although in some patients a long-term remission can be induced with surgery. And if you combine surgery with medical therapy afterwards, the results can be quite good.

Elective surgery is usually planned in patients who have a stricture, in patients who medication is not controlling the illness, once a fistula or abscess has formed, and in patients who have pre-cancer or dysplasia. Surgery becomes emergent when the bowel perforates or ruptures or if there's a high grade blockage or obstruction that's not resolving with conservative therapy.

Now what about nutrition? This is clearly one of the top ten questions that patients ask in clinic. What can I eat, what should I eat? In general, there are no known diets that are going to alter inflammation and improve your symptoms. I tell patients it's important that you have a heart-healthy diet, which is going to be a diet that's high in fruits and vegetables, that's low in processed sugars, and that's low in red meat. And generally that tends to be a good diet for most Crohn's patients. The exception would be if you have a stricture or blockage, if you try to eat a lot of fruits and vegetables it can make obstructive symptoms worse. In addition, sometimes in patients that are flaring, a lot of

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fruits and vegetables can actually make you feel worse. And it's important, especially when you're flaring, to try to keep track of what symptoms make you feel worse and try to avoid those as much as possible. And the CCFA has a food diary that will help you track your symptoms.

We talked about good nutrition and what I tell my patients is good nutrition is heart healthy. Other things to consider as far as supplements for nutrition, a daily multivitamin can be a good idea, especially in men, who tend to have diets that aren't quite as good as women. And patients with inflammation at the end of the small bowel or ileitis, or in those patients who have had surgery or removal of the ileum, oftentimes B12 injections or B12 nasal spray is needed to either prevent or treat B12 deficiency. About 40% to 70% of patients with Crohn's disease can have deficiency in Vitamin D, so it's common for patients to undergo repletion and maintenance with Vitamin D. And in patients who have bone loss, we often recommend calcium supplements. And in patients on methotrexate and sulfasalazine, we recommend a folic acid supplement to minimize or prevent side effects.

We talked a little bit about complementary or alternative medicine. And it can be defined pretty broadly by the National Center for Complementary and Alternative Medicine as any medicine such as a natural product, a supplement or probiotic. It also includes mind and body medicine such as meditation and acupuncture. And can include manipulation and body-based practices such as massage and spinal manipulation. And I mentioned that some studies have shown that about – that 50% of patients with Crohn's use some type of complementary medicine.

This is of interest for many reasons. Despite improvements in our medical therapy, medications sometimes don't control the disease, so patients are seeking other therapies to help get them completely into remission. Some of the symptoms are difficult to treat. Some patients will have chronic pain, whether it be chronic muscle pain, chronic joint pain, chronic abdominal pain, and sometimes therapies such as acupuncture, meditation, massage and other things can be a nice supplement to conventional treatment.

Some patients, in particular patients with Crohn's for reasons we don't understand, may experience more side effects of medications than other patients. And when you experience side effects of conventional therapy, it's very natural to want to look outside of conventional medication for treatment.

I also think that patients, from my own experience, patients seek out complementary medicine based on preconceived beliefs about medicine. I also think that Crohn's in general, patients, they feel out of control. And using things like complementary medicine when you're empowering yourself and you're advocating for yourself, it helps patients feel like they're getting control of their illness.

I think it's important to point out with complementary medicine two critical points. One, it's unlikely that complementary medicine alone is going to control your disease. It's usually going to be a supplement to conventional therapy. And then importantly it's very critical that you talk to your healthcare provider about what complementary therapies you're using.

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One complementary medicine, probably most frequently used, is probiotics. These are essentially good bacteria. We talked about all of those bacteria in our intestines. You can think of it sort of as a Yin and Yang of good and bad bacteria and probiotics are good bacteria. So the thought would be if you take probiotics you restore good bacteria in your intestines and you'll lessen your symptoms. Unfortunately there haven't been good studies in Crohn's showing that that's effective. It's also not clear which probiotic of the thousands out there on the market you should use. Some of the probiotics that have been studied the most include VSL#3, E. coli Nissle 1917, which is called Mutaflor, and then Flora-Q is another example. But as I mentioned, there's thousands out there on the market.

I typically use these agents most in my Crohn's patients when they're using antibiotics for some other reason. One of the best uses of probiotics is to prevent antibiotic-associated diarrhea and perhaps to prevent infection with *C. diff*.

So that leads us to our third polling question. "Have you used complementary and alternative medicine for Crohn's in addition to other medications?" A is yes. B is no.

So the majority of you have used complementary or alternative medicine in addition to your Crohn's medications.

So what about monitoring? So one of the key messages here is that even when you're well it's important to be monitored. This is going to include assessing your symptoms, but also looking for markers of inflammation in your blood and in your stool potentially, as well as monitoring the safety of your medication through blood and stool tests. Increasingly we are monitoring patients with some form of endoscopy, colonoscopy or upper endoscopy, to assess if the inflammation has improved with treatment. And sometimes we're also using imaging, CAT scans or MRIs to monitor improvements after we initiate treatment.

Blood and stool tests can be used to check medication levels. This is especially true with azathioprine, 6-MP and the anti-TNF agents such as infliximab and adalimumab. We can also see how medications are affecting your body systems and looking at response to treatment to see if the inflammatory markers have gone down. We can use blood tests to monitor your risk of infection. The typical tests that we order include a complete blood count, a comprehensive metabolic panel which looks at your electrolytes, kidney functions and liver function. And we talked about inflammatory markers, so we measure the CRP or C-reactive protein, the sedimentation rate or ESR, and increasingly we're assessing inflammation by looking at a stool test called a fecal calprotectin.

The most commonly used endoscopic procedure in patients with Crohn's is a colonoscopy. This is a tube with a light and camera that's inserted through the anus, once you've undergone a colonic prep and sedation. And it allows us to look at the rectum, the entire colon and the lower part of the small intestine called the terminal ileum. Importantly, we mentioned the prep, but it also requires an overnight fast.

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A flexible sigmoidoscopy is very similar, except it's a smaller scope and it only looks at the lower part of the colon, typically the rectum and the sigmoid, sometimes all the way to the entire left colon. The prep is a little less for this. Technically you don't have to have an overnight fast and you could just use an enema or two before the procedure to get clean enough to allow your provider to examine the colon. This procedure is used more often in patients with ulcerative colitis than Crohn's.

A capsule endoscopy is a pill camera essentially. It's the size of a penny. It has a light source and it takes thousands of pictures as it tumbles through the intestines after you swallow it. So that we can see the results of those images, you need to wear a utility belt basically for eight hours, similar to what Batman would wear, and it transmits the pictures from the pill camera to the recorder, which are then downloaded on the computer and read by your healthcare provider. And this allows us to look at the 18 feet of small intestine between where we can reach with an upper endoscope and a colonoscopy, so that problem area of the small bowel can be visualized with the pill camera.

We sometimes do an upper endoscopy in our Crohn's patients, especially in pediatric patients, patients with more upper abdominal pain, nausea, vomiting, difficulty swallowing, or those with known Crohn's disease of the stomach or duodenum can have an upper endoscopy completed.

Endoscopic ultrasound is used in some centers to look at perianal fistulas, so this is similar to a sigmoidoscopy where a special scope is inserted into the rectum. There's an ultrasound probe. And it allows us to look at fistulas where they course in the perianal region, whether there's associated infection, and it helps us monitor response to treatment.

External imaging procedures, so non-endoscopic. Let's start with the easiest one first, which is an X-ray. So when a patient presents to the hospital with signs or symptoms of a bowel obstruction or blockage, an X-ray is usually the first test ordered. It also can be used when we suspect a perforation or a hole in the bowel or a patient who has a colon that's severely inflamed, to look at dilation of the colon.

We don't really use ultrasounds very much in the United States, but in Europe they're often used to look for patients who have a stricture or blockage in the terminal ileum.

We rarely use white blood cell scans, but they can be used to look for segments of bowel that are inflamed.

Barium enemas can be used. Basically a catheter is inserted into the anal canal into the rectum, barium is put into the catheter, and it allows us to look at the rectum and colon to look for active disease, and more typically to look for blockages in the colon.

An older test that we don't do as much anymore is a small bowel series, where you drink barium and you undergo a series of X-rays as we watch the barium course through your small bowel. This is a good exam to look at narrowing or blockages in the small bowel, as well as for fistulas.

DR. RAYMOND CROSS:

Now more commonly today in 2014 we're doing either a CAT scan or an MRI. And MRI is increasingly being favored over CAT scan because generally speaking, you can get equal results to a CAT scan with no radiation exposure. And this is a critical point in younger patients. As you undergo more and more CAT scans, you have an independent risk of cancer associated with the radiation of a CAT scan. So if your doctor is recommending repeated CAT scans, it's important that you ask if maybe an exam like an MRI would be appropriate to decrease radiation exposure.

So how about some helpful tips to help you prepare for your doctor's visit? So first you want to write down a list of questions that you have. When you get into the office it can be intimidating and it's important that you make sure that you've gone through the agenda that's important to you.

Prior to the visit, especially in that very critical interval in the week or two before you go into the doctor's office, try to keep a diary of your symptoms. Do a 1 to 10 scale of abdominal pain, document the number of bowel movements a day you're having, and any other symptoms, and any potential side effects you think you may be having from your medications.

I think it's critically important, especially when something is changing with your Crohn's, to bring someone with you you trust. Doctors try to do a good job in explaining things, but there are many concepts that are going over, and it can be very helpful to have another person there to take notes and help you remember everything that happened in that 15, 30 or 45 minute office visit.

When you're going to the doctor for the first time and you're establishing care with a new doctor, it is very important to map out a timeline. When were you diagnosed, what were your symptoms, what treatment was tried, did it help you, did you feel worse, what did you try next, and so on and so on. When were you hospitalized, where were you hospitalized, did you have surgery, what was done. These are all critically important. And if you can sit down a night or two before the visit and map that all out on a piece of paper to help gather your thoughts, it can be very important and make that first visit much more meaningful.

The CCFA has a number of tools to help you track symptoms. On this slide you'll see mention of GI Buddy. That can be a very helpful app that you can download onto your device to help you track your symptoms. And it can help – these type of things can help keep you relaxed while you're waiting for your next visit.

So this leads us to our fourth poll question. "How comfortable do you feel discussing concerns about managing Crohn's disease with your doctor? A, very comfortable; B, comfortable; C, somewhat comfortable; or D, not comfortable at all."

So the majority of you say you feel very comfortable talking to your doctor about your concerns about managing Crohn's, and that's good.

What questions do you want to ask your doctor? The CCFA has a discussion guide that you can use to help you, but some things you might want to consider, and this will help you as you transition to

DR. RAYMOND CROSS:

another doctor as well, is what parts of your intestine are affected. Perhaps more importantly, what treatment plan is suitable for you. You can ask about probiotics. It's important when you're starting new drug therapy to inquire about potential side effects, so you're not blind-sided by them. It's another important question to ask how soon you should feel better, so you need to know what to expect, both good and bad from your therapy. It's important to ask about changes in your diet or any supplements before making changes or taking supplements. It's a good question about activity restriction, about work restriction. And then how often do you need follow up, not just for colonoscopy, just when do you need to be followed up in the office visit, how often do you need to have labs, how often do you need to have imaging or colonoscopy. Those are all important questions to ask.

So my final slide before I turn it back to James, the key points of Crohn's. Crohn's is an inflammatory condition of the GI tract with patchy or discontinuous inflammation and in severe patients it can involve the full thickness of the intestinal wall. Importantly, symptoms and prognosis differ for each person. So just because one person had the worst symptoms and worst prognosis doesn't mean that that's going to be the same for you. It's important to know the goals of the individual treatment strategy. So for example, the steroids you're giving me are going to get me into remission and then the azathioprine is going to help me come off of steroids and keep me in remission. So it's very important to have clear goals for each aspect and each phase of your treatment. It's important you talk to your doctor about how you're going to be monitoring and what monitoring is going to entail. Is it going to be just symptoms, is it going to be blood work, is it going to be scopes or is it going to be all three? Prepare for your visits. Be prepared. Make sure you write down your questions, make sure you have the information that your doctor is going to need. Bring someone with you when you're making changes in treatment to help you remember all aspects of the visit. And it's very important, this is a chronic illness and if you find a good provider, you're probably going to have a relationship with that person for years. It's very important that you can talk to him or her about your symptoms, about over-the-counter medications, about complementary medication, about goals that are important to you. So it's very important that your communication is open.

And with that I'm going to turn it over to James.

JAMES TESTAVERDE:

Thank you, Dr. Cross, for that informative presentation.

Now it's time for the question and answer part of our program. So for everyone's benefit, please keep your questions general, in other words, without personal details, so that Dr. Cross can provide an answer that will be helpful for everyone listening. And in the interest of time, I would also like to ask that you keep the questions related to the topic. You're always welcome to contact CCFA's Help Center if you have other questions.

So, Operator, can you please give instructions to the telephone and webcast audience for submitting questions?

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.

JAMES TESTAVERDE:

Thank you. So while people queue up, we'll take some first few questions from our webcast audience. So, Dr. Cross, first question is about surgery. How common is it for someone who has had surgery, for their disease or Crohn's disease to come back?

DR. RAYMOND CROSS:

So old studies from the 1990s have shown that about 70% of patients are going to require at least one surgery. And then about a third of patients are going to require two or more. So a third of patients are going to require two or more surgeries. In patients who have had surgery, the Crohn's disease comes back endoscopically in about 70 to 80% of patients within a year. About 50% of patients have symptoms five years after surgery. And about 20% of patients have had surgery again eight years after that initial surgery. And that's without treatment. So that's untreated without any medications onboard.

OPERATOR:

If you'd like to submit a live question, it is star-1. And our next question comes from Joyce in California. Joyce, please state your question.

JOYCE:

Hi. My daughter had the endoscopy and she had the colonoscopy and the biopsies and the diagnosis was possible Crohn's. So how does she really know that it is before going on all the medications? Like she does have stomach is bothering her, she does have pain. But there are other things that could be causing that. And, you know, no one seems to help. Somebody looked at the biopsy and they said that it might be Crohn's and she really doesn't know what to do.

DR. RAYMOND CROSS:

So sometimes it can be confusing. Usually patients with Crohn's have had symptoms for months, sometimes for years before they come to medical attention or before they have a diagnosis. In patients whose symptoms are more abrupt in onset, it can be difficult to figure out whether the symptoms are from an infection. We talked about nonsteroidals like aspirin, Motrin®, Naprosyn®, Aleve®, those type things can sometimes confuse us and look like Crohn's. So we do the endoscopic work-up, we do the imaging, we do the biopsies, and we're looking for specific changes on the biopsies to help us

DR. RAYMOND CROSS:

confirm the diagnosis. In some cases we don't see that. And so the diagnosis will be unclear. If that occurs, often we'll see what happens over time. And maybe we'll provide supportive care, maybe we'll provide the more milder treatments that have less side effects and then we'll reevaluate. If it's Crohn's disease, those changes we look for on biopsy should evolve over time and we should be able to then confirm the diagnosis.

JAMES TESTAVERDE:

Thank you.

We'll take another webcast question. So the next question has to do with cancer. And if you could talk a little bit about cancer as it relates to treatments and then cancer as it relates to having the disease for a long time.

DR. RAYMOND CROSS:

So let's start with the disease itself. So we talked about colon cancer. So if patients have – Crohn's patients that have involvement of more than a third of their colon have an increased risk of colon cancer. And I think a good number to remember is once you've had the illness, once you've had colitis for 30 years, your risk of colon cancer is about 7 or 8%. Your risk, if you don't have Crohn's colitis, is about 4%. So your risk is doubled, but the absolute chance of you getting colon cancer is low. You're also – patients with Crohn's are also at increased risk, men with Crohn's are an increased risk for lymphoma, and there's an increased risk of small bowel cancer, which is very rare, but the risk is increased in patients with Crohn's.

Now as far as risk specific to therapy, patients who take azathioprine and 6-MP have a higher risk of lymphoma or blood cell cancer. Depending on your gender and if you're on anything other than 6-MP or azathioprine, let's just say that the risk is about 1 in 1,000. Patients also have a higher risk of non-melanoma skin cancer, especially as they get older. Patients that are on the anti-TNF agents such as Remicade®, Humira® and Cimzia®, have a higher risk of lymphoma – of melanoma, excuse me, melanoma, but we don't think that those drugs in and of themselves increase the risk of lymphoma unless they're combined with the immune suppressants. The newer biologic drugs, Tysabri® and Entyvio™, the early trials haven't shown an increased risk of cancer, but these drugs are newer and we need more long-term data before we can conclusively say they're not associated with risk of cancer.

JAMES TESTAVERDE:

Great, thank you.

Next question has to do with steroids. What is considered a long period of time to be on steroids?

DR. RAYMOND CROSS:

It's a good question, James. I think that, you know, it's very reasonable to start steroids and once you've achieved remission and I usually tell my patients three straight days without symptoms, your doctor should start tapering, and usually within a couple of months you should be off of the steroids. If you're still on steroids after a couple of months, if you're having trouble tapering because you get recurrent symptoms or if you taper off and the symptoms come right back, that's an indicator that you need something else. And the something else would be azathioprine, 6-MP, methotrexate or one of the biologic drugs to facilitate coming off of the steroids.

JAMES TESTAVERDE:

Thank you. Operator, could we have another question from the telephone?

OPERATOR:

Our next question comes from Charles in Michigan. Charles, please state your question.

CHARLES:

Hi. I was wondering if there is any connection between flare-ups and someone who has Crohn's disease who drinks cow's milk? Is there any information that the doctor has about that?

DR. RAYMOND CROSS:

Well, no. Generally speaking, if you're drinking pasteurized milk there's not a flare that I'm aware of, there's not an association that I'm aware of between drinking cow's milk and a flare. Patients with Crohn's can be lactose-intolerant like any other patient and lactose intolerance patients can have bloating, gas and loose stools. Oftentimes when patients are flaring, if they drink milk products they might feel worse until the flare is under control.

If you're talking about drinking unpasteurized or raw milk, that in fact can be quite dangerous in patients that are in immune suppression. There is a bacterial infection called Listeria or listeriosis that's associated with drinking unpasteurized or raw milk, and that can be a lethal infection. So if you're on immune suppressants, steroids or the biologic agents, you absolutely should not be drinking raw or unpasteurized milk.

JAMES TESTAVERDE:

Great, thank you. I believe we have time for one or two more questions.

The next question, you mentioned monitoring for early relapse. Is there an amount of time remission typically lasts?

DR. RAYMOND CROSS:

Not in particular. I have patients that have had one flare and never had a relapse again and there are some remissions that are very short-lived. I think the take-home message is that when we find the right medication for you, we can put you in a prolonged remission without flares. And that would be expected to last for years.

JAMES TESTAVERDE:

Great, thank you. One more question. Could you discuss combination therapy? Could adding something like an immunomodulator to a biologic help boost my response?

DR. RAYMOND CROSS:

Absolutely. So there are two good studies, one done in Crohn's disease and one done in ulcerative colitis, showing that newly diagnosed patients with Crohn's or colitis, if we give you a combination of a biologic and an immune suppressant like azathioprine, that we achieve better results.

Now in the long term, there's some consequence to that. There is a higher risk of infection, a higher risk of unusual infection, there is probably a higher risk of some cancers like lymphomas and skin cancers, and it's also more costly. And it can be more inconvenient to the patient. So it's not necessarily appropriate for every patient that we do combination therapy.

Why does combination therapy work? There are two theories and I'll give you mine. One theory is that the two drugs may work in synergy, so one part of your disease may respond to the biologic and one part responds to the immune suppressant. So that's synergy. The other idea is that the immune suppressants can raise the drug levels of the biologics and prevent antibodies from forming, which makes the response more durable and more vigorous. My thought is it's probably a little of both. And some patients do need two drugs and some patients that start on one can do better by adding a second drug to their treatment.

JAMES TESTAVERDE:

Great, thanks. One more question. It has to do with extraintestinal manifestations. Could you talk a little bit more specifically about arthritis and what to do to treat it?

DR. RAYMOND CROSS:

Yeah, so the most common – so when we talk about arthritis, the most common form that patients experience is achy joints when their Crohn's is active. When we treat the Crohn's the achy joints go away.

The other form is arthritis involving typically one or a few joints, often a large joint in the body like the knee. And that typically will become active when the Crohn's is active. Again, if you treat it, the arthritis gets better.

DR. RAYMOND CROSS:

There's another type of arthritis that will involve multiple joints, often small joints in the hands, and it can be confused with rheumatoid arthritis. The challenging thing about that is it can happen before you're diagnosed, it can happen when your bowel symptoms are inactive, and it can even happen in patients who've had removal of the colon. So it can be hard to figure out and we often rely on a rheumatologist or our joint doctors to help us diagnose that better.

And then lastly there's a form of spinal arthritis that can develop that can affect the spine or basically the joints that connect your hips to your pelvis, called the SI joints. And those typically, they may not be active when your bowel symptoms are active, they typically present with significant morning stiffness and pain that improve with activity, whereas degenerative arthritis typically will get worse during the day and it's better with rest. And these occur in maybe 5 to 10% of patients and if you're just looking at joint ache, it can occur in over 25% of patients with Crohn's disease.

JAMES TESTAVERDE:

Great. Thank you, Dr. Cross, for your presentation and for answering tonight's questions. So we will close the Q&A session here.

Before we review some helpful resources, I wanted to remind the audience of two things. First, the recording of today's webcast will be placed on CCFA's website next month. And you will receive an update via email once that is made available. And second, upon exiting today's webcast, again you will be prompted to complete a brief program survey and we ask that you please take a few moments to provide your responses as your feedback is extremely important to us.

Now I would like to take a few minutes to review some available IBD resources.

So the American Gastroenterological Association offers a wealth of information on IBD. From the AGA website you can access their Patient Center. And from the Patient Center you can access informative patient guides covering various topics from GI procedures to diets to medications. And to access these valuable resources, simply visit www.gastro.org or visit the links shown on the slide.

The Crohn's & Colitis Foundation of America is also here to help. CCFA's IBD Help Center is a free service designed to provide members of the IBD community with disease-specific information, guidance and support. It is open Monday through Friday, 9 AM to 5 PM Eastern Standard Time, and can be reached via telephone at 888-694-8872, via email at info@ccfa.org or via live chat from our website at www.ccfa.org.

If you would like to watch previously recorded webcasts or register for an upcoming webcast, you can also visit www.ccfa.org/resources/webcasts.

JAMES TESTAVERDE:

CCFA also offers several opportunities to connect with other IBD patients. Through our Community website you can participate in discussion forums, read or share personal stories and access our online support group. And by visiting your local chapter home page, you can join the local support group, participate in the Power of Two peer mentor program, or learn about upcoming education programs. And to access your chapter's home page, simply visit www.ccfa.org/chapters.

And as Dr. Cross mentioned before, GI Buddy is CCFA's online disease management tool that allows you to keep track of your IBD from your computer or a mobile device. And to access the GI Buddy app, you can visit [www.ccfa.org/GI Buddy](http://www.ccfa.org/GI+Buddy).

CCFA Partners is an online registry of over 14,000 adult and pediatric IBD patients from across the country. And by enrolling in this program, you have the opportunity to play a key role in helping the IBD community better understand these diseases as well as inform the direction of IBD education, as well as IBD research. So to learn how you can get involved, simply visit www.CCFAPartners.org.

And if you're looking for other ways to get involved with CCFA, you can join a local Take Steps walk or train for a Team Challenge event. So these fun, family-friendly events help raise mission-critical funds as well as awareness of IBD. And to find out more, visit www.CCTakeSteps.org or www.CCTeamChallenge.org.

At this time, CCFA would like to extend a special thank-you to the American Gastroenterological Association for cosponsoring this program, and we would also like to thank Abbvie, Janssen Biotech, Inc., administered by Janssen Scientific Affairs, and Takeda, for their support of this program.

We hope you will join us on October 30th for our webcast and teleconference on biologic therapy, and to register for that program simply go to www.ccfa.org/resources/webcasts.

And on behalf of the Crohn's & Colitis Foundation of America, thank you for joining us.

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