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Getting It Right: How to Manage Nutrient Deficiencies in IBD CME

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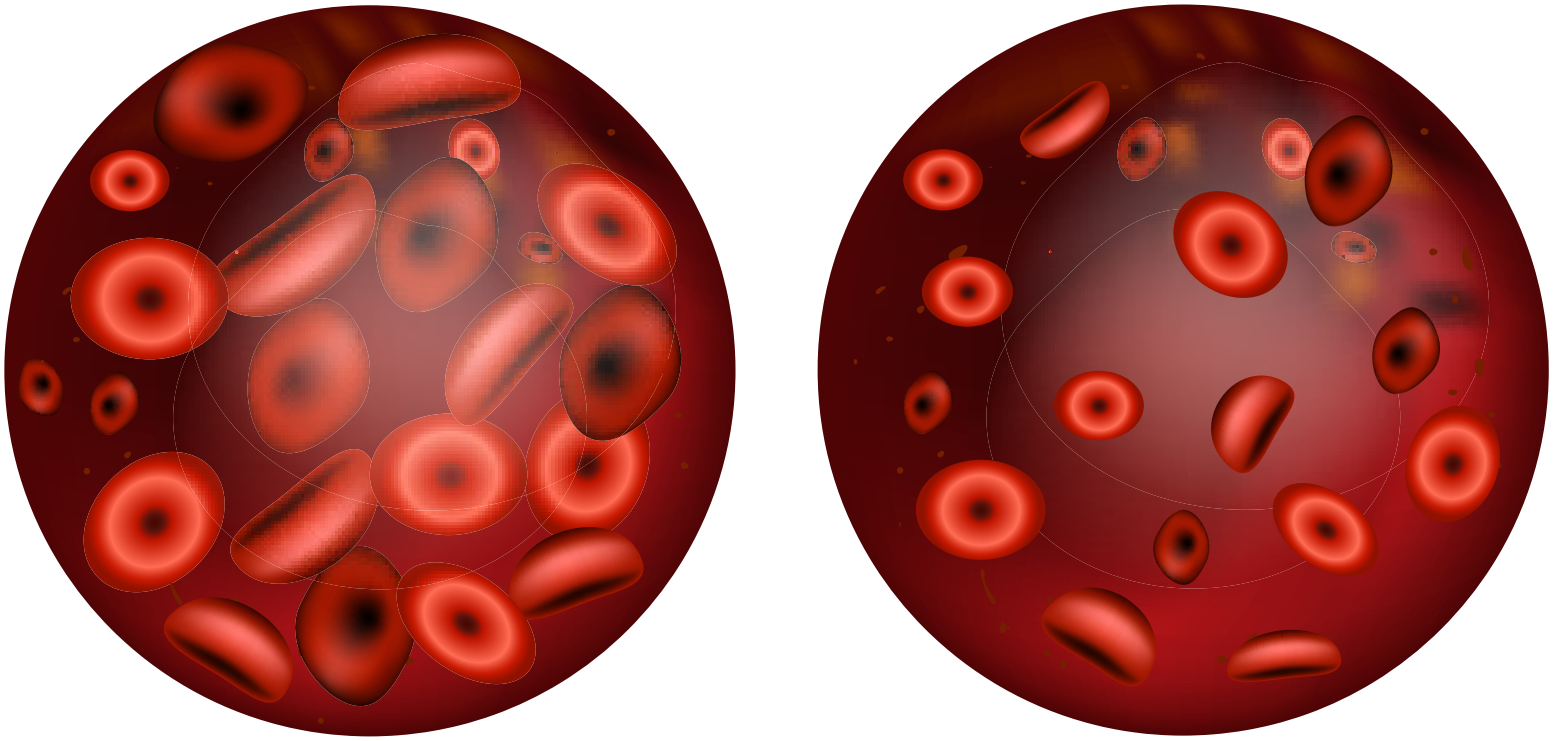

Normal

Anemia

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Target Audience
This activity is intended for gastroenterologists, nephrologists, and primary care physicians.

Goal
The goal of this activity is to increase clinicians' awareness of nutrient deficiencies in inflammatory bowel disease (IBD) and clinician's confidence in assessing and managing nutrient deficiencies in IBD, particularly iron deficiency anemia (IDA).

Learning Objectives
Upon completion of this activity, participants will:

Have increased knowledge regarding the
- Clinical data on intravenous iron preparations to guide treatment decisions

Have greater competence related to
- Implementing a team-based approach to assessing patients for common nutrient deficiencies in IBD
- Tailoring treatment options for IDA based on patient presentation and clinical data

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- Occasionally other additional software may be required such as PowerPoint or Adobe Acrobat Reader.

Disclosures

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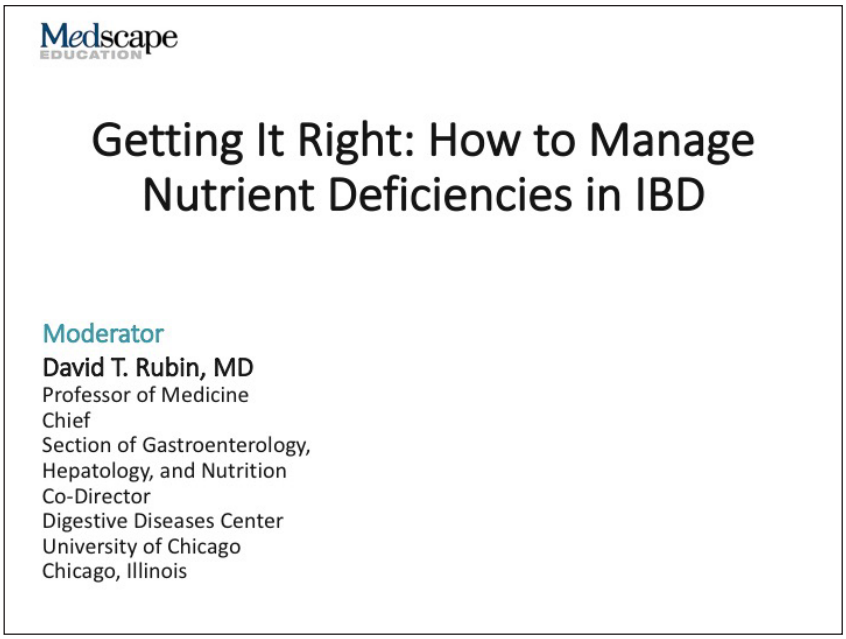


Getting It Right: How to Manage Nutrient Deficiencies in IBD

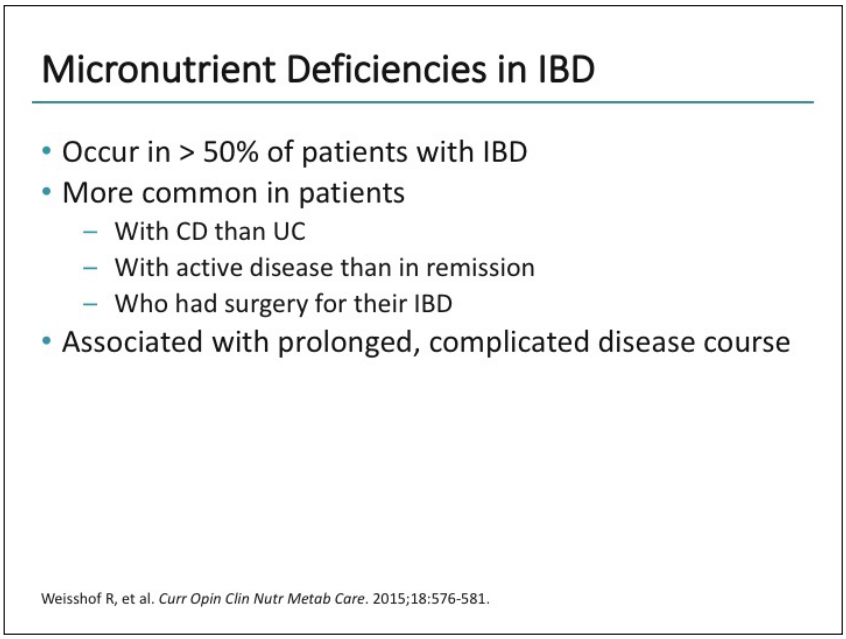
David T. Rubin, MD: Hello, I am Dr David Rubin, Professor of Medicine at the University of Chicago. Welcome to this program titled Getting it Right: How to Manage Nutrient Deficiencies in Inflammatory Bowel Disease.

Panelists

Dr Rubin: Joining me today at the American College of Gastroenterology meeting in Philadelphia is Jason Hou, Assistant Professor of Medicine and Research Director at the IBD Center at Baylor College of Medicine in Houston, Texas. Welcome, Jason.

Jason Ken Hou, MD, MS: Thanks.

Dr Rubin: Also joining me today is Raluca Vrabie, who is Assistant Professor of Clinical Medicine at the NYU Winthrop University Hospital in Mineola, New York. We are also joined by Kelly Issokson, Registered Dietician at Cedars Sinai Medical Center in Los Angeles. Welcome, Kelly. Welcome, Raluca. Welcome, Jason. We are very excited to have this conversation about a very important topic.

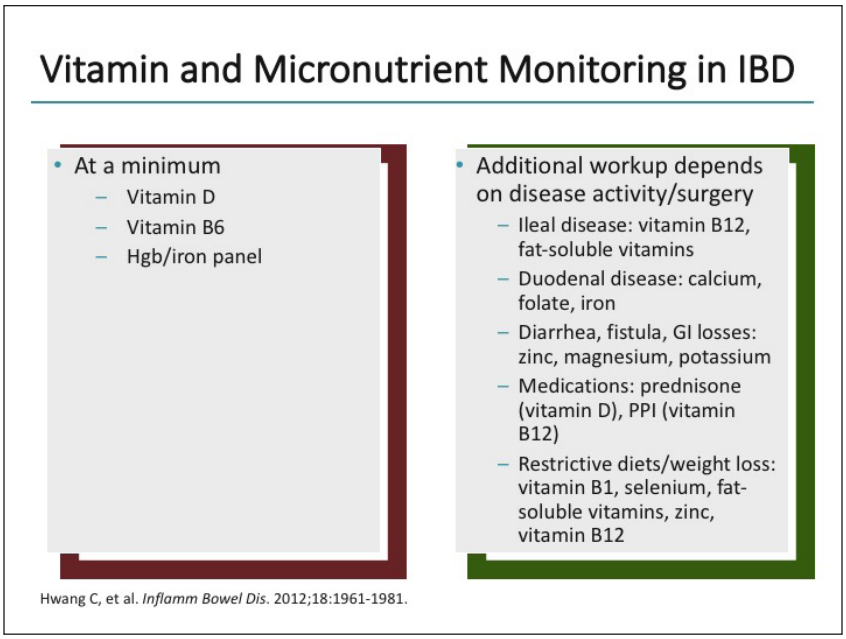


Micronutrient Deficiencies in IBD[1]

Dr Rubin: IBD is a complex disorder. It requires a lot of care, not only to manage the inflammatory condition of the intestines but, of course, we recognize that our patients have a variety of other issues. The one we are focusing on today has to do with nutrient deficiencies, which is really under-appreciated. As much as our colleagues know and understand that this can happen, we often find that these are issues that are left to the background or not addressed properly. I am excited to have a discussion with you today about some of these challenging issues.

Micronutrient deficiencies occur in more than half of the patients who have IBD. They are more common in patients with Crohn's disease than in ulcerative colitis. Not surprisingly, they are also more common in people who are actively inflamed or whose disease is not under good control.

We also see that these can be more common in people who have had surgery for their IBD, whether they have had a limited bowel resection or whether they have had a bowel resection with an ileostomy. Because of these challenges, we need to talk about how to approach these patients, when to know that these are issues, and then, very importantly, how to manage them. I am going to rely on my experts today to help us. Kelly, why don't you kick it off? Can you tell us a little bit about the general approach to understanding nutrient deficiencies in IBD patients?

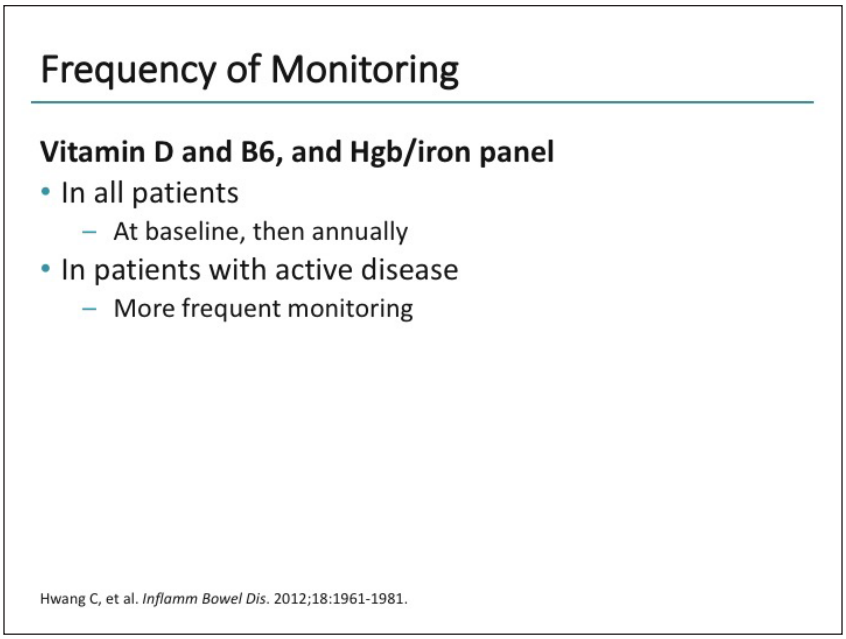


Vitamin and Micronutrient Monitoring in IBD[2]

Kelly Issokson, MS, RD, CNSC: At minimum, we should really be monitoring vitamin D, hemoglobin, an iron panel, as well as vitamin B6 in our IBD patients just because they are more at risk of developing those deficiencies. Additional nutritional workup will really depend on the clinical scenario.

For example, in our patients with terminal ileal disease, there is surgical resection of the ilium, we want to be more careful about monitoring vitamin B12 and fat-soluble vitamin deficiencies. In our patients on certain medications, such as proton pump inhibitor therapy, we want to look at B12 levels. In our patients who are on restricted diets or who have had significant weight loss, maybe a more comprehensive nutrition panel is warranted there, looking at nutrients such as selenium, magnesium, zinc, fat-soluble vitamins, and B12.

Dr Rubin: How often should we be checking all these? Is this an annual check in patients who are at risk, or is it specifically after surgery, or just 1 time when we first meet them? What are your recommendations in that regard?



Frequency of Monitoring[2]

Ms Issokson: For the vitamin D, B6, hemoglobin, and iron panel, we recommend baseline, as well as annual checking of those nutrients. If our patients have histories of deficiencies, we should really be monitoring them more closely, maybe every 3 or 6 months, or after we have given them repletion doses, just so that we can make sure those levels are back to normal range.

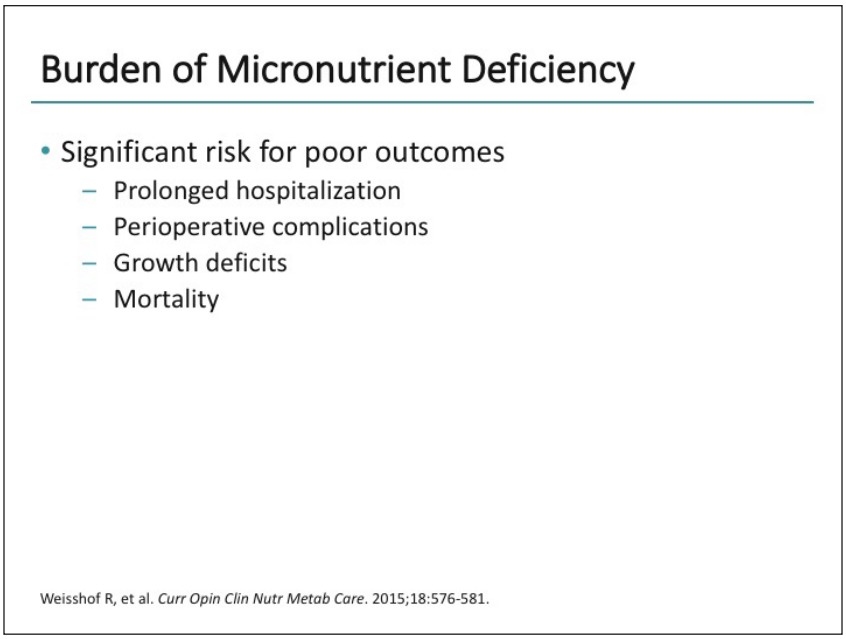
Dr Rubin: How long does it take for somebody to become B12 deficient after they have had their ileum resected?

Ms Issokson: It is a great question. It can take years, because vitamin B12 is stored in the liver, so patients can have normal levels even though they are malabsorbing B12. It is important that we continue to monitor that, as well as recommend sublingual therapy or intramuscular B12, or even nasal B12 administration in our patients with everything else.

Dr Rubin: Right. So if the B12 is normal initially, we should not be reassured that it may not go down over time in an at-risk patient.

Ms Issokson: Exactly.

Dr Rubin: Good, that is really helpful. Why do we not see more people evaluating all this? Why is this left to the background, or why is it not more emphasized by all of our management strategies and by our colleagues? What is going on out there?



Burden of Micronutrient Deficiency[1]

Ms Issokson: I think the role of nutrition can be underappreciated in IBD. A lot of practitioners do not realize the complications that are associated with vitamin deficiencies in IBD. Malnutrition or micronutrient deficiencies lead to poorer outcomes in IBD, such as prolonged hospitalization, increased perioperative complications, and growth deficits.

Between 15% and 40% of our patients are zinc deficient. A third to two-thirds of our patients are vitamin D deficient. B6 deficiency, again, is common in IBD. However, iron deficiency is considered to be one of the most prevalent global nutritional deficiencies.

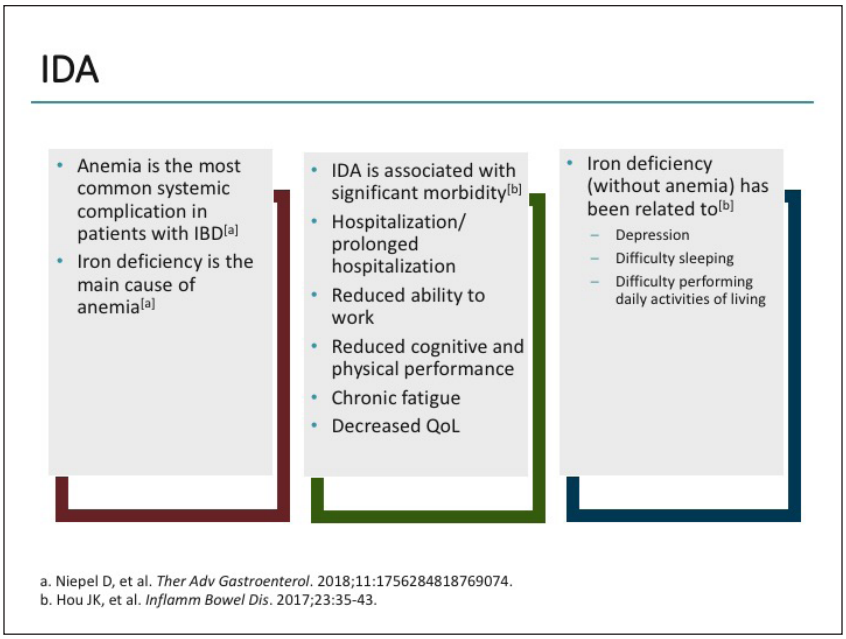
Dr Rubin: It is a bit ironic that we are missing nutritional deficiencies or not thinking about them as often as we should when, in fact, our patients are so focused, appropriately, on diet and understanding what they're taking in and how it may be driving their disease. How do you separate diet and nutrition when you are talking to patients or to our colleagues?

Ms Issokson: It is important to realize the distinction between the two. A diet really involves the foods that we eat, and nutrition is more the science of how that food works in our bodies. Some of our patients go on pretty restrictive diets, certain diets that are proposed to decrease inflammation in IBD or prevent recurrence of disease. And it is important that they realize that these restrictive diets can lead to malnutrition or nutrient deficiencies.

It is also important that we, as providers, open up those conversations with our patients, because they commonly go on these restrictive diets. We need to help them manage these diets in a nutritionally balanced way.

Dr Rubin: I think that is really important and emphasizes also the importance of a team approach in having a registered dietician and other members of your team who can work with the patient to educate them properly. Thank you for getting us started here.

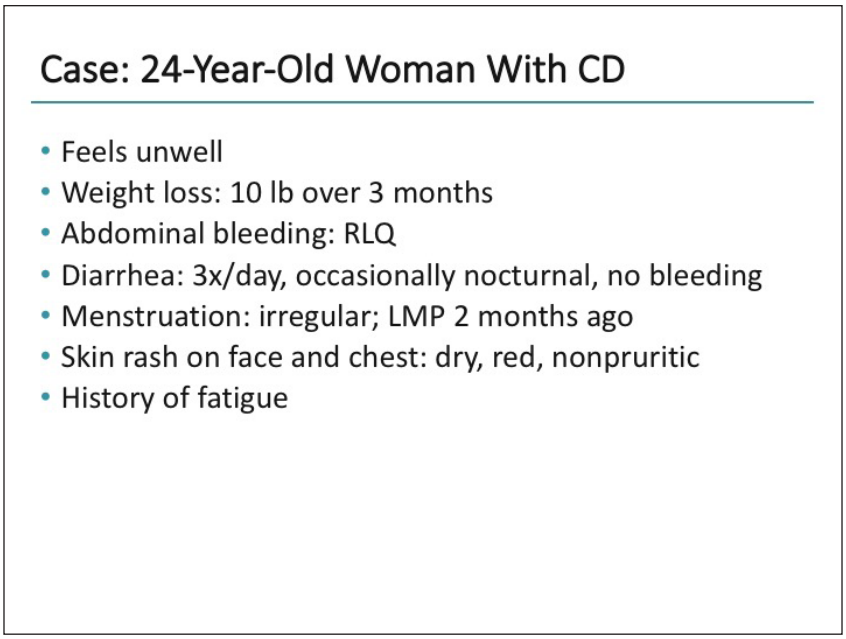
Let us talk a little bit about iron deficiency. Iron deficiency is common in IBD, and it is a challenge that we face. There are lots of questions when you get into the details of how to assess it, how to manage it, and we are going to have some of our colleagues help us understand that here today. In general, what should we know about iron deficiency from your side of things?



IDA[3,4]

Ms Issokson: In IBD, iron deficiency anemia, or IDA, is a common trigger for hospitalization or prolonged hospital stay. Further, iron deficiency itself without anemia is related to chronic fatigue and symptoms of depression, including difficulty sleeping and problems performing regular daily activities.

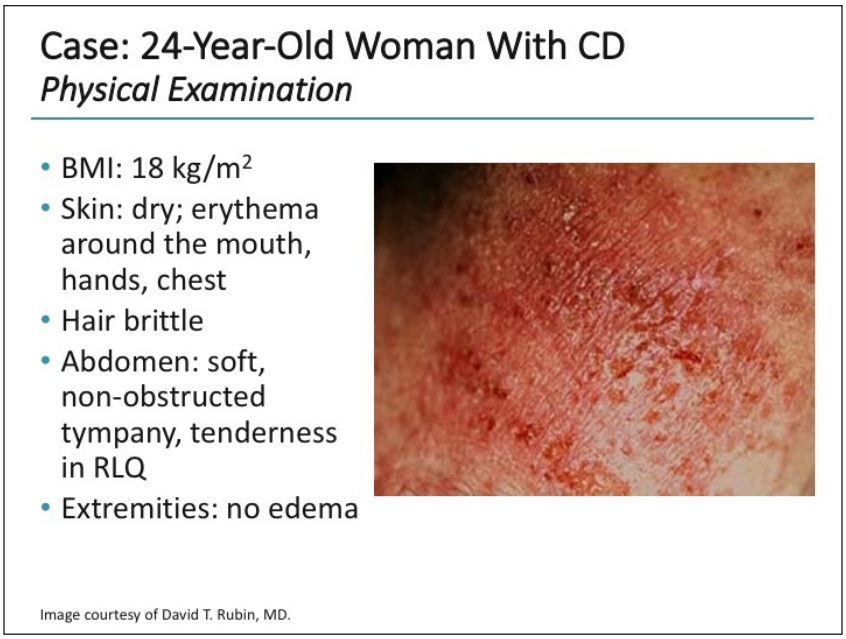
Dr Rubin: It is a big deal, and it happens more often than we may realize in some of our patients. Let me turn to some of my colleagues here and think about this. Put on your clinical hats, everybody. I am going to present a case from my own practice.



Case: 24-Year-Old Woman With CD

Dr Rubin: I recently saw a 24-year-old woman with Crohn's disease of the ileum and colon who had just moved to Chicago. She was not feeling well, and she wanted to establish care for her Crohn's disease at our center and came to see me. She had lost about 10 pounds in the last 3 months. She had been having a variety of abdominal systems and GI complaints, including right lower quadrant pain. She had noticed some bleeding. She had also been having bloating and discomfort.

She said that she was having up to 3 stools a day. There was a little bit of urgency. She was sometimes waking up from sleep with these symptoms. Also, her menses had become irregular. Her last menstrual period was 2 months ago, and she knew she was not pregnant. She noted a skin rash that had appeared on her face and chest, which was dry, and red, and not pruritic. She also felt quite fatigued, which of course is a common symptom and a very troubling one for our patients.



Case: 24-Year-Old Woman With CD: Physical Examination

Dr Rubin: On physical exam, she looked thin. Her BMI actually was calculated at 18. Her skin looked dry, and there was some erythema and eruption around her mouth, and also noted on her hands and chest. We have an image of it that you could all see. We noted separately that her hair seemed somewhat brittle, and she just did not look like she felt well.

On abdominal exam, her abdomen was soft and not obstructed, but there was mild tympany, most notably on the right side of the abdomen and some tenderness in the right lower quadrant without a mass. Her extremities revealed no edema.

Case: 24-Year-Old Woman With CD
Laboratory Results

Test	Value	Reference Values[a]
Hgb, g/dL	9.1	≥ 12[b]
Hct, %	28	35.5-44.9
MCV, fL/red cell	78	78.2-97.9
Ferritin, µg/L	8	11-307
Iron, µg/dL	22	35-145
TIBC, µg/dL	500	250-400
Albumin, g/dL	3.1	3.5-5
Vitamin D, ng/mL	18	20-50
Zinc, µg/dL	0.5	0.66-1.10

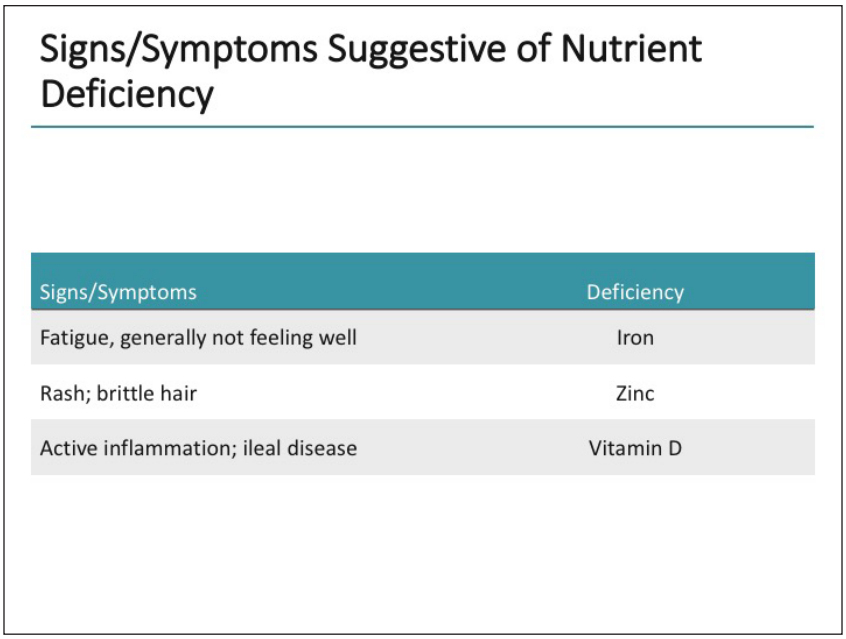
a. Mayo Clinic. 2018 Rochester handbook; b. WHO. 2017 nutritional anaemias.

Case: 24-Year-Old Woman With CD: Laboratory Results[5,6]

Dr Rubin: When we looked at some routine labs, importantly, her hemoglobin was 9.1. Her hematocrit was 28%, and her MCV was low, at 78. Her ferritin was 8. Her iron was 22. Her TIBC was 500. Importantly, select labs that I am sharing with you, her albumin was 3.1, which is low. Her vitamin D was 18, also low, and her zinc was 0.5, also low.

We have some labs that demonstrate a variety of challenges for this young woman. Obviously, we wanted to think carefully about what we might do. Let me turn to you now, Raluca, and ask you a couple of questions.

Are there some clues here in terms of the physical exam that point to nutrient deficiencies, or even in the history of this patient? What are you thinking?



Signs/Symptoms Suggestive of Nutrient Deficiency

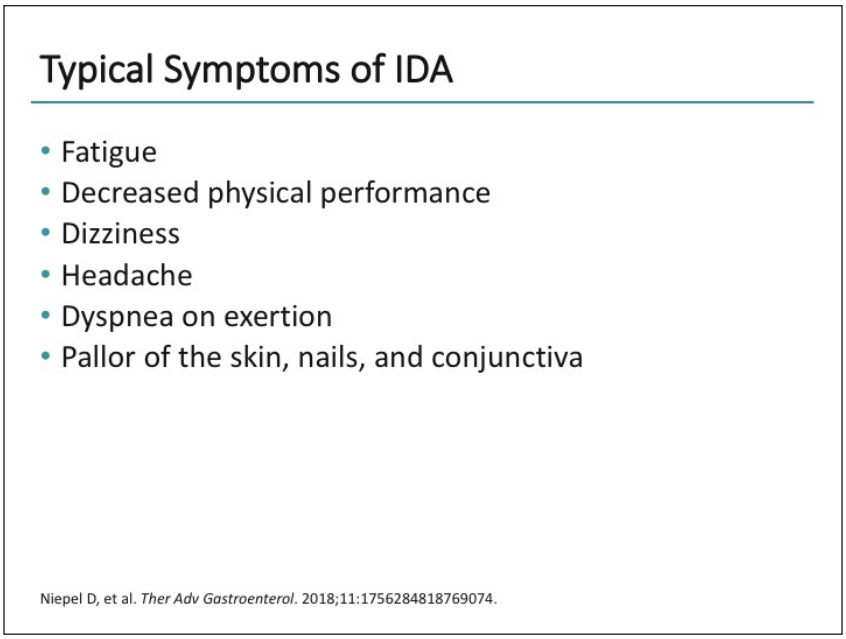
Raluca Vrabie, MD: Yes, so this patient is fatigued and generally not feeling well, which would go with iron deficiency. Additionally, she has this rash, which is concerning for perhaps zinc deficiency, and her hair is brittle. She has also some evidence of general malnutrition in her albumin, being 3.1. Perhaps some evidence of ongoing inflammation because her vitamin D level is low, which usually vitamin D is an anti-inflammatory vitamin. That goes also with her ileal disease, as vitamin D is absorbed in the terminal ileum.

Dr Rubin: We also see, sometimes, vitamin D that is low even in people with intact ileum and in ulcerative colitis patients, too. It is a fascinating problem that we have to understand a little bit more about. Kelly, why do you think she lost 10 pounds? What is going on here? What usually happens to patients who are losing weight with Crohn's disease?

Ms Issokson: In active inflammation, we see an increase in inflammatory cytokines, which can decrease or suppress appetite in our patients. That could be one reason why she has lost weight. Maybe she is eating less. She might be malabsorbing her nutrition as well due to her active disease, or she might have started a restrictive diet to help control her IBD. These are all certainly factors I would suss out when I am talking to my patient, to help to identify what could have led to that weight loss.

Dr Rubin: Yes, so consciously or subconsciously not eating as much because patients learn that it causes more symptoms. Being hypermetabolic because they are inflamed, so getting back to the cytokine issue, or putting themselves on a diet to try and manage the problem because somebody told them they might, or they just saw it on the internet, or they just thought it might work for them.

These are some challenges that we are facing here. Raluca, focusing on her iron deficiency, she has a low ferritin, a low iron, and her MCV is low; tell us a little more about that.



Typical Symptoms of IDA[3]

Dr Vrabie: Other typical symptoms of iron deficiency anemia could include decreased physical performance, dizziness, headaches, dyspnea on exertion, pallor of the skin, nails, and conjunctiva. My patients sometimes describe an inability to concentrate or brain fog, which might be related to this or to the disease itself.

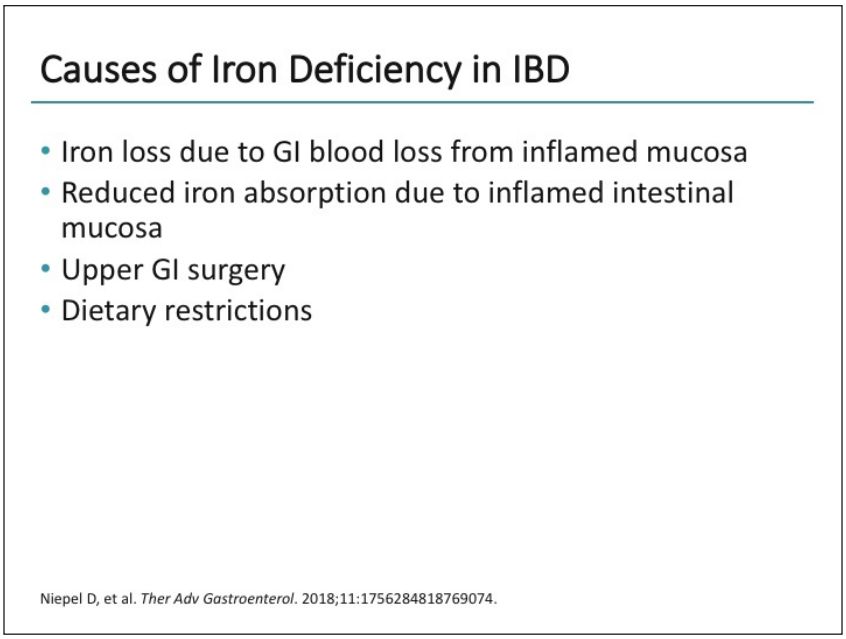
Dr Rubin: Brain fog is something that comes up a lot. It is hard to put our hands around. You hear about brain fog in your clinic?

Dr Hou: Yes, we hear that.

Dr Rubin: Do you ever feel brain fog?

Dr Hou: I have, yes, not uncommonly. Brain fog, I agree a lot with what Raluca was saying. The challenge with anemia is it can be very insidious. I think as clinicians, when we are talking with our patients who are sick and not feeling well, or we focus on the GI on their bowel symptoms, we sometimes lose the picture of their overall feeling because fatigue is very common. Many of us feel fatigue fairly commonly, as well. It is important that we recognize that could be a marker of something else going on.

Dr Rubin: Right. Obviously, these are nonspecific symptoms. There are many things that could be contributing to all this. We should not exclude the possibility that she has developed hypothyroidism, contributing to many of the same symptoms we are seeing here. Remember, we have to think clinically about the whole patient when we are evaluating these people. Getting back to iron deficiency, what are the reasons this young woman might have become iron deficient?

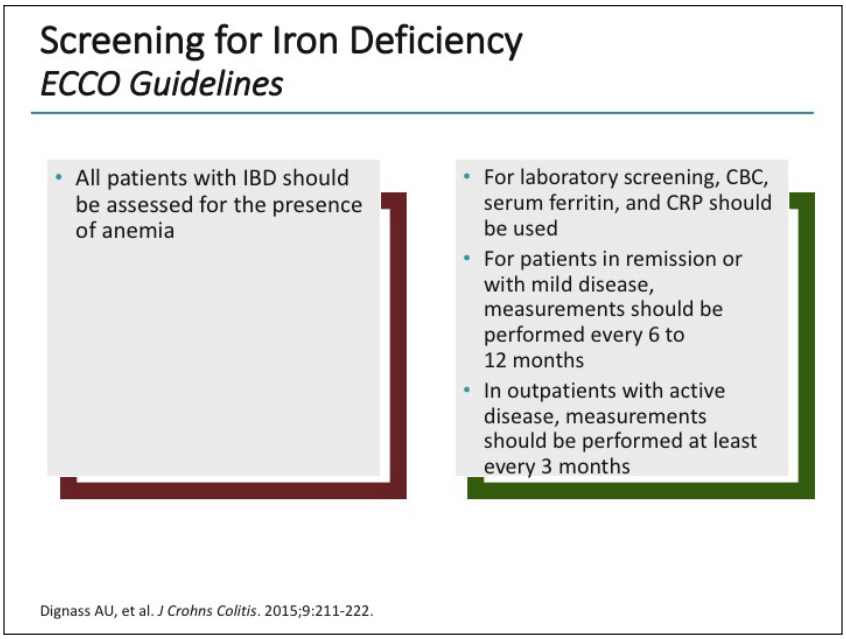


Causes of Iron Deficiency in IBD[3]

Dr Vrabie: The state of having inflammatory bowel disease sets you up for difficulties in terms of absorbing iron. Intestinal inflammation interferes with your ability to absorb iron. Additionally, there could be some compromise in your ability to have productive erythropoiesis during an active inflammatory state.

It is noteworthy here that she is not menstruating, so that is not part of the reason, but it is significant that she stopped menstruating because that might be a marker of a more generalized malnutrition problem that she is having, which could tie into her other anemia symptoms.

Dr Rubin: Sure, very important. In your practice, Raluca, tell me how you screen for iron deficiency? Do you get a ferritin with everybody when you see them in the clinic, or do you wait for the CBC to come back, rather than rely on the MCV? What are the things that you do?



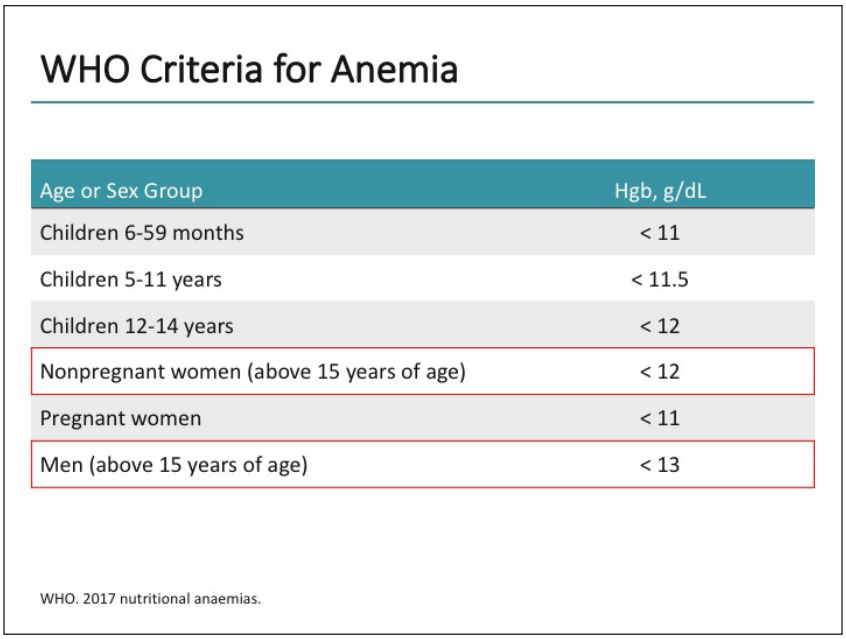
Screening for Iron Deficiency: ECCO Guidelines[7]

Dr Vrabie: I do actually get an iron profile along with a CBC on all my IBD patients. I do that even if I know that patient, and I know that they do not have a history of anemia. I will still separately get an iron profile every 3 to 6 months because, in my practice, I do find that repeating that iron is actually helpful in terms of symptom control.

Dr Rubin: Every 3 to 6 months, you are checking the iron panel. I presume that is in people who have previously had problems, or is that routine for all your follow-ups?

Dr Vrabie: In the patients who come every 3 to 6 months, and I am presuming that there is a reason they are coming as frequently as they are.

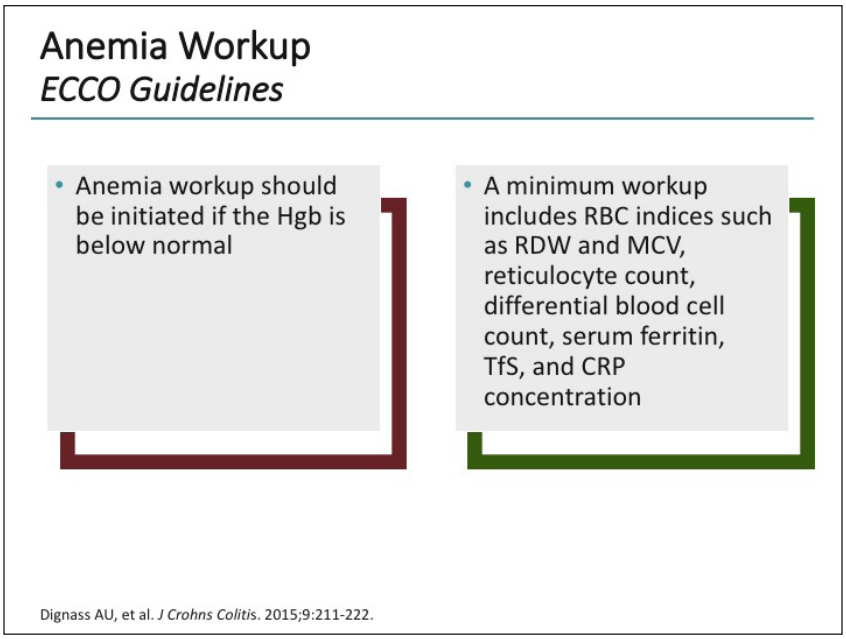
Dr Rubin: Right. So, certainly, stratifying that. What are the diagnostic criteria for diagnosing somebody with iron deficiency? What guides our colleagues?



WHO Criteria for Anemia[6]

Dr Vrabie: The World Health Organization has some criteria here. It is age and gender dependent. There is a hemoglobin cutoff of 11 in children under 5, 11.5 in children between 5 and 11, 12 in children between 12 and 14. Pregnant women, as we know, become anemic as part of that pregnancy course, so their cutoff is 11. Nonpregnant women over the age of 15, the cutoff is 12. Men over 15, the cutoff is 13.

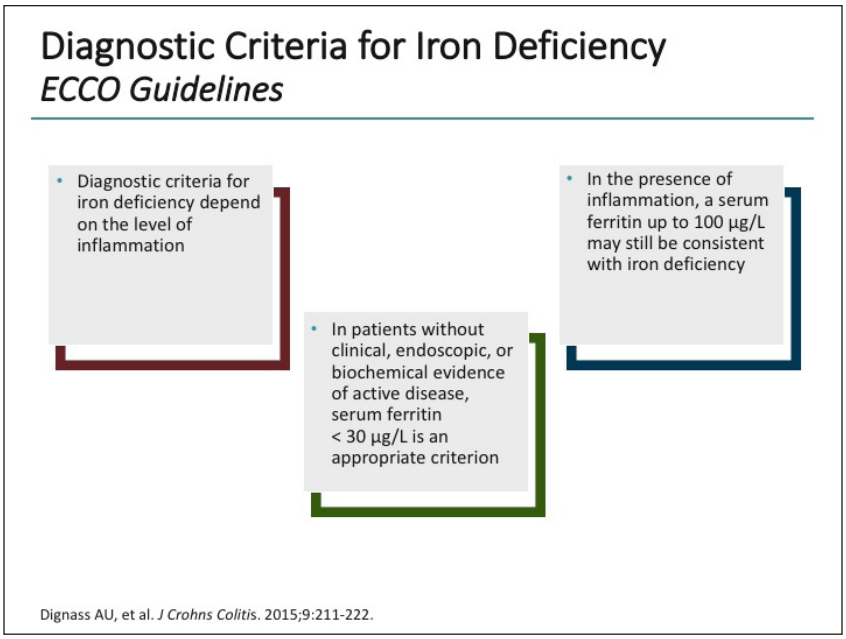
Dr Rubin: Okay, and then you look at other criteria as well, or it is just starting with the hemoglobin and then you work them up beyond that?



Anemia Workup: ECCO Guidelines[7]

Dr Vrabie: I check the iron studies along with the CBC. If I see an MCV that is low, if I see a ferritin that is low, if I see a TIBC that is elevated, sometimes it is just the markers of inflammation that I worry about. If the platelets go up or the CRP or the calprotectin, I start thinking perhaps there is more to this person's generalized fatigue than just fatigue. Perhaps I should look into their iron situation.

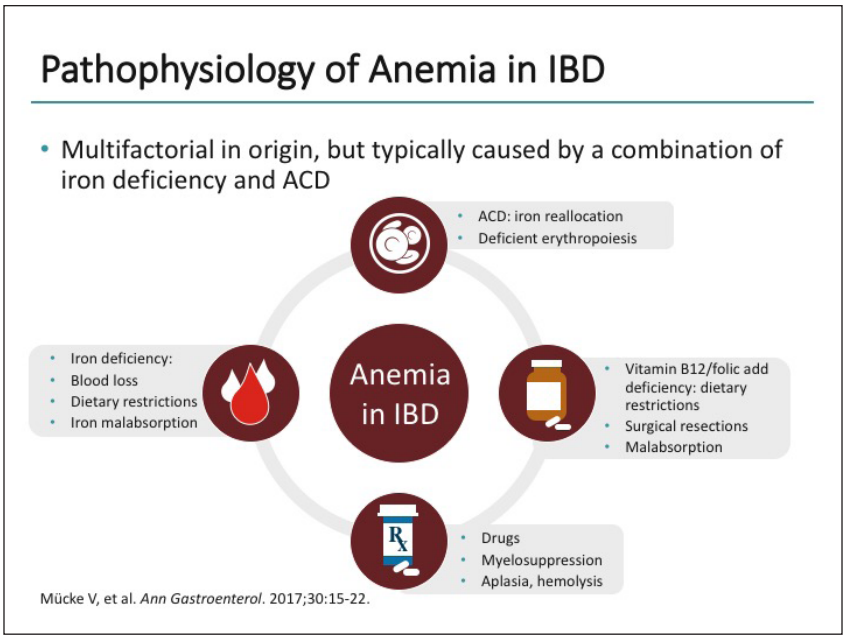
Dr Rubin: Sure. Now ferritin is interesting because it is also an acute phase reactant. We can see an elevated ferritin when people are inflamed. Does ferritin go up in the presence of iron deficiencies? Can we be fooled and have a falsely normal ferritin, Jason?



Diagnostic Criteria for Iron Deficiency: ECCO Guidelines[7]

Dr Hou: We can. This is a tricky situation because, I think, in med school, depending on where you train, you learn certain cutoff points. Some of our colleagues in hematology and other parts in general medicine use different cutoffs for our noninflamed patients. What I do in my practice with patients is I use a cutoff of 30 or lower of ferritin. It does not really matter, the rest of their indices. If their ferritin is less than 30, I consider that patient to be having low iron and may benefit from additional iron therapy.

Dr Rubin: Let us now focus a little bit more on this, the pathogenesis of anemia. Take us back to a little bit of medical school and remind us that all anemia is not iron deficiency. What else should we be thinking about here, Jason?



Pathophysiology of Anemia in IBD[8]

Dr Hou: Absolutely. We are talking about iron deficiency because it is the most common reason IBD patients are anemic. As you mentioned, we have to think of the whole patient. We have to think of all the other issues. The next most common reason for anemia in our IBD patients is anemia of chronic disease. That term is somewhat being changed over time. They are calling it anemia of mixed origin.

In general, the concept as you already referred to is that patients with IBD have inflammation. When you have your systemic inflammation, there is a reduction in your body's ability to absorb and incorporate iron properly. You may be consuming, orally, a significant amount of iron, but your body is not able to use it and incorporate it productively into hemoglobin. That is the other consideration that we think about.

In our IBD patients in particular, Kelly already mentioned some of the risk factors for anemia. We worry about B12 deficiency, primarily in patients with ileal disease or prior resection. We also do have to keep in mind certain medications can result in anemia. They can lower the blood count.

Dr Rubin: Patients may have multifactorial causes for anemia. That can confuse interpretation of some of the results. That is why, for example, an MCV that might look normal may in fact be a mixed picture where you have a B12 deficiency as well as iron deficiency, right? How do you make the diagnosis of anemia of chronic disease?

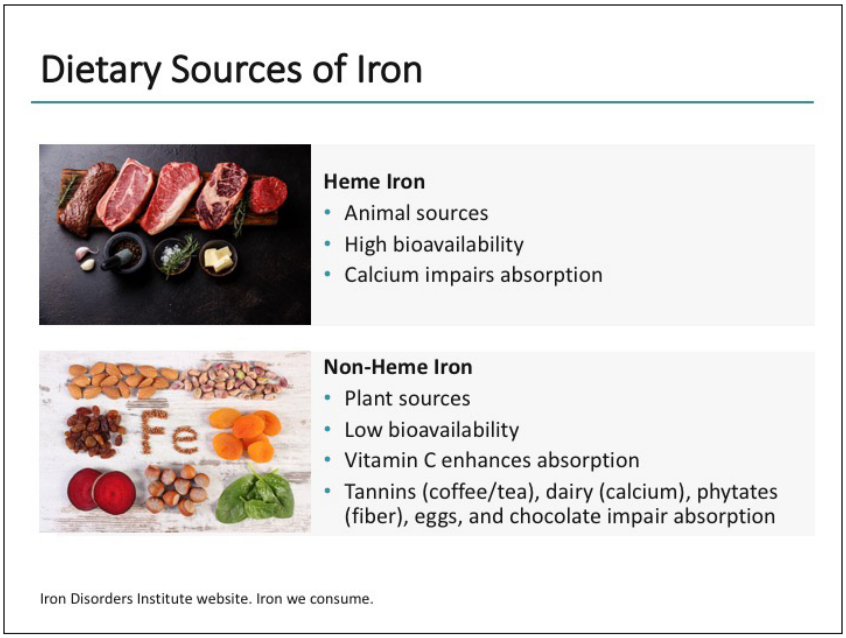
Dr Hou: Usually I look at that where patients have anemia, but their ferritin levels are above where I would consider that their iron stores are sufficient.

Dr Rubin: Do you ever check an EPO level, erythropoietin?

Dr Hou: In my practice, I do not because, honestly, I do not know how to act on that. When my patients are not responding like I expect them to, I usually would refer them to our hematology colleagues to help us out and look at some of those more nuanced components.

Dr Rubin: Right, so now let us shift gears to management. This patient we have seen has a low albumin. She has a low vitamin D. She has a low zinc, and she is iron deficient, as we have all discussed. There may be multifactorial contributors to all of this.

Kelly, teach us a little bit about what dietary recommendations we might make. Maybe, specifically, how can our patients get more iron in their food? How can they get more vitamin D and zinc in their food? How do we advise them in this regard?



Dietary Sources of Iron[9]

Ms Issokson: When we are talking about iron, there are 2 types of iron in the diet. We have heme iron, which has the highest bioavailability. That comes primarily from animal sources such as oysters, beef, and liver. Then there is non-heme iron, which has a slightly lower bioavailability. That comes from plant sources such as nuts, vegetables, and fortified grains.

In fact, in the United States, about 50% of our iron comes from fortified grain products.

Dr Rubin: Just to specify, fortified grain means that when you are buying a grain product, I presume you mean bread or other product, pasta. What kind of grains are you talking about?

Ms Issokson: It is breads, cereals, grains, pastas.

Dr Rubin: You want to read that it is fortified with iron on the label?

Ms Issokson: Exactly, yes. Vitamin C-rich foods can enhance the bioavailability of these non-heme sources. I encourage my patients to include maybe berries in their cereal or spinach with their beans or grains that they are eating with their meals so that they can absorb more of their iron from these plant sources.

Other components in vegetables and grain products, such as phytates and polyphenols, can decrease iron absorption. Usually, the effects of that are attenuated by a mixed diet.

Dr Rubin: Special considerations for people who are vegetarians or vegans, what do you tell them?

Ms Issokson: I encourage them to eat grains that are fortified with iron and include those vitamin C-enriched foods at their mealtimes. Sometimes, taking a multivitamin with iron is recommended, as well, if they do not have active disease.

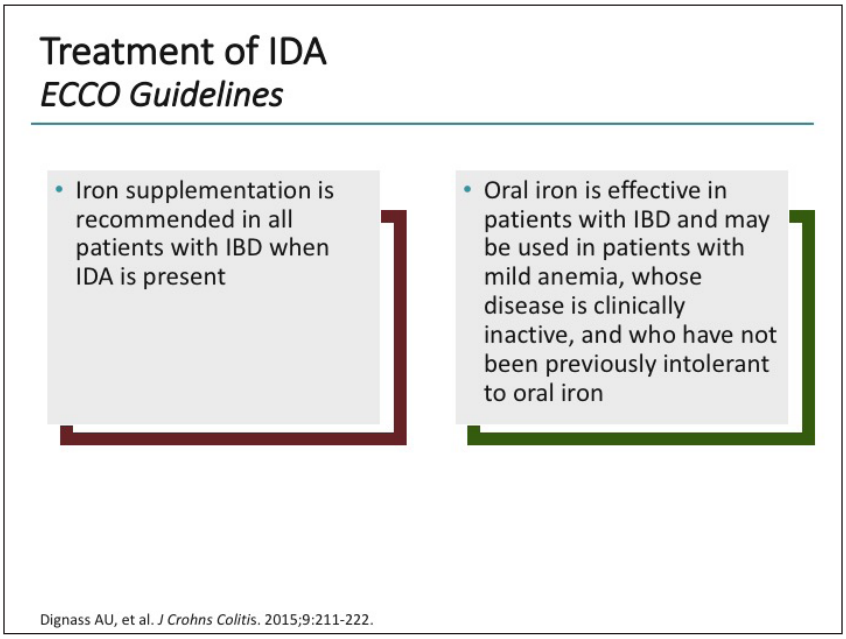
Dr Rubin: What about other things like vitamin D and zinc? Can we get some of that in our diet, or do we need to supplement?

Ms Issokson: It is really hard to get enough vitamin D in the diet, especially in our patients who can require up to 5000 units a day for just maintenance levels to keep their vitamin D in a normal range. To give you an example, a serving of fatty fish has about 400 IUs of vitamin D, so they would have to eat about 10 servings of fatty fish a day to get that need in. Most of my patients will need to supplement with vitamin D, but I do encourage the fatty fish and fortified dairy products. Then for zinc, whole grains are a good source, and then also taking a multivitamin with zinc can be helpful there.

Dr Rubin: Okay, very helpful. Some of my patients who take calcium as a supplement, it of course causes some GI side effects, sometimes, calcium combined with vitamin D. Sometimes it has magnesium in it. There are all sorts of things that can confuse how the patients are feeling.

One of the challenges we face, of course, is GI side effects with the supplements we want to use or the nutrition that we add to supplement them. That would include, of course, oral iron, which is one of our challenges.

Let us talk a little bit about how we can address the issue of treating iron deficiency. Maybe we can start with Jason and think about when do we use oral iron supplementation, and what should we know about that?



Treatment of IDA: ECCO Guidelines[7]

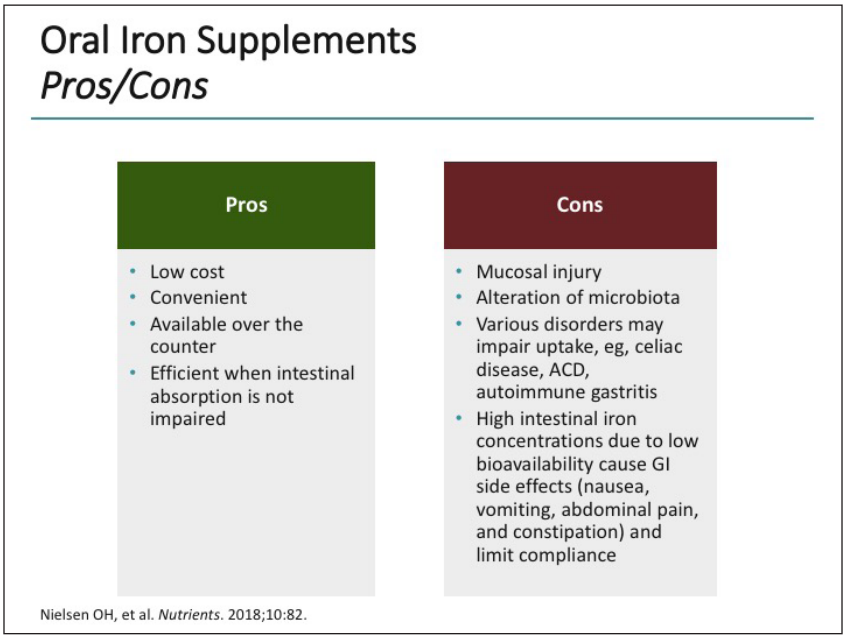
Dr Hou: Sure, oral iron is a good first approach in many patients. Oral iron is readily available. It is not expensive. They can get it over the counter or it can be given via prescription. Oral iron is easy for patients to take. I typically will offer that for patients who have maybe more mild aspects of iron deficiency, mild anemia, and, importantly, if they do not have any active inflammatory bowel disease.

As I mentioned earlier, systemic inflammation can reduce the bioavailability, the absorption, and incorporation of iron when it is taken orally. Patients who I know have active IBD, like the case you described, probably would not be a good candidate for oral iron supplementation.

Dr Rubin: What is the dose?

Dr Hou: Typically, your goal would be 30 to 100 mg of iron a day.

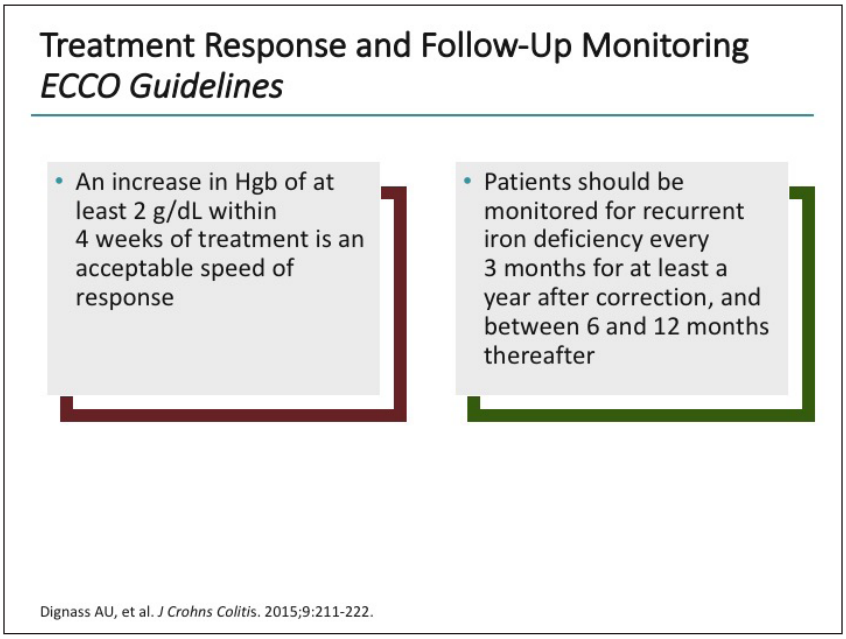
Dr Rubin: There are some pros to this. Obviously, it is available over the counter, less expensive. What are some of the reasons not to use oral iron?



Oral Iron Supplements: Pros/Cons[10]

Dr Hou: The 2 biggest reasons that I would not recommend oral iron are, as I mentioned, if they already have active IBD, they are unlikely to absorb enough iron to make a dent. The other reason, as you have already mentioned, is the side effects. They can have issues with GI upset and the patient, again, in the middle of an IBD flare, the last thing you want to do is give them more abdominal pain or nausea. It can also alter the color of their stool. Our patients in the middle of a flare are usually paying very close attention to their stool, so little changes can be actually very disturbing to them.

Dr Rubin: Right, so then how soon after you start any kind of oral iron supplement will you recheck or reevaluate to know if you are making progress? This is a question that comes up all the time. Do you just put them on oral iron and wait until their next visit in months and months, or should you do something in 6 weeks? What do you recommend?



Treatment Response and Follow-Up Monitoring: ECCO Guidelines[7]

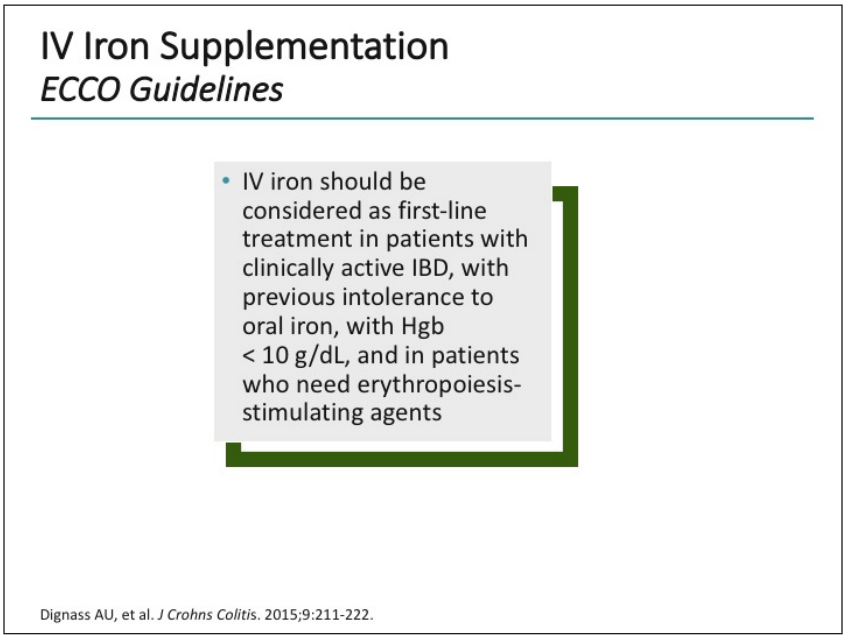
Dr Hou: That is a great question. This happens a lot and is something I know I am not that great at doing when we are looking at processes to improve our way to follow up patients more quickly. Usually, our expectation is that they should have an increase of their hemoglobin or a normalization within 4 weeks of iron supplementation, either oral or IV. If they are not hitting that mark, then we need to take a step back and see what else can we do to fix this.

Dr Rubin: Right. And obviously, there is balance because if their disease is active, they may be losing blood and malabsorbing iron faster than you can replace it. You definitely want to get a sense for whether you are making appropriate progress in that patient. Good. So when do you follow up after you have gotten them back on track? Let us say that they are iron deficient and you have given them an oral supplement. In follow-up, you see that you have actually made progress. Do you shift back to checking less often, or do you worry that in 90 days all those red blood cells are gone and you need to know what is going on again?

Dr Hou: The key question is, we have already talked about this, the baseline of the patient. The patient who is already in remission and they are just a little bit below target, I would probably recheck it again in 3 months. If they are doing well, then I would slowly expand that over time. That is in contrast to the patient you described who is actively inflamed. They probably have continued GI blood loss. I would be keeping a closer eye on that patient.

Dr Rubin: This is a little bit more intensive management for something that I think many of our colleagues are not thinking as much about. We have really had it ingrained in us to recheck labs when we put people on immunomodulators or immunosuppressants and biological therapies. But we have not really talked about some of the more fundamental aspects of managing IBD and thinking carefully about how these issues can really affect the well-being of our patient. I think it is an important point that not only should you be addressing this, but then you need to follow up adequately to make sure you keep people on track.

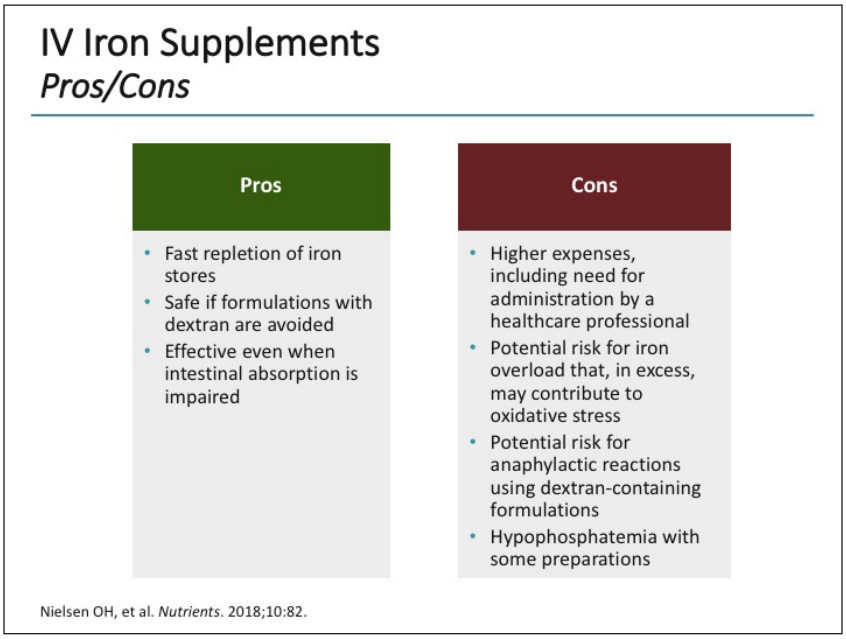
Raluca, you have told me before that oral iron causes side effects and some of the concerns Jason has already raised. When do you use IV iron?



IV Iron Supplementation: ECCO Guidelines[7]

Dr Vrabie: I use IV iron on my patients with clinically active IBD, and people that were unable to tolerate oral iron before, or did not respond adequately to it, or if their hemoglobin is below 10.

Dr Rubin: What are the relative pros and cons of IV iron compared to what we talked about with the oral?



IV Iron Supplements: Pros/Cons[10]

Dr Vrabie: I find that IV iron is faster. It is more efficacious if you are concerned about that person's iron stores, you could load them up quickly with intravenous iron. I do find similar concerns to Jason that intravenous iron bypasses the GI side effects or the change in stool color. I find that it's a more easy-to-tolerate means of delivering iron in my patients.

Dr Rubin: What are the downsides to it?

Dr Vrabie: There is the fact that you need an appointment at the infusion center, and you need your insurance to approve that. It is time out of work. With some of the older formulations of intravenous iron, there were some allergic reactions that happened with those infusions, which is less of an issue now.

Dr Rubin: Yes, so now that you bring that up, Jason, there are several different IV iron formulations that have been available and are still available. How do we distinguish them, and what should we know about that?

IV Iron Formulations

Formulation	Test Dose	Dosing Schedule
Low-molecular-weight iron dextran	Required: 0.5 mL before first dose	Single dose (full deficit correction) OR multiple doses until total dose
Ferric gluconate	Recommended in patients with history of drug allergies	Multiple doses
Iron sucrose	Not required	Multiple doses
Ferumoxytol	Not required	2 doses of 510 mg IV push, given within 3-4 days
Ferric carboxymaltose	Not required	2 doses 7+ days apart
Iron isomaltoside	Not required	Single dose of 20 mg/kg

Hou JK, et al. *Inflamm Bowel Dis*. 2017;23:35-43.

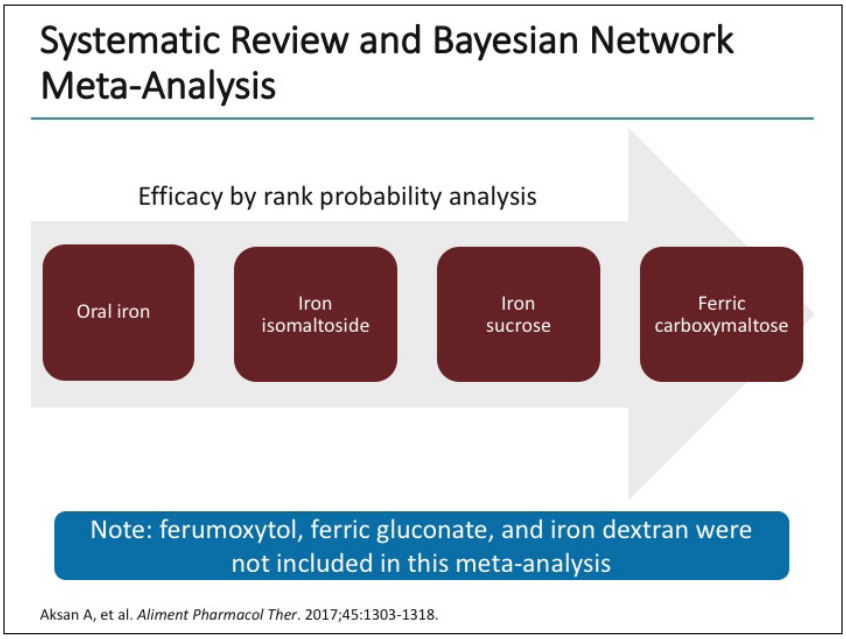
IV Iron Formulations[4]

Dr Hou: There are many formulations. I think the walkaway point for me would be as long as you can give IV iron in patients who need it, that is the important one. I tell my providers that we are working with that you find one that you feel comfortable with. You have to know which one is covered by your local insurers because, as Raluca mentioned, cost can be a big barrier.

The other subtle differences, one of the iron formulations, iron dextran, one advantage of that is that it can be given as a single dose. You have to calculate the iron deficit, and you can technically give it as a single dose. That is the one formulation that does require a test dose because of concern of anaphylaxis.

Dr Rubin: I see. Is there one that you find is best tolerated or is a little easier to administer?

Dr Hou: Each one, again, has its advantages. Most of them, though, do require multiple doses.

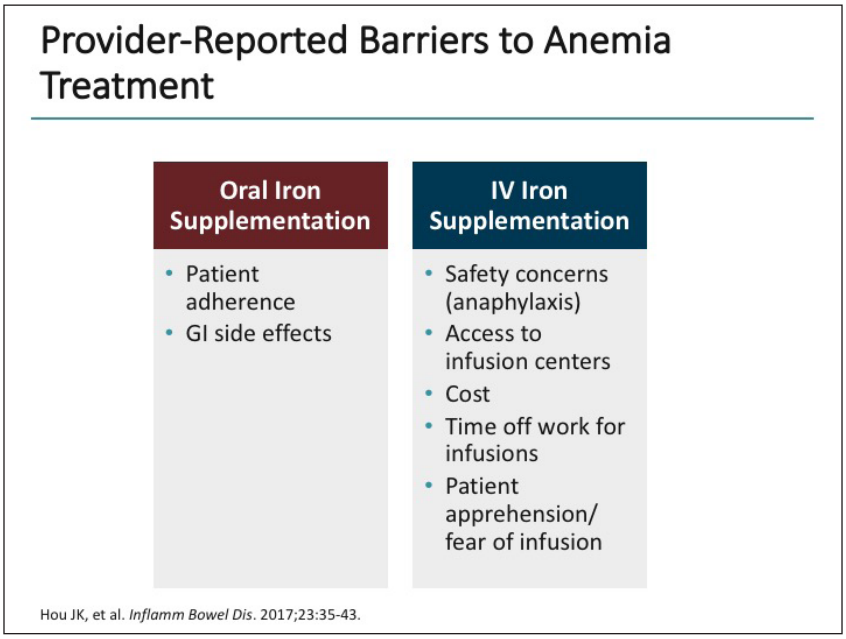


Systematic Review and Bayesian Network Meta-Analysis[11]

Dr Hou: There have been some data comparing different IV formulations in patients with inflammatory bowel disease. There is a network meta-analysis which did show ferric carboxymaltose was somewhat better. Again, there has been fairly limited study specifically in the IBD literature. It is important to remember that all the IV formulations have been approved to treat IDA, which is what we are addressing in our patients.

Dr Rubin: Sure, and one of the major themes in managing IBD that has emerged has been this concept of treating to a target, right? Whatever you use, whether it is dietary or other oral supplements or you use IV iron, you want to make sure you are following up and getting to the target of addressing their iron deficiency in a stable and sustained way. Clearly, that is a good guide for our colleagues if they are having trouble figuring out what to do with their patients.

Should we be thinking about anything else in regard to supplementing this? Do patients who get IV iron need repeated IV iron periodically, or do they get caught up and then we can let them be on oral iron? Do you guys ever combine these approaches? What do you do?

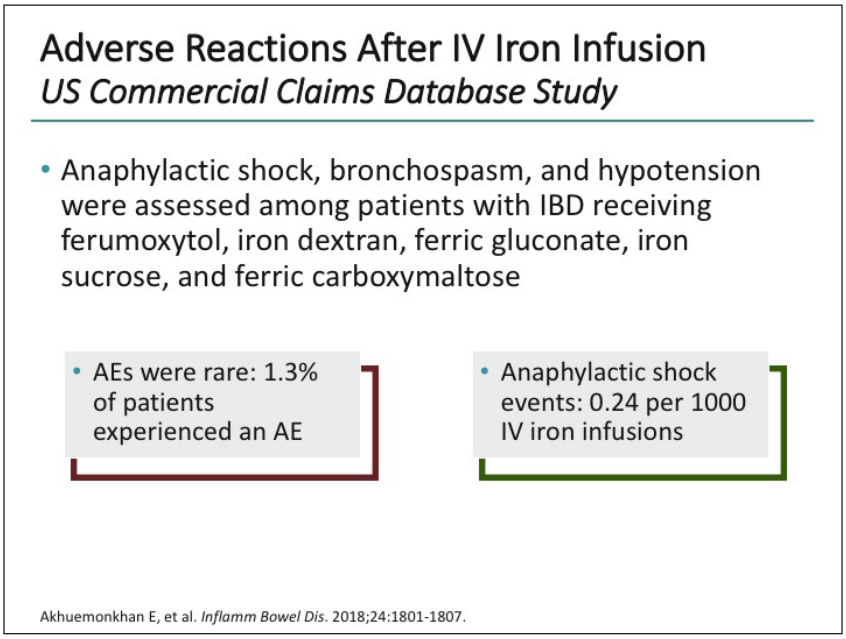


Provider-Reported Barriers to Anemia Treatment[4]

Dr Hou: We do. Some of our patients, again, as Raluca mentioned, sometimes, there are barriers to access for IV related to cost, access. Sometimes we will start with an oral iron if they are on the fence, but in the process of moving them to get their IV formulation. As you mentioned, the monitoring, in some ways it does not matter so much which type you are using. The most important part is the follow-up to make sure they have responded.

Dr Rubin: As you mentioned, the older IV iron formulations certainly had many side effects, including even anaphylaxis. Certainly, taking a careful history about what your patient may have been exposed to in the past and how they tolerated it will be very important before you make those recommendations.

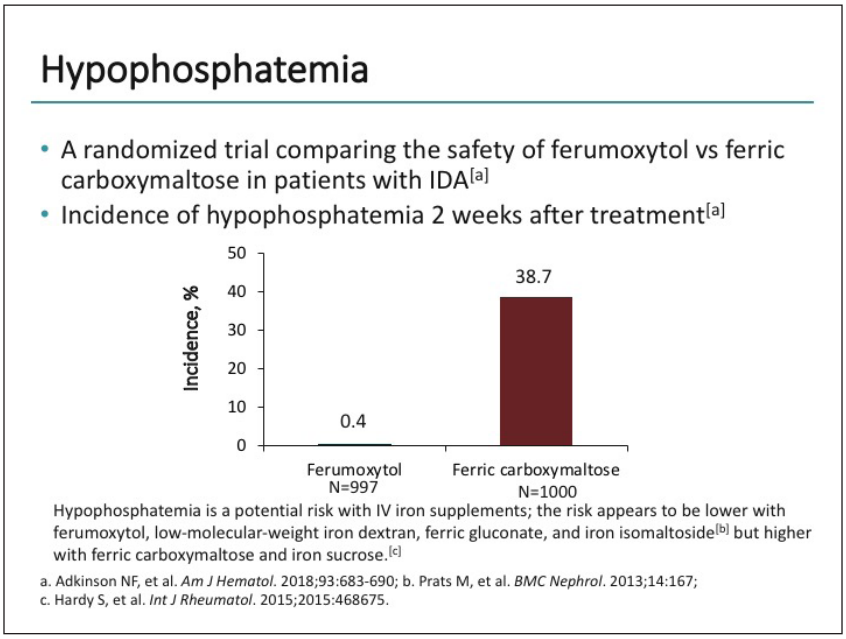
Dr Hou: Yes, the comment about anaphylaxis is important because, like I said, we did some focus groups with providers about this before. A lot of docs, especially those who have been in practice longer, remember those IV formulations and are worried about anaphylaxis.



Adverse Reactions After IV Iron Infusion: US Commercial Claims Database Study[12]

Dr Hou: In reality, there is a recent large study using a large, nationwide database which showed serious adverse reactions to intravenous iron was very low, only about 1.3%. It is something to be aware of, especially with the one iron formulation I mentioned. For most of them, anaphylaxis rates are something we need to be aware of but are not common.

Dr Rubin: Should we be checking any other labs while we are giving IV iron? Is there anything else to be worried about?



Hypophosphatemia[13-15]

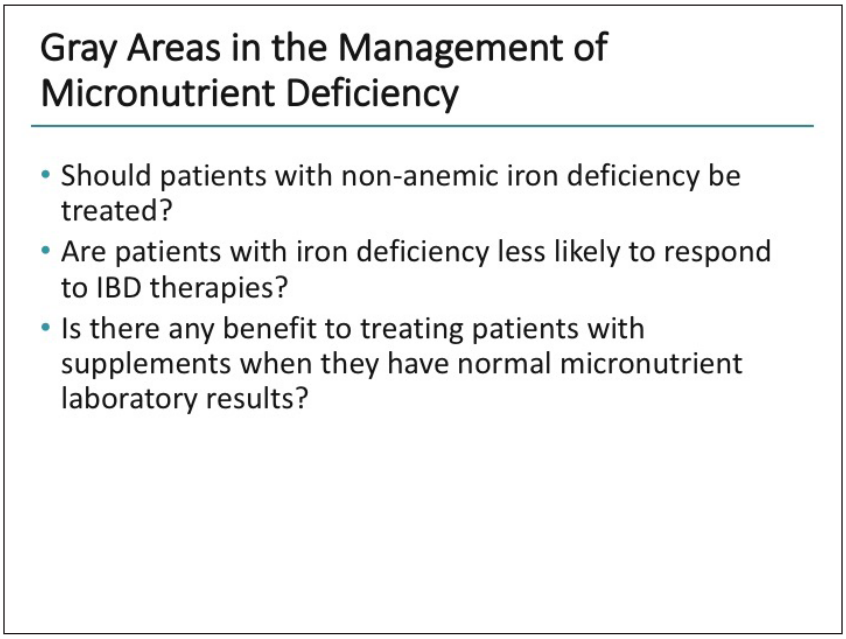
Dr Hou: One other side effect or thing to take note of that I think many of us do not think of off the top of our heads with IV formulations is hypophosphatemia. There was one trial which showed that ferumoxytol compared to ferric carboxymaltose, that hypophosphatemia rates were somewhat lower or lower in the ferumoxytol group. It is something that we should be aware of in keeping an eye on it for using IV iron.

Dr Rubin: Yes, I definitely learned something while we were preparing for this about that. I will definitely be following up on that.

Kelly, anything we should think about in terms of other nutrient deficiencies while we are replacing the IV iron? Should we be addressing phosphate? Should we be proactive in that regard, or is that a little overkill? What do you think?

Ms Issokson: It sounds like that is a concern with some of the iron formulations. I think it is important to monitor that and replace it where appropriate. Vitamin D deficiency can also contribute to anemia, so it is important that we monitor that as well.

Dr Rubin: Yes, I think vitamin D deficiency is a very important one to keep in mind. Remember, too, that in patients who are in a starvation state where they are malnourished and they are not absorbing, as their disease gets under better control, they are going to start utilizing phosphate. They can drop their phosphate levels. I think our colleagues need to remember that as part of the management in some of these complex patients.



Gray Areas in the Management of Micronutrient Deficiency

Dr Rubin: What about the patient with a normal hemoglobin and their MCV is a little lower, their ferritin is low? Do you treat those patients for iron deficiency? Let us say they are feeling well. They are in remission. You get a routine CBC and the ferritin, and you find out that they are iron deficient. Should we be treating them? What do you think?

Dr Hou: I think this is a bit of a controversial area. We use the term non-anemic iron deficiency in these patients. There are data, not in the IBD space, but in the other general population, primarily young women who are anemic related to menstruation, but there are data to show if you address those patients, even if they are not anemic but their iron levels are low, they have reduced fatigue.

In my practice, I have been keeping a closer eye on these patients still, depending on their symptoms. But I have observed some of the patients who identified as non-anemic iron deficient, even if they were not having symptoms, we may have just decided to watch. Over time, their hemoglobin trends down. I have been taking a more proactive role in some of those patients in getting them on iron therapy.

Dr Rubin: Raluca, what are you doing?

Dr Vrabie: That has been my experience as well. I rarely see the patient that has a low ferritin and is feeling well with that low ferritin, in spite of normal hemoglobin. Perhaps, I rarely see the patient that is feeling well. I recognize that is a provider bias on my part, but I will have the conversation about iron, oral or intravenous. I have had very good personal, clinical success with intravenous iron in my patients where I have had patients report feeling much better just getting up out of that infusion chair, a sense of pep or less fatigue that day.

Dr Rubin: One of the issues that has come up and has been at least discussed or considered is if a patient is anemic or, more specifically, iron deficient, are they less likely to respond to any of our medical therapies? In other words, if we are trying to treat their IBD, should we be simultaneously addressing this very aggressively so that it improves their likelihood of responding? Do we know anything about that?

Dr Hou: I see that as having 2 different components. The first comment you made is we do not need to wait until we treat their IBD to treat their anemia. That is a very common misconception. We can treat them both at the same time.

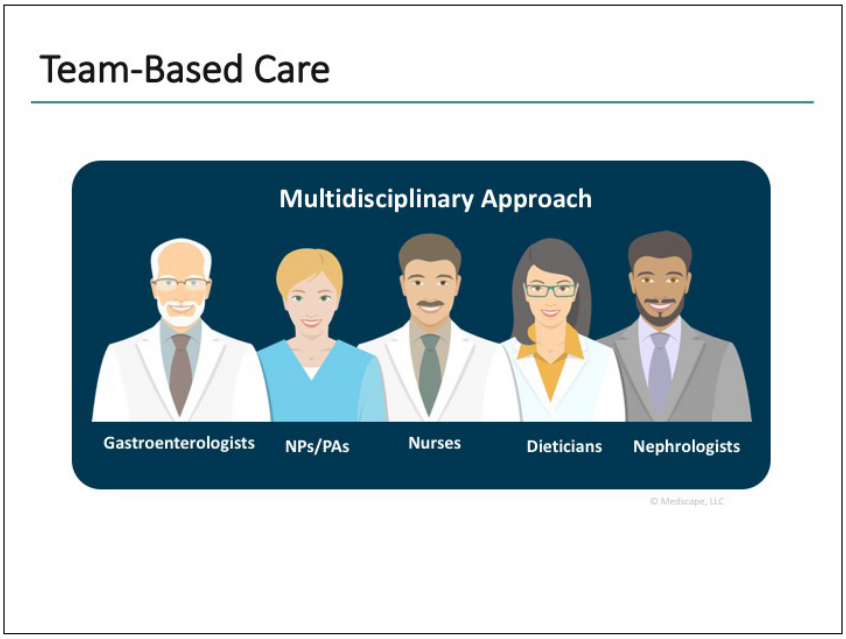
Dr Rubin: We should treat them both at the same time.

Dr Hou: Yes, absolutely. The other component is usually if a patient who has severe anemia iron deficiency, they probably have more severe disease. As you know, the patients that have more active inflammation are the ones that are typically harder to treat. That is something that we do need to keep thinking about.

Dr Rubin: Yes, I think that is important. Kelly, let me ask you a question. Sometimes, patients who have fatigue want extra B12 or they want us to address some of the other micronutrients even when they are normal. How do you approach that general concept? Is there any benefit to treating people with these supplements when they actually have normal labs?

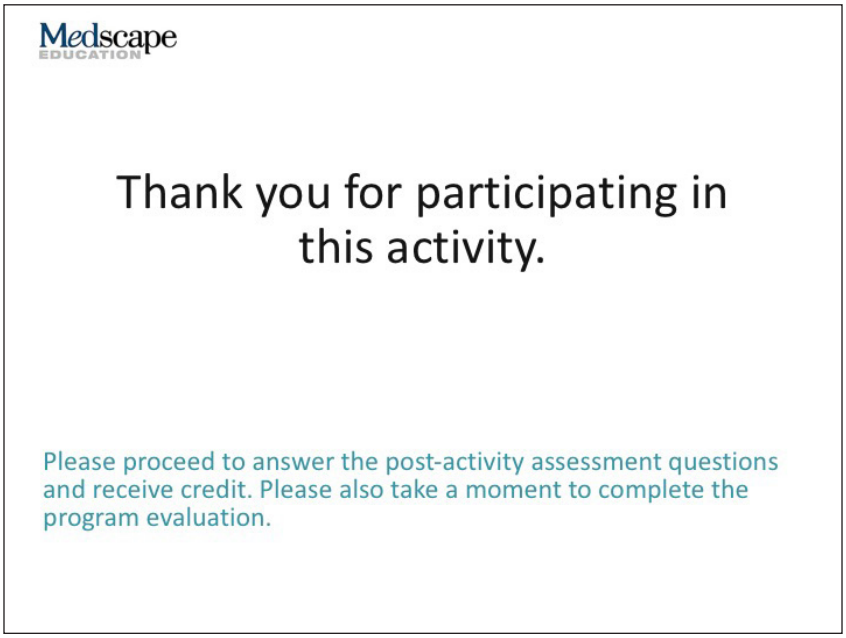
Ms Issokson: Sometimes, patients can have low B12 levels but still have normal serum B12. I think that giving them B12 injections or sublingual B12 can be helpful, and patients do report improvement in energy levels. Routine supplementation beyond multivitamins is not generally recommended unless our patients have documented deficiencies. They are not going to necessarily benefit from a supplement if they do not have a documented deficiency.

Dr Rubin: Great. I want to thank my expert panel today. I think this was a really helpful discussion for an important area that is really underappreciated by many of our colleagues. I am sure that our patients will benefit from what we have talked about today. Kelly Issokson, Raluca Vrabie, and Jason Hou, thank you for joining me today.



Team-Based Care

Dr Rubin: Obviously, it is complex to manage IBD patients. I think working with a team of experts, as well as your nurses, nurse associates, advanced practice providers, your dieticians, your nutrition colleagues, there are a variety of individuals who should all come together to take best care of your IBD population.



Thank You

Dr Rubin: Thank you very much for participating in this activity. Please continue on to answer the questions that follow and complete the very important evaluation.

Abbreviations

ACD = anemia of chronic disease
AE = adverse event
BMI = body mass index
CBC = complete blood count
CD = Crohn's disease
CRP = C-reactive protein
ECCO = European Crohn's and Colitis Organisation
EPO = erythropoietin
GI = gastrointestinal
Hct = hematocrit
Hgb = hemoglobin
IBD = inflammatory bowel disease
IDA = iron deficiency anemia
IV = intravenous
LMP = last menstrual period
MCV = mean corpuscular volume
NP = nurse practitioner
NR = normal range
PA = physician assistant
PPI = proton-pump inhibitor
QoL = quality of life
RBC = red blood cell
RDW = red cell distribution width
RLQ = right lower quadrant
TfS = transferrin saturation
TIBC = total iron binding capacity
UC = ulcerative colitis
WHO = World Health Organization

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