I'd like to welcome you to the 4th session of Smilo shares with primary care. This is a series of talks that we think will be of interest and importance to our primary care colleagues as they are taking care of patients. And trying to best understand indications for referral and what happens when people are referred to the Smilo Cancer Center, which is such a valuable part of our health system. These talks are targeted towards primary care and the faculty panel.
has rotated on specific to the
NOTE Confidence: 0.881477285333333
speciality of the talk that’s being
NOTE Confidence: 0.881477285333333
addressed and today’s topic is anemia.
NOTE Confidence: 0.881477285333333
There are many other venues for
NOTE Confidence: 0.881477285333333
education for primary care clinicians
NOTE Confidence: 0.881477285333333
and we know your time is valuable,
NOTE Confidence: 0.881477285333333
so thank you so much for joining.
NOTE Confidence: 0.881477285333333
Just for convenience,
NOTE Confidence: 0.881477285333333
these talks will always be monthly
NOTE Confidence: 0.881477285333333
on the 1st Tuesday from 5 to 6
NOTE Confidence: 0.881477285333333
and there is a master schedule
NOTE Confidence: 0.881477285333333
and we’ll show you at the end the
NOTE Confidence: 0.881477285333333
previews of the next sessions.
NOTE Confidence: 0.881477285333333
These sessions are recorded and NE
NOTE Confidence: 0.881477285333333
Medical Group clinicians can find
NOTE Confidence: 0.881477285333333
those on the clinician website
under that and we will send out a link afterwards to all of those who attended. At the end of the session there will be a brief survey and please stay tuned for that.

This is the schedule we will move shortly into case presentations and then the best part of these sessions is the question and answer. As you hear the presentation, please use the Q&A field to queue up your questions. We will stop briefly after each of three cases to address the questions pertinent to the case and then have some open discussion at the end.
I'd like to introduce our speakers on the left, Bob Bona, who's the director of the benign hematology program and the medical director of the Hemophilia Treatment Center at Yale. He's originally from New York, and he and his wife Georgiana are current residents of New Haven and longtime residents of Connecticut, where they raised their three children. Prior to coming to Yale, he was a founding faculty member of the Frank Netter School of Medicine at Quinnipiac University. Prior to that, he was a professor of medicine.
at the UConn School of Medicine, having trained there and at Saint Francis Hospital in Hartford.

He did serve as the hematology and Oncology Fellowship program Director, chief of the Division of Hematology and a hemophilia treatment cancer director. He has a strong interest in his career in medical education and is a graduate of SUNY Upstate Medical College in Syracuse. I think you will see his teaching. Skills on broad display here. And Anna Crest received her medical
degree from Columbia University.

Vagelos College of Physicians and surgeons,

her internship and residency were completed at Columbia University,

New York Presbyterian Hospital.

Dr Crest completed her fellowship in medical oncology and hematology at the Yale Cancer Center and served as a Chief fellow in her third year.

Her clinical and research interests include various topics within classical and malignant hematology.

Frank Ciminello is an internist in Trumbull, Connecticut and has over 20 years of Experience in the medical field.
He graduated from NYU School of Medicine and completed his residency in Internal Medicine primary care at the University of Pennsylvania. He also has an MBA from the Yale School of Management and currently serves as both a Regional Medical director for Northeast Medical Group in the Bridgeport Region and also as the President of the Primed Medical Group, which is a PSA group within NE Medical Group.

Kelsey Martin, our final panelist, is an assistant professor of clinical medicine at the Yale.
Cancer Center and Cares for patients at the SMILLO Cancer Center.

In Orange, CT, she received her medical degree from the Royal College of Surgeons in Dublin and completed her residency in internal medicine at the Jacobi Medical Albert Einstein College of Medicine in New York.

She subsequently completed specialty training in hematology and medical oncology at Lenox Hill Hospital in New York City.

Doctor Martin’s clinical interests are patient communication,
hematology, hematologic disorders in women’s cancer prevention, including the role of nutrition. Obesity and an environment in cancer promotion. Doctor Martin is actively involved in the Yale community as a member of the Status of Women in Medicine and the Women Faculty Forum. With that said, I think you have a lot of learning in front of you and I’m going to turn to our panelist to begin. Frank,
00:05:16.610 --> 00:05:19.970 do you want to introduce the first case?
NOTE Confidence: 0.959529158333333
00:05:19.970 --> 00:05:21.059 Thank you and.
NOTE Confidence: 0.871126412
00:05:23.510 --> 00:05:24.940 Well you just put yourself on mute
NOTE Confidence: 0.851466764545454
00:05:25.750 --> 00:05:28.498 I muted unmuted and muted again
NOTE Confidence: 0.851466764545454
00:05:28.498 --> 00:05:30.850 myself so sorry about that.
NOTE Confidence: 0.851466764545454
00:05:30.850 --> 00:05:33.258 So we have three cases I’ll I’ll
NOTE Confidence: 0.851466764545454
00:05:33.258 --> 00:05:35.916 present them and then each of the
NOTE Confidence: 0.851466764545454
00:05:35.916 --> 00:05:37.851 our our panelists are specialists
NOTE Confidence: 0.851466764545454
00:05:37.851 --> 00:05:40.238 will will help guide us through
NOTE Confidence: 0.851466764545454
00:05:40.238 --> 00:05:42.710 some discussions some work up and
NOTE Confidence: 0.851466764545454
00:05:42.793 --> 00:05:45.264 and and we hope this is extremely
NOTE Confidence: 0.851466764545454
00:05:45.270 --> 00:05:47.340 educational and beneficial to you
NOTE Confidence: 0.851466764545454
00:05:47.340 --> 00:05:50.646 and and your patience and as I’m sure
NOTE Confidence: 0.851466764545454
00:05:50.646 --> 00:05:53.064 you know anemia is extremely common.
NOTE Confidence: 0.851466764545454
00:05:53.064 --> 00:05:55.542 And and it seems as patients get
NOTE Confidence: 0.851466764545454
00:05:55.542 --> 00:05:57.970 older the the chances are the
prevalence of anemia really does increase quite dramatically. So we hope these three cases which we picked from literally a week of my patients a few weeks ago is relevant for you as well. So case one is a woman 52 years old who is coming in for a routine physical she has a history of thyroid disease, sleep apnea, diabetes. And you can see her current blood work which showed anemia and the prior year showed a little less severe anemia, but you’ll notice a drop in
hemoglobin and a drop in her MCV

although MCV is still normal.

And then, uh,

next slide and there’s a routine village.

You had no symptoms at all.

Um, get next slide, please.

I am trying to move to the next slide and it’s not working.

I’ve been having some network problems.

Renee, can you pull up this slide deck?

I’m going to stop. Sharing.

Actually I can try resharing one more time and see if that works.

No, it’s not working right now.

Have you? Pull it up.

Apologies for the delay.
Um, oh, there we go.

Alright, so we sent her for some additional blood work and you'll see her iron levels, which is now high. Her ferritin is low and her B12 was normal.

She did have a colonoscopy the prior year that showed us a benign hyperplastic polyp and diverticulosis.

And uh, if we can go to the next slide, actually those questions,

So I'll hand it off to Kelsey,
by us or that we should do first and any recommendations for treatment and then when we would want to refer this person to hematology. Alright, thank you.

Alright. Thank you so much for the opportunity this evening. Frank, would you mind just flipping back to the labs that we did already perfect. So I think in looking at this case, I think what jumps off the page to me right away is that you know that hemoglobin hematocrit dropped in about a year’s time span as you mentioned the MCV started to decrease. The platelet count was also kind of
heading towards the upper limit of normal and the MCV and I'm sorry the RDW is also starting to increase as well. I think these labs as far really clearly consistent with iron deficiency. The ferritin being less than 30 really is as a number we would look at. So certainly if it’s less than 10, I think that this is clear cut iron deficiency, a retic count I think is helpful just to sort of to show sort the lack of narrow response. The peripheral smear is always I think useful to in hematology and I
think actually truthfully I think if the patient is not describing significant bleeding or history of bleeding. I may even be content with stopping there. I think if a patient is giving a history of a long standing history of bleeding, particularly something like a menstrual bleeding will come into that in a second. And as a hematologist, I do start to think about bleeding disorders as well, things like von Willebrands disease that are common in the population and can manifest as iron deficiency. And so I actually would probably not do too much more at this point.
I actually think we have enough of a diagnosis to make.

So and.

Iron deficiency is extremely common. A significant burden globally and disproportionately impacts children and women.

Most commonly here we’re seeing things like chronic blood loss, particularly in a man until proven otherwise and postmenopausal.
women's menstrual bleeding,

NOTE Confidence: 0.8466977675

gynecological bleeding and and Gu bleeding,

NOTE Confidence: 0.8466977675

sort of the second sort of

NOTE Confidence: 0.8466977675

major category be malabsorption.

NOTE Confidence: 0.8466977675

And this we see commonly I

NOTE Confidence: 0.8466977675

think in our patients with a

NOTE Confidence: 0.8466977675

history of bariatric surgery as

NOTE Confidence: 0.8466977675

obesity and continues to rise.

NOTE Confidence: 0.8466977675

And also Umm H pylori is another

NOTE Confidence: 0.8466977675

quite common thing I feel that

NOTE Confidence: 0.8466977675

we see in the outpatient setting.

NOTE Confidence: 0.758115975

And then there is sort of another second,

NOTE Confidence: 0.758115975

third major category would

NOTE Confidence: 0.758115975

be sort of physiologic need.

NOTE Confidence: 0.758115975

So you know, periods of growth,

NOTE Confidence: 0.758115975

childhood, adolescence and certainly
during pregnancy where nearly half of pregnant women are iron deficient. So we could flip the next slide. So we think specifically looking at more pathologic disorders associated with iron deficiency and as mentioned in this patient’s case, she had seen. Gastroenterology not in the recent future right played Frank. It was in the last year or two in this case. But always important for us to think about the entire job GI tract. I think particularly about H pylori again as an as an NPI, that’s something that we see that
can contribute to or hydria,

which can also contribute to iron deficiency.

We sometimes are screening patients for celiac disease as well, I think UM and that it comes up often in our patients who are also refractured iron which I’ll come back to in a couple slides. And then there is a number of conditions as well that we see frequently and particularly in the primary care setting of anemia associated with chronic disease where those patients or maybe have poor utilization of iron and and that’s patients with chronic heart failure,
chronic kidney disease and other.

Chronic inflammatory disorders, particularly things like inflammatory bowel disease, I listed on the right hand side here just a couple of other things I feel that we see often in our practice as hematologists. So I think food insecurity and sort maybe for access to diverse diet, diet is something that we should probably dig into a little bit deeper with our patients as we take a history. Blood donation and I have a a number of patients who are those...
frequent blood donors you know who
NOTE Confidence: 0.758217754166667
donating their blood every you
NOTE Confidence: 0.758217754166667
know between 50 to 60 days and and
NOTE Confidence: 0.758217754166667
there's and they're saying to just
NOTE Confidence: 0.758217754166667
support those types of patients
NOTE Confidence: 0.758217754166667
should be on oral iron supplementation
NOTE Confidence: 0.758217754166667
to prevent iron deficiency.
NOTE Confidence: 0.758217754166667
So I think again a good history
NOTE Confidence: 0.758217754166667
comes in handy there as
NOTE Confidence: 0.758217754166667
mentioned before gynecologic bleeding
NOTE Confidence: 0.758217754166667
you know iron deficiency again
NOTE Confidence: 0.758217754166667
disproportionately impacts.
NOTE Confidence: 0.758217754166667
And then?
NOTE Confidence: 0.758217754166667
And have you menstrual periods is
NOTE Confidence: 0.758217754166667
is common and so working closely
NOTE Confidence: 0.758217754166667
with our gynecologists can be
tremendously helpful in improving the quality of life of women with iron deficiency and asking about hematuria and other sources of blood loss.

And then patients who receive erythropoietin stimulating agents or darbepoetin for example, those patients use up their iron stores over time and it’s important that they are. Also receiving iron supplementation so important as we look in patients medications to see if that’s playing a role. And we also know by researchers
from here at Yale that Trimberg for example that there are genetic conditions where some people do not absorb iron adequately and that’s due to inappropriately increased levels of hepcidin which is our master regulator of iron. So we think about that a lot in patients who have been taking iron supplements appropriately, but are not not achieving an adequate response. Next slide, please.

And a couple of just clinical pearls perhaps are things to consider? An iron deficiency can be due to more than one thing at a time.
And in dual pathology for example, both upper and GI tract involvement is found in about 1 to 10% of cases and with our aging population this becomes more common. In both males and postmenopausal women, cancer of the GI tract is found about 8 to 10% of cases, which is quite significant. In our premenopausal women, heavy menstrual periods would be playing a major role in that case. Cancer of the GI tract is much less common and and heavy menstrual periods would be playing a major role in that case. Next slide, so for the ferritin is probably the most single most
useful test we can have performed. And going back to your question about what additional testing can be done and if it’s low which is really characterized by less than 15 and then you’ve already confirmed absolute iron deficiency and that’s why with that prior case I think with a ferritin of three that was very helpful to have an iron saturation of less than 20% is also another useful. A target and when doctor bonus speaks, I think he’s going to you know interpret situations where patients
may still be iron deficient yet have anemia of chronic disease. So, so important to pay attention to that iron saturation, the peripheral smear can show us classic findings of iron deficiency and the reticulocyte count, RDW and platelet count are also all factor into my decision making process as I evaluate these patients. Umm. I think in history, I will come back to that in that I don’t think much additional lab work is required,
but I think a strong history taking skills are really useful and asking patients if they’re craving ice or being crunchy things. I think it’s also very helpful and also quite specific for iron deficiency. And so I asked that often of my patients and other things like restless leg syndrome, cold intolerance which I feel like patients mention often and I do find that patients mention alopecia as a as a concern should I’ll bring our attention to iron deficiency and maybe out of the scope of today, but certainly patients maybe carries a beta thalassemia and it can be
sometimes challenging when someone has a microcytic anemia to help make that distinction. And the Mentor Index is a tool worth the MCV over the RBC Count, which can help us, you know, try to make that distinction. And excited. Something I’ve thought about and I thought maybe others might do is you know should our patients be fasting when we check iron levels and I think it can be, but it doesn’t have to be. It’s how I interpret the data.
I'm not sure if my colleague should answer this but I think that there are some diurnal variations and also some changes after meals that impact serum iron and so our serum iron levels peak in the late morning and it also increases after a meal. But it also decreases after fasting. So my interpretation of this is that I think it is not crucial to measure iron studies fasting but. On the other end of the spectrum, sometimes we see very high
levels of iron and we’re sending patients to that for hemochromatosis and those patients I will often have them repeat it fasting in that circumstance and it appears that the tscp performs just as well in non-fasting versus fasting patients so.

Next slide, please.

So our goals of treatment or management of iron deficiency, we want to first and foremost identify and treat the underlying cause of the end deficiency and working typically closely with our gynecologist and gastroenterologist colleagues is key.
And maybe less commonly, urology, we want to replete the iron stores and we want to normalize the hemoglobin if someone’s anemic and improve or reverse the symptoms that they’re experiencing. And usually, you know, the craving of ice ships, you know, response quite quickly. And I often remind patients to bring that to our attention if they notice it in the future because it’s such a sensitive sign and the goal is not to keep patients on lifelong iron. And as I’m sure, as we’ve all seen, sometimes it’s a medication that seems to linger on medication.
Lists.

And I think it's always worth reevaluating whether the patient really truly still needs to be on it.

So. Next slide, please.

So what is the best approach?

Case that patient team was around 9:00

and I think this patient has Frank you said was largely asymptomatic you said was largely asymptomatic and probably this patient could be managed with oral iron supplements.

Patients often I find ask you know can they just eat eat more meat or or make a change and I think that’s is
limited and it’s in its efficacy once
patients are becoming progressively anemic but but could be considered if someone has a normal hemoglobin but maybe borderline iron levels.
I think it’s that reasonable to to try and I’ve just listed some some foods that are rich in iron and Anaheim iron from from meat or poultry and fish is is absorbed more efficiently than iron that comes from plant based sources. But I would you know certainly doesn’t have to be what someone needs if they’re vegan for example. I think if there’s one thing that
people in the audience want to listen
to today is how to give oral iron.
And we now have a growing collection
of data that tells us that every other day iron supplementation is,
and it’s easy to remember
about 100 milligrams of elemental iron every other day.
I think I can’t go wrong and this
is the the the reason behind this is.

Sort of.

If,

if there's a really simplistic way

is if there’s kind of too much

consistent iron that hepcidin,

which again is sort of our master

regulator of iron absorption,

starts to impair our ability to

absorb further iron,

starts to impair our ability to

absorb further iron,

and taking the iron every other day is best.

It’s also best on an empty stomach,

hour before 2 hours after a meal.

You know,

regarding the rule of vitamin C

from from from my understanding,
there’s really no data to sort

of fully make this

I often personally don’t.

I’m not sure if my colleagues

would answer that,

but I never really push for it.

But it doesn’t bother me

if someone’s taking it.

And it really needs to be

continued for a few months.

At least three to six months

after the iron deficiency has

been corrected in order to

to replenish those stores.
So it takes a few months for it to be effective and I would just keep that in mind as again as we make decisions about which patients might need to have. Their anemia improved quicker and as we talked about intravenous iron. Also, a lot of patients can’t tolerate it. You know, somewhere between 30 to 70% of patients have, usually GI upset. As a result, there’s a number of different brands on the available. Usually do recommend fair.
00:22:42.666 --> 00:22:44.640 sulfate because I think it has
00:22:44.705 --> 00:22:46.722 the most data supporting it,
00:22:46.722 --> 00:22:51.102 and I I personally am weary of
00:22:51.102 --> 00:22:53.598 slow release formulations because
00:22:53.598 --> 00:22:56.486 its absorption is passed the
00:22:56.486 --> 00:22:58.066 duodenum where iron is absorbed.
00:22:58.070 --> 00:22:59.869 So I’m personally wary that I’d be
00:22:59.869 --> 00:23:02.029 curious with my colleagues say about that.
00:23:02.030 --> 00:23:04.280 Umm.
00:23:04.280 --> 00:23:04.912 Next slide, please.
00:23:08.300 --> 00:23:10.484 We as hematologists offer
00:23:10.484 --> 00:23:13.214 a lot of intravenous iron.
00:23:13.220 --> 00:23:15.512 And the patients who I consider
00:23:15.512 --> 00:23:18.022 it in are largely those patients
00:23:18.022 --> 00:23:20.358 Umm.
who are either intolerant or sort of failed oral iron therapy.
Many of our patients also have malabsorption medical conditions, patients with gastric bypass for example, or patients with inflammatory bowel disease where the utilization of iron given intravenously is much more efficient. As I mentioned, it takes a few months for oral iron to be effective, so sometimes we need to improve things quickly. Maybe someone is going to have surgery or if someone is. 34 weeks pregnant and we need to
improve their anemia in a shorter time.

frame and I think intravenous iron is extremely helpful in those situations.

It is also common in patients who are with chronic kidney disease on erythropoietin stimulating agents often benefit from intravenous iron. Umm.

We have ways of calculating the iron deficit. That calculation is stated there.

It usually ends up being somewhere around 1000 milligrams that someone needs repleted,

and there’s a number of different brands that are available.

They. At the end of the day, can I think we choose which brand
based on patients, insurance and and?

Potentially, how many visits it might be to the clinic.

Some of them require more than one visit. Umm.

There is evolving literature about the risk of infusion related reactions that can happen with iron.

Including our own published data that seems to be maybe relevant to patients blood type,

but I think it still is quite rare,

maybe maybe somewhere around 1%

of patients have what we call an infusion related or which is a sort of allergic type reaction.
But for the most part there’s no brand preference at the end of the day.

Next slide, please.

So who should be sent to hematology, I think patients who benefit from IV iron will always happy to see those patients and I think if the patient is having a history with significant bleeding and that includes a heavy menstrual periods. Patients who have prolonged menstrual periods, patients who see clots of blood during their periods, patients who say every woman in their family had heavy periods,

43
I think it can be very helpful for us to make sure those patients do not have a bleeding disorder. Patients who bleed after pregnancy, these are patients who are frequently missed in their diagnosis and then patients who are refractory to patients who have been taking oral iron appropriately. So again, I just think back on, are they taking it every other day, are they taking it, are they taking on empty stomach, are they, are they taking it the way we’ve recommended for patients that really are or? I think it can be helpful for
us to think outside the box a little bit as to what the cause of their iron deficiency is.

Good. I'll just pop in one of the questions on Katie Reeve, who's one of our EMG internist in the New London region or the Far East region, says other than pill burden is there a downside to long-term iron that people aren’t feeling side effects are their harms? Well because the there’s no real way for our the human body to get rid of excess iron. I do worry about iron overload.
and occasionally I think we do.

We do see patients who start to have high duration and high ferritin from being on you know a long standing iron.

So I do think, I do think, it really should just be done for a fine out amount of time.

Alright. And Doctor Zarko Power just points out that you know chronic blood loss especially angiodysplasia and other GI issues on seems to be really common.

Sometimes we use the platelet count as a kind of approximator of how acute the bleeding is.

Is there any truth to that that people
who have a high platelet count with their iron deficiency are more likely actively bleeding than not?

I'm not aware of that. I don’t know the answer to that.

And I actually think so when I did some of the research that the platelet count is often high in iron deficiency through its own mechanism. So I don’t know how bleeding offsets that’s why I actually just don’t know the answer to that question. I don’t know I’ll defer to my colleague. someone else has a nose of more than
I do but I and I but I absolutely agree with interact with ours about Andrew dysplasia and and we do have some patients I think that are kind of chronic leaders and and for those patients I think yes they could stay on iron. As long as you’re someone’s like tracking it and measuring.

OK. But.

So I’ll, I’ll take this back. Thank you, Kelsey, very much.

And even though I prepared these cases and knew what you’re going to say, I still learned three things just now.

So thank you. So this woman did have manraja on more directed questioning.
and ultrasound that showed polyps. She had a GYN who took her surgery. She did well after surgery. And she’s had a normal hemoglobin postop and since still without any symptoms which is great. So and I think she had just oral iron I believe in the end. Thank you. I think we answered. Yes, I think we answered all of our questions for case one. So I’m going to move us through to case two. So SN is another patient of mine, 76 year old gentleman a little older, 76 year old gentleman a little older, a little bit thicker coronary artery disease,
prefer all disease Tia, stroke, COPD,
chronic kidney disease stage 3.
Which is not in there but that’s what
he has who came in with the subacute
der of one to two-month history of chronic
Here’s his most recent blood work
and I was calculating his GFR by
memory but I might have overshot.
But you can see he is anemic
hemoglobin of nine his ferritin.
Was in the normal range of B12 in the upper
normal range and his platelets were normal,
his MCV normal.
We’ll go and through the next slide
for a little bit more history.

We did a fit card that was negative because of his comorbidities.

Um, he was probably just about due for a colonoscopy now and the decision really wasn’t to do unless we had to.

But his colonoscopy exactly 10 years ago was essentially normal as well, diverticulosis and internal hemorrhoids.

So I’m going to pass it on to Bob Bona and the questions first.

Bob Bona and the questions first.

Would be what other testing would you recommend in this case? Thank you.

Thanks, Frank.

And just to echo Kelsey,
00:31:21.820 --> 00:31:23.878 I appreciate the opportunity to be here
NOTE Confidence: 0.85454854
00:31:23.878 --> 00:31:26.160 this evening to speaking with all of you,
NOTE Confidence: 0.85454854
00:31:26.160 --> 00:31:28.188 it’s a it’s a real pleasure.
NOTE Confidence: 0.85454854
00:31:28.190 --> 00:31:29.670 And so just to recap,
NOTE Confidence: 0.85454854
00:31:29.670 --> 00:31:32.560 this is a a man in his 70s who has
NOTE Confidence: 0.85454854
00:31:32.651 --> 00:31:35.765 multiple medical issues who now has
NOTE Confidence: 0.85454854
00:31:35.765 --> 00:31:38.460 some symptoms of dyspnea and has what
NOTE Confidence: 0.85454854
00:31:38.546 --> 00:31:41.626 I would characterize in many of us
NOTE Confidence: 0.85454854
00:31:41.626 --> 00:31:44.449 would characterize as a moderate anemia.
NOTE Confidence: 0.85454854
00:31:44.450 --> 00:31:46.270 And I think what other
NOTE Confidence: 0.85454854
00:31:46.270 --> 00:31:47.726 tests would you recommend?
NOTE Confidence: 0.85454854
00:31:47.730 --> 00:31:51.194 I think it’s always helpful to know what
NOTE Confidence: 0.85454854
00:31:51.194 --> 00:31:54.107 the previous CBC values are certainly
NOTE Confidence: 0.85454854
00:31:54.110 --> 00:31:56.546 is this anemia developed rather quickly,
NOTE Confidence: 0.85454854
00:31:56.550 --> 00:31:58.090 has it been present for
NOTE Confidence: 0.85454854
00:31:58.090 --> 00:31:59.630 many years or many months,
in which case the dyspnea may not be related to the anemia. So having those values is really very helpful and also keeping in mind that individuals who develop anemia slowly have a great capacity. To compensate for that and may or may not have symptoms until they get quite anemic. The Reticulocyte count is really a must in this situation, I think where we're looking at in anemia where it's not so straightforward. And then a peripheral blood smear I think is always a very reasonable
thing to request from our pathology colleagues to get any clues about what this anemia could be due to. The maybe I'm going to come as we go through this case if I could. So if you could please just advance the slide. So I just want to spend a minute talking about reticulocytes if I can because I think there's a lot of confusion about how these are reported and how these are interpreted. So most of us know that these have been reported as percents, reticular site percent and then where we've been taught to calculate...
00:33:12.418 --> 00:33:14.218 a reticular site production index

00:33:14.218 --> 00:33:15.298 or a curriculum.

00:33:15.300 --> 00:33:16.608 Corrected reticulocyte count.

00:33:16.608 --> 00:33:20.600 And then look at that number and to determine

00:33:20.600 --> 00:33:23.186 if the anemia is hypo proliferative.

00:33:23.190 --> 00:33:24.714 That is from the point of

00:33:24.714 --> 00:33:26.150 view of the blood smear,

00:33:26.150 --> 00:33:30.958 bone marrow not producing blood

00:33:30.960 --> 00:33:32.370 cells or hyperproliferative.

00:33:32.374 --> 00:33:37.080 a lot of blood cells,

00:33:37.080 --> 00:33:38.440 the bone marrow are producing

00:33:38.440 --> 00:33:39.800 a lot of blood cells,
many of us do that.

The absolute reticulocyte count is probably the best way to think about this.

And just a moment,

So if the normal red count is 5

So our reticulocyte count is 1% * 5

And sometimes this is reported as 50,000.
Sometimes in the Yale lab it’s reported as a number of times 10 to the 6th. So it comes out to point. And so if a person has an anemia and has a reticulocyte count of 50 or 60 or 70,000, they are under producing red blood cells and the bone and the bone marrow is not able to compensate for the anemia. And on the other hand, if the articular side can is 150,000 for instance, that suggests that the bone marrow is producing a lot of red blood cells despite the anemia.
And this is critically important because there are only a couple of things that give an anemia with an elevated reticulocyte count. And one of those is of course hemolysis. With an adequate bone marrow response, you can have homolysis and not have an elevated reticular site count. So if you have iron deficiency for instance. Plus hemolysis, the bone marrow can’t respond. The other thing that will give an increased reticulocyte count is that there’s some recovery from an anemic process. So someone’s had a bleed and you’re seeing them a week or two.
00:35:31.332 --> 00:35:32.608 later and they’re recovering.

00:35:32.610 --> 00:35:34.866 Or as in the previous case

00:35:34.866 --> 00:35:36.370 that Kelsey discussed you,

00:35:36.370 --> 00:35:37.900 you’re giving someone iron and

00:35:37.900 --> 00:35:39.430 their anemia is getting better.

00:35:39.430 --> 00:35:40.720 And in those cases, again,

00:35:40.720 --> 00:35:43.758 you’d expect the reticulocyte count to be

00:35:43.758 --> 00:35:47.090 increased as the bone marrow is recovering.

00:35:47.090 --> 00:35:48.476 And just as a quick reminder,

00:35:48.480 --> 00:35:48.775 those.

00:35:48.775 --> 00:35:50.250 Particular sites are the bigger,

00:35:50.250 --> 00:35:52.145 bluer cells on the peripheral

00:35:52.145 --> 00:35:54.500 blood smear indicated by the arrow.

00:35:54.500 --> 00:35:55.922 So for me,

00:35:55.922 --> 00:35:58.292 absolute reticulocyte count is a

NOTE Confidence: 0.760395563076923
Very important number that I look at to try to help decipher the anemia. And then if, yeah, if we could move. Thank you.

The blood smear is also very important and especially if there are some characteristic abnormalities described. For instance, if there are teardrop cells noted on the peripheral blood smear, we're often thinking of myelofibrosis or myelopoiesis. Myelopoiesis, of course, is where there's something invading the bone marrow. That could be cancer. It could be infection like tuberculosis.
It could be granulomas with sarcoid for instance. So the presence of teardrops is helpful. Burr cells are often seen in uremia spur cells and liver disease target cells and liver disease, etcetera.

So I won’t go through the list, but these things you know can really help us a lot and give us clues as to why the patient is developing anemia. And we would either look at the smear in clinic ourselves or ask our pathology colleagues to look. And then give a formal. Report in the chart.
Thank you. And so back to this case, I think represents one of the harder cases of anemia for me as a practicing hematologist because you have a patient who has multiple medical problems who has a moderate anemia, one that we can’t just say is just a tiny bit off. You know, there’s something going on here with the hemoglobin of 9 grams. And it’s normal chromic and presumably normochromic. And I’m going to assume here that the reticulocyte count is low in this case.
So these are hard, hard anemias to decipher because there are many things that can cause the anemia and there are likely multifactorial causes of the anemia. And at the end of the day when I see someone like this, the question that’s in my mind is do they need a bone marrow biopsy, do we need to suggest a bone marrow aspiration biopsy, determine the cause of the anemia? And on the left there is just kind of a broad overview of the classifications.
for anemia, bone marrow failure,
NOTE Confidence: 0.8488761725
bone marrow replacement,
NOTE Confidence: 0.8488761725
nutritional or hormone deficiency,
NOTE Confidence: 0.8488761725
etcetera.
NOTE Confidence: 0.8488761725
And then on the right is kind of
NOTE Confidence: 0.8488761725
the thinking that I will go through
NOTE Confidence: 0.8488761725
when I see a patient like this.
NOTE Confidence: 0.8488761725
So is this anemia urgent and we do,
NOTE Confidence: 0.8488761725
we needs to do something today.
NOTE Confidence: 0.8488761725
Tomorrow. So is it new and severe?
NOTE Confidence: 0.8488761725
Is the patient significantly symptomatic
NOTE Confidence: 0.8488761725
where they might need an intervention,
NOTE Confidence: 0.8488761725
for instance,
NOTE Confidence: 0.8488761725
like a blood transfusion from the anemia?
NOTE Confidence: 0.8488761725
We don’t usually expect that
NOTE Confidence: 0.8488761725
with the hemoglobin of nine,
but if someone had a hemoglobin of 14 yesterday and they’re nine today, they are going to be symptomatic and will likely need some urgent intervention. And so the history is quite important here to help us understand that in terms of the development of this anemia. And then the other thing to think about is there some other process that’s life threatening going on here that we need to deal with right away? Is this TTP, for instance, so are there just a sites on the blood smear? Is there thrombocytopenia as well? Are there myeloblasts on the blood smear?
So this may be an acute leukemia.

So those are kind of things that we often need to think about right away.

Because those patients really need to be seen right away and triaged differently.

If those things are not present,

so I'm thinking about it, could this be bone marrow invasion with cancer for instance?

And so a good history, a good physical exam are really, really important here.

Has there been weight loss, other sweats, fevers, is there a mass, is there a history of cancer?

Is there frequent urination with
00:39:58.108 --> 00:40:00.384 prostate enlargement and a possibility
NOTE Confidence: 0.8488761725
00:40:00.384 --> 00:40:02.839 of prostate cancer for instance,
NOTE Confidence: 0.8488761725
00:40:02.840 --> 00:40:05.018 because prostate cancer and bone marrow.
NOTE Confidence: 0.8488761725
00:40:05.020 --> 00:40:08.368 Invasion is not uncommon.
NOTE Confidence: 0.8488761725
00:40:08.370 --> 00:40:10.090 I always will think about
NOTE Confidence: 0.8488761725
00:40:10.090 --> 00:40:11.810 multiple myeloma in this setting.
NOTE Confidence: 0.8488761725
00:40:11.810 --> 00:40:13.865 So a normochromic anemia in
NOTE Confidence: 0.8488761725
00:40:13.865 --> 00:40:15.920 an older individual I think
NOTE Confidence: 0.818529248823529
00:40:16.001 --> 00:40:19.067 who also has some chronic kidney disease.
NOTE Confidence: 0.818529248823529
00:40:19.070 --> 00:40:21.638 We we need to make sure we’re not
NOTE Confidence: 0.818529248823529
00:40:21.638 --> 00:40:23.631 missing multiple myeloma and it often
NOTE Confidence: 0.818529248823529
00:40:23.631 --> 00:40:26.086 I will get protein studies in these
NOTE Confidence: 0.818529248823529
00:40:26.086 --> 00:40:28.396 individuals and those will include
NOTE Confidence: 0.818529248823529
00:40:28.396 --> 00:40:30.850 a serum protein electrophoresis and
NOTE Confidence: 0.818529248823529
00:40:30.850 --> 00:40:33.250 immunofixation electrophoresis and serum
NOTE Confidence: 0.818529248823529
00:40:33.250 --> 00:40:36.406 free light chains because about 20% of individuals with multiple myeloma.
00:40:36.406 --> 00:40:38.666 Will not have an M spike on their serum protein electrophoresis and the serum.
00:40:38.670 --> 00:40:42.912 free light chains will be abnormal.
00:40:42.912 --> 00:40:45.772 chronic inflammation here.
00:40:45.772 --> 00:40:49.189 There are a number of disorders this patient has that cause chronic inflammation.
00:40:49.190 --> 00:40:51.675 I’m often thinking about a SED rate or CRP.
00:40:51.675 --> 00:40:53.166 So I might be thinking about a superfluous at this point,
00:40:53.170 --> 00:40:55.326 or I might think that’s superfluous at this point,
00:40:55.326 --> 00:40:59.815 that the patient does have chronic inflammation and I don’t really need to get a SED rate.
00:40:59.815 --> 00:41:00.970 SED rate or CRP,
But one of the things that I'm also thinking about is temporal arteritis. And in my history I'm asking about headaches, weakness in the shoulders, and I'm pressing on the temporal arteries when I examine a patient. Arteries when I examine a patient cause another diagnosis that you certainly don't want to miss and is a common diagnosis. And even though this anemia is not microcytic or macrocytic with the way we usually think about nutritional deficiencies, I am going also going to think about a nutritional deficiency here as combined.
with anemia of chronic inflammation or as a possible multifactorial process.

So even though this is not normal, not microcytic or macrocytic.

I certainly will worry about this. Anemia of chronic inflammation is also something we would think about and if you could go to the next slide please.

So this person does have stage 3 chronic kidney disease and about 17% of patients with chronic kidney disease stage three will have anemia.

And the next slide please, a very important slide here because I think this slide demonstrates to us that if you have a ferritin that is.
00:42:20.660 --> 00:42:23.481 200 or less with an iron saturation
NOTE Confidence: 0.818529248823529
00:42:23.481 --> 00:42:24.934 of 20% or less,
NOTE Confidence: 0.818529248823529
00:42:24.934 --> 00:42:27.188 you can still have iron deficiency if
NOTE Confidence: 0.818529248823529
00:42:27.188 --> 00:42:29.451 you have chronic kidney disease and
NOTE Confidence: 0.818529248823529
00:42:29.451 --> 00:42:32.296 the ferritin might even be as high as
NOTE Confidence: 0.818529248823529
00:42:32.296 --> 00:42:35.020 500 if you have more advanced kidney disease.
NOTE Confidence: 0.818529248823529
00:42:35.020 --> 00:42:38.620 And then so the final slide.
NOTE Confidence: 0.818529248823529
00:42:38.620 --> 00:42:40.130 Is that what I would do?
NOTE Confidence: 0.818529248823529
00:42:40.130 --> 00:42:42.790 I would certainly do the things we
NOTE Confidence: 0.818529248823529
00:42:42.790 --> 00:42:45.821 talked about the previous red cell CBC
NOTE Confidence: 0.818529248823529
00:42:45.821 --> 00:42:48.545 values or ticad peripheral blood count.
NOTE Confidence: 0.818529248823529
00:42:48.550 --> 00:42:51.196 I would probably give this person oral
NOTE Confidence: 0.818529248823529
00:42:51.196 --> 00:42:53.925 iron and see what happens with their
NOTE Confidence: 0.818529248823529
00:42:53.925 --> 00:42:57.552 anemia before I went off on a on a a
NOTE Confidence: 0.818529248823529
00:42:57.552 --> 00:42:59.763 workup that included a bone marrow biopsy.
NOTE Confidence: 0.818529248823529
I think if this person didn’t get better with oral iron or had monoclonal proteins in their blood or there was some other reason to suspect cancer, I would refer this patient to hematology. So I would hope that this patient gets better with iron, but otherwise I think I would refer this patient for an evaluation by a hematologist.

Great, thank you very, very much. I had one questions on the retic count, I had one questions on the retic count. I had one questions on the retic count. I had one questions on the retic count. I had one questions on the retic count. You know one of those hallmarks of teaching that I still remember is.
Uh if you have someone with who might have iron deficiency anemia and you give them iron and the, you know the first thing that might improve before their hemoglobin is the retic count to know that if they’re responding and just would just sort of ask if that’s still common teaching and something that we can follow because we’ll see someone in two weeks. Let’s say we put them on iron and if we hadn’t had the retic before but check it now it, would it still be helpful to know that maybe we’re on the right track?
Yeah, absolutely, frank.
The reticulocyte count should be the first thing to respond.
And now we get some additional fancier tests that articulus reticulocyte, hemoglobin content.
So that’s just what it is, the amount of hemoglobin in particular sites and that often will respond even before the reticular site count does.
OK. All right. Thank you. Ohh. All right. And we do have one, it totally falls into this question here.
How quickly do we expect to see a rise in the hemoglobin with iron supplement? If they’re appropriately dosed, it’s usually 1 gram and three to four weeks. All right, great. Thank you.
00:45:19.955 --> 00:45:22.280 comes in for routine physical.
NOTE Confidence: 0.902869432

00:45:22.280 --> 00:45:24.644 Her CBC is pretty much identical
NOTE Confidence: 0.902869432

00:45:24.644 --> 00:45:27.410 to the the year prior and we’ll
NOTE Confidence: 0.902869432

00:45:27.410 --> 00:45:30.490 point out that she has a high high,
NOTE Confidence: 0.902869432

00:45:30.490 --> 00:45:34.480 high platelets and a high MCV.
NOTE Confidence: 0.902869432

00:45:34.480 --> 00:45:35.548 I always think of before I
NOTE Confidence: 0.902869432

00:45:35.548 --> 00:45:36.480 was a doctor I was,
NOTE Confidence: 0.902869432

00:45:36.480 --> 00:45:39.603 I was actually a social worker in an HIV.
NOTE Confidence: 0.902869432

00:45:39.610 --> 00:45:41.845 Clinic and everyone had a
NOTE Confidence: 0.902869432

00:45:41.845 --> 00:45:45.640 high MCV back then, but.
NOTE Confidence: 0.902869432

00:45:45.640 --> 00:45:47.348 Otherwise, we don’t see it as often,
NOTE Confidence: 0.902869432

00:45:47.350 --> 00:45:50.556 but we thought that discussing a case
NOTE Confidence: 0.902869432

00:45:50.556 --> 00:45:53.750 of macrocytosis might be helpful to the
NOTE Confidence: 0.902869432

00:45:53.750 --> 00:45:56.360 to the participants and the attendees.
NOTE Confidence: 0.902869432

00:45:56.360 --> 00:45:59.030 So here’s the what we have,
NOTE Confidence: 0.902869432

00:45:59.030 --> 00:46:01.508 we’ll go to the next slide please.
Before we turn it over to Anna, here’s a list of her medications. There is an AC is not AZT or Combivir, but you can see she is on some medications for her colitis and a similar question. To the other two cases, what other testing or treatment would you recommend? And once again, one is a good time that we should be sending a referral to hematology. Alright, Anna, thank you. Thanks, Frank. Umm, just to touch on sort of
00:46:35.976 --> 00:46:38.720 macrocytosis and macrocytic anemia briefly.
NOTE Confidence: 0.628829122
00:46:38.720 --> 00:46:40.848 I wanted to start off by saying that,
NOTE Confidence: 0.628829122
00:46:40.850 --> 00:46:43.649 you know, I think you know as as Bob
NOTE Confidence: 0.628829122
00:46:43.649 --> 00:46:46.477 Donna mentioned also that the lines are
NOTE Confidence: 0.628829122
00:46:46.480 --> 00:46:48.840 not so clearly delineated sometimes.
NOTE Confidence: 0.628829122
00:46:48.840 --> 00:46:50.478 So even though we like to think of anemia
NOTE Confidence: 0.628829122
00:46:50.478 --> 00:46:52.009 and the three buckets of microcytic,
NOTE Confidence: 0.628829122
00:46:52.010 --> 00:46:54.908 normocytic and macrocytic.
NOTE Confidence: 0.628829122
00:46:54.910 --> 00:46:56.527 You know, using just the cut offs,
NOTE Confidence: 0.628829122
00:46:56.530 --> 00:46:58.612 you know for example an epic
NOTE Confidence: 0.628829122
00:46:58.612 --> 00:47:00.000 is is not always,
NOTE Confidence: 0.628829122
00:47:00.000 --> 00:47:01.757 is not always the way to go.
NOTE Confidence: 0.628829122
00:47:01.760 --> 00:47:03.800 Someone might be slightly macrocytic.
NOTE Confidence: 0.628829122
00:47:03.800 --> 00:47:05.676 I would still include you know all
NOTE Confidence: 0.628829122
00:47:05.676 --> 00:47:07.399 the workup that Doctor Bona just
NOTE Confidence: 0.628829122
00:47:07.399 --> 00:47:09.115 went through for the most part.
Like patients who are enormous headache, I might include workup that I’m about to go through now. I think where that doesn’t hold true is that the extremes. So somebody who’s extremely microcytic or extremely macrocytic, you know those differentials are are very different but I think there’s a big gray zone in the middle. Umm, in terms of macrocytic anemia, I think you know two of the buckets that that falls into our, whether it’s megaloblastic or non megaloblastic.
which really has to do with whether DNA synthesis is actually being impaired, megaloblastic anemia. What we mean when we say that is we see some characteristic findings both in the bone marrow and on the peripheral blood, but just to speak about the peripheral blood for our purposes, things like hypersegmented neutrophils and also macrocytic. These are can be indications that there is a megaloblastic process going on or impaired DNA synthesis leading to ineffective erythropoiesis.
the major causes of megaloblastic anemia are B12 and folate deficiency, which could really be a whole talk on its own. But you know briefly how we work this up in the clinic, the gotos are just serum B12 and folate levels. I will say that you know, again just relying on the normal range and. especially in the case of B12 level is sometimes be a pitfall because for a couple reasons. Umm, you know,
I sort of consider things in the less than 400 range to be very borderline. And though that's an area where I would always send an MMA to confirm, I put over here on the right an image to remind us, you know why we check homocysteine and MMA in B12 and folate deficiency and only homocysteine in folate deficiency. But so borderline B12 levels are a case where I would always send it.
also very strong clinical suspicion.

So even with a normal B12 level, if the story if everything else you know is really suspicious for B12 deficiency, I will send it.

It’s also worth being aware that patients with pernicious anemia. So auto antibodies to intrinsic factor or to parietal cells due to actually a lab interference due to issues with the assay with the presence of these antibodies can have a normal serum B12 on lab testing when they’re actually B12 deficient. So again, if you’re suspecting this,
you’d want to check an MA as well, Umm.

And then a reminder that B12, severe B12 deficiency, we can see neurologic deficits. And that’s why, you know, there’s the classic teaching that you want to be cautious not to treat folate deficiency without making sure that the patient does not have concurrent B12 deficiency, because you could have progression of neurologic symptoms in that setting because you’re not correcting the B12 deficiency. So B12 and folate deficiency can happen for a variety of reasons,
and I’ll go through some of the common ones between the two of them in a second, but particular to B12 is pernicious anemia. She just spoke about PPI, which can inhibit absorption of B12. Strictly vegan diet, as B12 is often found in animal products. Fully deficiency. Less commonly seen from a dietary perspective because at least in the US, flowers routinely supplemented with folic acid to prevent neural tube defects. So it’s less common to see this, but we do see an Alcoholics also in in patients who have high cell turnover.
For a variety of reasons.

So any patient with a chronic hemolytic anemia, including sickle cell anemia or psoriasis, these would be clinical scenarios in which you’d be more suspicious of folate deficiency.

And in cases of macrocytic anemia will pretty much always at minimum, you know send these two tests. So just very quickly in terms of causes, etiologies of both B12 and folic deficiency with which have to do with how these micronutrients are absorbed. So B12 when it’s consumed in the upper GI tract, binds to transcobalamin,
one, goes to the stomach, intrinsic factor is produced by the parietal cells of the stomach, binds to B12, goes into the small intestine where it's absorbed in the terminal ileum and then binds to transcobalamin 2. Absorbed into the bloodstream and taken up into the tissues, whereas folate is sort of a more passive absorption process but also absorbed in the small intestine. So for this reason anyone who’s had some kind of small bowel pathology including resection, whether that be small bowel resection,
bacterial overgrowth,
NOTE Confidence: 0.91861876125
inflammatory bowel disease,
NOTE Confidence: 0.91861876125
celiac disease,
NOTE Confidence: 0.91861876125
these patients are all at risk for deficiencies of both of these micronutrients.
NOTE Confidence: 0.91861876125
And then in particular you do have gastrectomy as a.
NOTE Confidence: 0.91861876125
to consider gastrectomy as a.
NOTE Confidence: 0.91861876125
Potential cause of loss of parietal
NOTE Confidence: 0.91861876125
cells and therefore intrinsic factor,
NOTE Confidence: 0.91861876125
which could also lead to B12 deficiency.
NOTE Confidence: 0.893134962857143
So this is just a very short list
NOTE Confidence: 0.893134962857143
of an otherwise very long list of
NOTE Confidence: 0.893134962857143
medications that can cause macrocytosis.
NOTE Confidence: 0.893134962857143
The ones I’ve included here and
NOTE Confidence: 0.893134962857143
many of the medications that that
NOTE Confidence: 0.893134962857143
do this in general actually do
this via a megaloblastic process.

So they actually do interfere with DNA synthesis, which is why we see this macrocytosis.

There are others that can cause macrocytosis for other reasons, for example.

If somebody has G6PD deficiency and develops you know hemolytic anemia from a medication and can have a reticulocytosis in that setting.

And and as Doctor Bonner showed us particular sites are larger cells.

So a higher percentage of particular sites increases your average MCV.
But here included are just medications that through megaloblastic process can cause an elevated MCV. And as Frank pointed out, antiretrovirals for HIV are a common one, so definitely something to consider if you have a patient on HIV medication. But there's a host of them here including allopurinol and mercaptopurine, which the patient in this question stem was on both, but also anti epileptics. Bacitracin and some other commonly used medications. And so in terms of non megaloblastic causes of macrocytic anemia,
I know we’re running short on time and there’s a lot to go through. But in general, so these are a means by which causes of macrocytosis that don’t have to do with interference with DNA synthesis. So you wouldn’t see those classic megaloblastic changes like hypersegmented neutrophils etcetera. For example, blood loss or anemia of chronic disease, liver disease can cause anemia for a variety of reasons, some of which would not be macrocytic. For example, blood loss or anemia of chronic disease,
but other means which can lead to macrocytosis, such as alterations in the cholesterol content of red blood cells. Also hemolysis, which could be either from hypersplenism, portal hypertension or as Doctor Bona also mentioned on this the review of different smear findings spur cell anemia, which in liver disease in particular is a poor prognostic sign. You know this site. We'll consider as guided by history. So if someone has a history of liver disease, there's concern by imaging abnormal LFT's, maybe a low albumin,
00:54:58.990 --> 00:55:00.370 a slightly abnormal INR,

00:55:00.370 --> 00:55:03.170 any smear findings that could be consistent?

00:55:03.170 --> 00:55:03.822 You know,

00:55:03.822 --> 00:55:06.104 those are the situations where I would

00:55:06.104 --> 00:55:08.385 consider that liver disease could be the

00:55:08.385 --> 00:55:10.450 cause of the underlying macrocytosis.

00:55:10.450 --> 00:55:13.312 Alcohol use certainly can lead to

00:55:13.312 --> 00:55:15.800 macrocytosis and this can actually

00:55:15.800 --> 00:55:18.770 take months to resolve after the


00:55:20.790 --> 00:55:23.584 It’s always important to take an alcohol

00:55:23.584 --> 00:55:26.236 history when working out these patients.

00:55:26.240 --> 00:55:29.282 As I mentioned increased reticulocytes which

00:55:29.282 --> 00:55:32.910 are larger cells and mature red blood cells,

00:55:32.910 --> 00:55:35.612 a higher percentage of reticular sites in

NOTE Confidence: 0.868297492727273
the peripheral blood increases the MCV.

So this is always something to consider like any anemia should be. You know, one of your go to 1st test is a reticulocyte count and if elevated you have to consider whether there could be an active, you know, a bleed, but more likely. You know, if this patient is really macrocytic, some kind of hemolysis and you’d want to send sort of a hemolytic evaluation. So LDH, haptoglobin, direct bilirubin, total bilirubin and a peripheral smear.
hypothyroidism can also lead to macrocytosis. You know, I do send this very often in these workups, but I think this also should be guided by history. I think it would be unusual to see somebody with a macrocytic anemia from hypothyroidism without otherwise having other signs and symptoms of that. Copper deficiency can cause anemia of pretty much, you know, any size red blood cell. But again, as guided by history, if someone has some kind of absorptive issue, dietary deficiencies for other reasons.
or zinc toxicity and you know, one of the sort of curls is somebody who’s using a denture glue that contains zinc, you know, which can paradoxically cause copper deficiency. Again, I don’t routinely send this just if it’s a high clinical suspicion or an otherwise totally negative. Uh, work up monoclonal gammopathy. So as Doctor Bona talked about two. So my threshold to send this for macrocytic anemia is very low. I’ll send it on pretty much anyone unless there’s a very clear cut reason.
You know why they have a macrocytic anemia. So that includes not just the spec but as Doctor Bona said the Immunofixation and the free light chains. And this can be even in the absence of other crab criteria. So even if you know the renal function is normal, they have no Bony pain calcium. Normally I would still send it. And then macrocytic anemia, the last thing I'll say I think is that you know even more so than the other, you know Norma acidic or microcytic anemias.
The clinical suspicion for an underlying bone marrow process or malignancy has to be quite high and the threshold to refer to hematology very low because we wouldn’t want to miss something like an MGS or an under other malignancy, especially if this preliminary workup which is all pretty easy to obtain is negative or especially in the case where there are concurrent. symptoms which might be concerning, but you know, the bottom line being that if there’s
no clear reason for macrocytosis, whether it be medication, A B12, folate deficiency or any of these other things that you know, the threshold should be very low to refer to hematology for further workout. Good. So I’ll take the liberty of just asking the two final questions and then we’ll wrap up.

So I’m doctor Zarkov power ask again about frequency of B12 level whether it should be continued
to be checked in patients on a bike rides and at what interval? 
Oh yeah. So good question. 
So I’m like on metformin. 
So that’s a good question. 
I don’t know that I really know the answer to that. 
My suspicion would be you know, as long as the patient is continuing on metformin, if they develop B12 deficiency on metformin, I would probably just keep them on B12, you know, now and then you know you could check a serum level and see if it’s responding every, you know, six months.
So obviously most patients are on metformin for years and years. I don’t know that there’s a clear cut guideline for how often. Repeat that, but I would probably just leave the patient on it. And then Doctor Reeve asks patients, especially seeing naturopaths bring in reports of their methyltetrahydrofolate reductase testing. And the question is how? How much do they need this very special form of folate that’s often prescribed for them if
they’ve been asymptomatic?

Yeah, no, I’m not aware of there being any data, you know,

You know, somebody has fully 50.

Folic acid usually use in one to two milligrams per day orally as well.

It’s very orally bioavailable,

you know, people will respond to that.

So no, I’m not aware of there being any other formulations that any other formulations would be necessary in the setting of fully deficiency and especially not, you know, if there’s no fully

And now one final question.

102
Like iron, I understand that the B12 orally is actually more effective than we've given it credit for. We have a lot of people who are on injections. So, you know, I think it depends on the severity of the deficiency and also the D so for example, not that any of us really see this anymore or or often, but if somebody were to present to you with neurologic symptoms for example, that's somebody you'd want to
I am injections right away.

You wouldn’t want to wait you know for an oral supplement also if it’s somebody who has B12 deficiency for a malabsorptive reason either because of a gastric bypass surgery. Permission, yeah, they’re not going to respond to PO supplementation. So those patients need to be on, I am probably lifelong, but otherwise in somebody who has bowed pathology who has no reason to not be absorbing it orally. PO B12 is very effective, you know, usually 1000 micrograms daily. Good.
Well, I the pace kind of picked up at the end and I apologize for my time management that didn’t have us a little more evenly spaced, but tremendous gratitude to all of our panelists. This was really terrific information. Like Frank, I was part of the preparation and still learned. So there were a lot of both, you know, very practical tips here the upcoming speakers are demonstrated, you know on the slide. Here we do not have a talk in January. It’s just a little early in the
month after the holidays to do that.

So please join us and if you don’t mind, please stay on.

There will be a very quick survey at the end in order to.

Just make sure that we get your feedback to help us in the future.

So Anne Chang couldn’t be here.

But on behalf of Anne and myself, we thank you so much for your attendance and again, thank you to our panelists.

Goodnight. Thank you. Goodnight.