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Clinical Conversations: IBD aims to provide healthcare professionals with practical information on implementing evidence-based, guidelines-recommended care for patients.

**In this podcast, we'll hear from internist Dr. Doron Schneider, Chief Patient Safety and Quality Officer for Abington Health, and gastroenterologist Dr. Sunanda Kane, Professor of Medicine at the Mayo Clinic.**

**DORON:** So, good morning. I'm here, Doron Schneider with Susie Kane from the Mayo talking about inflammatory bowel disease. Good morning, Susie, how are you?

**SUSIE:** Good morning, Doron. How are you?

**DORON:** I'm well. We're going to jump right into this. We have a patient who has inflammatory bowel disease and for this conversation, we'll focus on the patients with Crohn's. They've been started down the road of treatment. As we reviewed in the last podcast, there are multiple different classes of medicines that patients have. Depending on the disease state, severity of the disease, the GI physician will select from those agents. And then it becomes really a partnership with the GI doc to ensure that we are thinking holistically about that patient's health over time, over years. As we know this disease strikes many young people who have decades of life in front of them. So let's just spend a few minutes just walking through how we think about that and how we can both play a vital role in thinking about that patient. Sound good?

**SUSIE:** Yes, I love the fact that you use the word holistic. I think the patient sometimes can get lost in the shuffle and that we can get so granular that really it is about treating the whole patient over an extended amount of time and that we partner to understand the preventable, you know, diseases that can often get lost in the shuffle and some that are being mitigated or that put our patients at an increased risk because of the treatments and because of the disease itself. So, I love that holistic approach.

**DORON:** Perfect. Let's just jump right in. So, I think what we did talk about again in the last podcast, we'll maybe put it in a box for now, is the idea of the sort of monitoring for drug toxicity, and based on the agent, we may need to do some routine monitoring of CBC, LFTs, CMP, just to make sure that the patient's not having side effects, right?

**SUSIE:** Right.

**DORON:** So if we put that in a box and then just focus on some of the other effects agents may have that are not straightforward side effects that need to be monitored like that, perhaps we shouldn't start with the idea of vaccines, right?

**SUSIE:** Right.

**DORON:** Help us think through, you know, the co-management that's required on vaccines, which should be – again I'm a primary care internist and I should feel very comfortable in that space, but there are some nuances that the IBD patient or the patient with IBD brings to the table. Help us think through what do we need to do. What do we need to know about immunizations?

**SUSIE:** As you know, and I know I don't have to tell you this, you're going to know this better than I, that there are immunizations that are age specific or age appropriate. There are ones that you give and then you do booster dosing throughout their life and then there are vaccines that can be stratified by whether they are a live viruses or attenuated. And so, those are the kind of issues that come up when we have a patient who has Crohn's disease and we're thinking about starting an agent that is going to be long-term and is going to suppress the immune system. And again, usually, the mechanism of action is such that certain kinds of infections are going to be more prevalent and at higher risk. So, the viral ones and some of the mycobacterial ones as opposed to bacterial. So, you have been recommending to your patients

who are under 26, male and female, you know, HPV vaccines. Depending on their situation they're getting annual flu vaccines, that they've had pneumococcal and hepatitis B vaccinations. So, all of those things we can check titers for and then if I need to start an immunomodulator, I feel comfortable that they have onboard the appropriate vaccines to prevent those conditions. Does that sound about right?

**DORON:** Yeah, absolutely. This is a disease state that has many of the agents impacting immune status so attending to the vaccinations for status of patients, that is the bottom line as it should be for all patients, right? That's good primary care. We don't want to forget the basics here. I do want to call out that just like the landscape of options is emerging and changing for IBD, so are vaccines. Vaccines, the options to us are changing. So for example, varicella vaccinations is one that we now have recombinant options that are able to be taken by people who are on biologics and on immunomodulators. So, for those that are listening, the idea of focusing on immune status and increased risk should lead you to be very careful about ensuring full vaccination and attending to the new vaccines that are on the market.

Susie, can you help us? Certainly, you want to do that before you have patients on these agents—the different medications for IBD. How about if people are already on them and we see that there's a gap?

**SUSIE:** So, that's a really good question. That's a whole field of science right there. The CDC every year puts out its recommendations in the Annals of Internal Medicine. The definition for immune suppression is if you are on a biologic, if you are on prednisone at greater than 20 mg per day for longer than, I believe, three months, if you are on methotrexate greater than 15 mg weekly and then a thiopurine, so azathioprine or 6-MMP, that if you are on more than 2.5 ml per kilogram body weight. So, in theory, our IBD patients are chronically immunologically "suppressed" only if they are on long-term steroids, which they shouldn't be, and a biologic.

So, if a patient is on a thiopurine that is a dosage which we use to treat IBD, they are not considered at higher risk for immunological suppression and for the vaccine algorithm. So you should feel comfortable that if the patient is age appropriate for whatever vaccine, that you don't have to worry about it at all. You know, so certainly, the PNEUMOVAX, if they're due for PNEUMOVAX, that shouldn't be a problem. If they need the herpes zoster, you can give that. And now, like you said, the new formulations are such that it's not an issue at all and that's been taken off the table.

**DORON:** Perfect. So, that's vaccines—a lot to know and a lot to say. Let's transition over to the fact that patients with IBD have increased cancer risk and some of these agents also, just by the nature of how they work, may increase cancer risk themselves. So what do we need to do in mitigating the risk of morbidly, mortality from cancer in these patients?

**SUSIE:** Right. So, when we talk about cancer, there are specific ones that we keep in mind. One is colon cancer if the colon is chronically inflamed. Interestingly, Crohn's patients are at increased risk for cancer in their small intestine, but it is so exceedingly rare that even if you increase the risk over rare it's still rare. So, we don't do any kind of monitoring or surveillance for small bowel cancer in Crohn's disease. So that's sort of off the table.

The ones that we worry about are lymphoma because you are interfering with normal function of the lymphocytes because that's the part of the immune system that we're dealing with. Anytime that you are interfering or intervening with normal function you can cause interference pathway that leads to cancer. So lymphoma is the big one and what are we talking about? We're talking about a four-fold increase in the risk of lymphoma with using either an immunomodulator or a biologic. And that sounds horrible, right? You tell your patients that they're four times more at risk. Let me put it, though, into absolute risk because relative risk is four times the normal. That's relative. But absolute risk, so the risk for lymphoma in the U.S. is 1 in 10,000. If you are on any of these agents, four times that means that the risk now is 4 in 10,000.

**DORON:** So really what you're saying is that we're not doing anything in addition to screen for lymphoma.

**SUSIE:** Correct. Exactly. Except emphasizing the point that this is still uncommon and that you certainly want to have your antenna up if you see that the patient starts to develop B systems—so unintentional weight loss, night sweats, fevers and the like—but that there's no surveillance or screening that we do. They're just at increased risk so it's worth the discussion and having our antenna up. But, certainly, skin cancers are the other big cancers that IBD patients are at risk for in the therapies that we use. So, we do recommend that if you feel comfortable as the primary doing a skin exam annually, that that occurs. I don't, so I will send the patient to the dermatologist. But that would be in discussion with the primary care provider how comfortable they feel. But skin cancer screening annually should occur. So, a skin exam and then we should

both be telling the patient wear sunscreen, wear long sleeves and don't sit out in the sun so much and so prolonged that you burn continually. Because it's really the sunburn history that ends up causing the most risk.

**DORON:** Perfect. So, we're looking at GI risk, specifically increased risk of colon cancer, lymphoma where there's no additional screening, just awareness and annual skin exams. Perfect.

So, let's transition then beyond the vaccines.

**SUSIE:** Doron, before we move on. For young women, actually, if you are on an immunomodulator and you are a young woman, there are data for an increased risk for cervical cancer. So, we do think it's important that women get annual PAP smears—not every third year if you've had a negative one. So, annual PAPs.

**DORON:** Very good, very helpful. And, of course, one of the things that people do from a lifestyle that increases the risk of cancer is smoking. And there is a lot of biology now that we're increasingly understanding between the effect of smoking and IBD. So, is there any lesson you can tell us about how to approach the patient who is smoking? That's something we should feel comfortable with as to how to guide people through smoking cessation. Is that even more important for the IBD patient?

**SUSIE:** You know, it's interesting that you say that. I think that smoking in and of itself is such an increased risk for cancer, but in the IBD patient it's not any higher than the non-IBD patient who's a smoker. We are also trained internists at heart as well as gastroenterologists, so it's a discussion about, for your overall health, why you shouldn't smoke cigarettes. From a Crohn's standpoint, tobacco makes Crohn's disease worse and so it's harder for me to do my job if you smoke. But the cancer risk around tobacco is the same discussion you would have. So again, it's nice emphasizing messaging that we're giving that patient.

**DORON:** Yes, I'm on the same page. Now, let's transition just for a moment to bone health. Of course, we're familiar with steroids, which increases the risk of osteoporosis. Beyond steroids is there anything else we need to be thinking about as it relates to some of the other classes? And what about doing early screening of bone density?

**SUSIE:** Right. So, actually, there are several different risk factors that Crohn's patients may have that advises a DEXA Scan well before menopause in a female, and age 65 in a male. So these folks are avoiding dairy products because it gives them increased symptoms so they're not getting enough calcium and vitamin D. They may feel poorly so they are not physically active, so they're losing bone health in that way. We already talked about the fact that Crohn's patients smoke more than the background population so smoking is a risk factor. Methotrexate also has its impact on bone health and then certain other dietary restrictions that are self-imposed, patients put themselves at risk for malnutrition and osteomalacia as well as osteopenia. So those are the other things we look for in order to consider their bone health. What's interesting is that the anti-TNF agents actually has been shown to improve bone health. Whether that has been improved through efficacy and mucosal healing versus that there are a secondary benefit and effector that we just can't explain yet in terms of the actual physiology of bone health that the anti-TNF is playing a role.

The other thing to remember too is that, at least the Europeans will say, the osteoporosis is actually an extraintestinal manifestation of IBD. So, it's not unreasonable to just go ahead and screen all of your patients with the DEXA scan after they get their diagnosis. I don't think that's unreasonable if it's non-invasive, relatively inexpensive and certainly, if you find osteopenia, it's reversible. So, I do tend to emphasize that to my patients.

**DORON:** Perfect. And for many patients, the burden of a chronic disease of any kind can be overwhelming and life-changing and that can have an impact on mental health. So, should we be screening for anxiety, depression in this population?

**SUSIE:** Absolutely. That's a really important point. You know, a patient who has confirmed healing on their x-rays, but still comes in and, you know, "Dr. Kane, I'm so tired. I just don't feel well. I've got pain." That patient could be depressed. They could have a completely normal CBC, completely normal CRP, but yet they are still sick. It is the under-diagnosed or undertreated depression that is driving their symptoms. So absolutely, every patient should get screened and no, of course, I'm not a mental health professional trained, but we have really effective screening tools which are just simple questions that are available online and different checklists for either IBD or well-being checklists in the internal medicine space that can help just screen patients and if they have a score that is above a certain threshold, then boy, you either have to broach that subject with the patient, you communicate that to their primary provider or you can decide that

you want to just go ahead and refer them on to a mental health professional. Or, there are some folks that feel very comfortable with prescribing an anxiolytic or an antidepressant. They are very well tolerated by the GI tract by the way. So, there isn't a contraindication to giving any of these therapies to an IBD patient. Interestingly, bupropion has some anti-TNF effect. I'd use that one as my anxiolytic of choice. It is good for pre-menstrual syndrome, it is great for smoking cessation and for depression and if there's a little bit of an anxiety component, and it might even treat their Crohn's disease as well.

**DORON:** What a wonderful pearl. Thank you so much. You alluded to the scale. I'll just mention the PHQ-2 as one of the standards. It doesn't matter what you use, but that's a validated one. So screen this population.

As we wrap up I just want to bring special attention to young women and the issue of pregnancy and what we need to do to be on the same page as it relates to how we handle questions regarding pregnancy in this disease state and with the different agents that people are on. What do we need to know in the primary care space?

**SUSIE:** Yes, thank you so much for asking that. You know, we forget that these patients have lives and interest in starting families. I think that one of the big pearls and takeaway messages here is that having Crohn's is not a contraindication to getting pregnant and carrying children. There may be times when it's inappropriate to be thinking about trying to get pregnant because the disease is not controlled, but just having that diagnosis in and of itself should not be an impediment or a barrier to thinking about fertility and pregnancy.

So having said that, a female patient who has Crohn's disease and has had an operation is at increased risk for infertility, and we believe that it's because of the scar tissue that can form in the abdomen and pelvis from that surgery as well that surgery is a marker for more aggressive, active disease, and because Crohn's is a transmural disease that in the abdomen and pelvic space in and of itself that there can be an inflammatory environment, a hostile environment, such that her eggs and ovaries don't work as well and that they're not as healthy. So in the Crohn's patient who has had surgery, fertility rates are lower. But if she gets pregnant, that she can carry to term, there is no increased risk for congenital anomalies or what we call birth defects. She will likely have a baby that is a little bit early and small for gestational age, but the good news is that once that baby is born, their APGAR scores are normal and they catch up really quickly with their peers in terms of weight gain and certainly there's no increased risk for neurologic dysfunction or pathology.

**DORON:** Wow. So, a lot to think about, a lot to remember for patients with IBD and in particular, with Crohn's, which was the focus this morning. I want to thank you Susie for that broad overview of how we can really think holistically together with the patient in the middle as their primary care doc and their GI physician looks to maintain a longitudinal therapeutic relationship over time to bring them the best of health, whether it's in the GI tract or outside of it.

So, with that, I'd like to conclude and thank you so much for your energies here this morning. Thank you.

**SUSIE:** Well, thank you.

**This has been Clinical Conversations: IBD.** This podcast was developed for the American Gastroenterological Association by Knighten Health and was supported by a medical education grant from Takeda Pharmaceuticals.