

# Webinar Transcript Common Infections with CLL: Prevention and Treatment December 13, 2024

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00:05:35.000 --> 00:05:38.000 Hello and welcome to today's webinar.

00:05:38.000 --> 00:05:45.000 I am Robyn Brumble, a registered nurse and CLL Society's Director of Scientific Affairs and Research.

00:05:45.000 --> 00:05:53.000 At the CLL Society, we are dedicated to bringing credible and up-to-date information to the CLL and SLL community...

00:05:53.000 --> 00:05:57.000 because we believe smart patients get smart care.

00:07:05.000 --> 00:07:12.000 This program was made possible through support from both our donors and our industry partners.

00:07:12.000 --> 00:07:16.000 At this time, I would like to introduce our moderator.

00:07:16.000 --> 00:07:21.000 Thank you. Thank you, Robyn. I would like to welcome our audience...

00:07:21.000 --> 00:07:26.000 to today's event. I'm Dr. Brian Koffman, co-founder, Executive Vice President...

00:07:26.000 --> 00:07:29.000 and Chief Medical Officer of the CLL Society.

00:07:29.000 --> 00:07:39.000



And today we're joined by Dr. William A. Werbel. He's the Assistant Professor of Medicine, Division of Infectious Disease, Section of Transplant and Oncology Infectious...

00:07:39.000 --> 00:07:44.000 Diseases at Johns Hopkins University School of Medicine.

00:07:44.000 --> 00:07:53.000 He's also the Associate Director of Epidemiology and Quantitative Science at Johns Hopkins Transplant Research Center.

00:07:53.000 --> 00:07:58.000 And we'll be answering audience questions at the end of this event...

00:07:58.000 --> 00:08:04.000 so, please take advantage of that opportunity and ask your questions in the Q&A box.

00:08:04.000 --> 00:08:10.000 Before we begin, I'd like to share a few important disclaimers.

00:08:10.000 --> 00:08:13.000 The information provided during today's webinar...

00:08:13.000 --> 00:08:19.000 is for educational purposes only and should not be considered medical advice.

00:08:19.000 --> 00:08:23.000 For any personal health or treatment questions,...

00:08:23.000 --> 00:08:26.000 please consult your healthcare team.

00:08:26.000 --> 00:08:31.000 Please note that while te CLL Society may have its own opinions and policies,...

00:08:31.000 --> 00:08:34.000 our speakers may offer differing viewpoints,...

00:08:34.000 --> 00:08:38.000 especially about the management of CLL...

00:08:38.000 --> 00:08:42.000 and its complications, including infections.



00:08:42.000 --> 00:08:51.000 Now it's our pleasure to welcome Dr. William Werbel.

00:08:51.000 --> 00:08:55.000 Well, thanks very much for the introduction. My name is Bill...

00:08:55.000 --> 00:08:58.000 Werbel and uh, you know I take care of...

00:08:58.000 --> 00:09:00.000 patients with CLL and...

00:09:00.000 --> 00:09:06.000 as an infectious disease doctor trying to prevent or treat infections if they come up. So, I'm not a cancer expert, but...

00:09:06.000 --> 00:09:10.000 I do work closely in trying to keep people with cancer healthy.

00:09:10.000 --> 00:09:19.000 So with that, I wanted to spend some time now to talk about common infections in people with CLL and their prevention and treatment.

00:09:19.000 --> 00:09:21.000 So as a brief outline,..

00:09:21.000 --> 00:09:27.000 we'll talk first about a respiratory infection kind of status report and a little bit of a forecast for the winter;..

00:09:27.000 --> 00:09:35.000 then some general and CLL specific factors for serious respiratory diseases with the focus on viruses which are the most common infections;..

00:09:35.000 --> 00:09:37.000 some ways to reduce risk,..

00:09:37.000 --> 00:09:40.000 and then we'll drill down in sort of the three most...

00:09:40.000 --> 00:09:44.000 common viruses in the winter, RSV, influenza, and COVID-19.



00:09:44.000 --> 00:09:50.000

And hopefully we'll have time for this, it's a little bit of a grab bag at the end, about some relationship between certain...

00:09:50.000 --> 00:10:00.000

CLL drugs and certain infections, being a little bit more specific, and then really hopefully, have time to talk about emerging infections, meaning things that are kind of coming up...

00:10:00.000 --> 00:10:07.000 this year that are a threat to people who are immunocompromised.

00:10:07.000 --> 00:10:09.000 So in terms of...

00:10:09.000 --> 00:10:16.000

the status reporting forecasting. It's actually been relatively difficult to understand which viruses are circulating at a given time...

00:10:16.000 --> 00:10:27.000 due to variation in testing and reporting by the CDC and others. So, some have looked to wastewater, basically sewage, to see what is being shed in the community. And so these are from...

00:10:27.000 --> 00:10:33.000 A publicly available resource called BioBot, which is similar to what the CDC does. And to orient you, this is a graph of RSV,..

00:10:33.000 --> 00:10:44.000 where the purple line denotes how much RSV virus is kind of being found in the wastewater. There's a little teal circle there that should be January 1st, which you see is a theme through these.

00:10:44.000 --> 00:10:54.000 And then most importantly, the arrow here showing an uptick in late November that's continued now in early December, showing us that we are indeed in the start of an RSV surge that will likely peak...

00:10:54.000 --> 00:10:56.000 in the next...

00:10:56.000 --> 00:11:02.000



four to six weeks. Influenza is relatively similar, also tends to peak...

00:11:02.000 --> 00:11:07.000 at a relatively similar time as RSV, but kind of a longer lag time. It's usually a second hump...

00:11:07.000 --> 00:11:11.000 in the late winter, early spring...

00:11:11.000 --> 00:11:16.000 and also is ticking up. It's likely to begin about a week or two after RSV.

00:11:16.000 --> 00:11:19.000 And like I said, have a longer season...

00:11:19.000 --> 00:11:26.000 so, this is a timely, timely webinar. And then lastly, the hardest one I save for last, which is COVID-19 or SARS-CoV-2.

00:11:26.000 --> 00:11:32.000 You can see here, these are teal dots, those four ones here for the last four years of circulation.

00:11:32.000 --> 00:11:37.000 As you can see, there is about a January 1st surge as well with COVID-19...

00:11:37.000 --> 00:11:39.000 but there's usually like a second hump...

00:11:39.000 --> 00:11:48.000 in the late summer or early fall for the last two years, in particular. And then if you zoom all the way to the right of the graph, this was that most recent hump that peaked around...

00:11:48.000 --> 00:11:52.000 September, mid-September,..

00:11:52.000 --> 00:11:54.000 a little bit later than in the previous year or two.

00:11:54.000 --> 00:12:00.000 And right now, we're actually at a relatively low circulation relative to what we would probably anticipate later...



00:12:00.000 --> 00:12:02.000 in the winter.

00:12:02.000 --> 00:12:08.000 And, there is uncertainty here. I would probably predict that we'll be seeing it more in January,..

00:12:08.000 --> 00:12:20.000 maybe January, February, but it's really hard to know. And part of it is you can see kind of the glaring obvious giant spike in the middle of that graph that corresponded to the first Omicron wave, meaning a major shift in the viral variant...

00:12:20.000 --> 00:12:26.000 led to a lot of people being susceptible and eventually infected. That is basically always possible.

00:12:26.000 --> 00:12:33.000 It's becoming less and less likely over time owing to increased immunity. But the virus is tricky.

00:12:33.000 --> 00:12:39.000 So, I actually wanted to talk a little bit about the variant forecast because it directly relates to what we're discussing.

00:12:39.000 --> 00:12:41.000 So, there's a lot of letters that end up in the...

00:12:41.000 --> 00:12:48.000 numbers and the sort of alphabet soup of variants that show up on headlines and CNN and such. But to kind of drill down,..

00:12:48.000 --> 00:12:55.000 all the variants that are circulating now are children or grandchildren of some of the early Omicron variants.

00:12:55.000 --> 00:13:01.000 JN.1 was the most recent successful child that was part of the peak that was happening in the...

00:13:01.000 --> 00:13:08.000 fall and its grandchildren are KP.2 and KP.3. And those are actually, the targets of the updated vaccine that...



00:13:08.000 --> 00:13:11.000 some of us received this past fall.

00:13:11.000 --> 00:13:13.000 And those are the sort of greenish,...

00:13:13.000 --> 00:13:20.000 green purple sort of parts of these bar graphs, which are week by week variant proportions. There's a light green...

00:13:20.000 --> 00:13:25.000 graph, part of the graph that's increasing. And that variant is called XEC,...

00:13:25.000 --> 00:13:32.000 the newest member, an X, if you ever see that in a variant, means two variants combined together.

00:13:32.000 --> 00:13:39.000 And basically, this was the product of two JN.1 variants combining together. And it's likely the one that's going to be the most common in December.

00:13:39.000 --> 00:13:48.000 And it does seem to be a little bit more immune evasive, meaning evades some of our antibodies, but not a dramatic shift necessarily as compared to prior variants.

00:13:48.000 --> 00:13:56.000 There is another one on the horizon that you might see, I would bet maybe January, February, called LP.8.1, but that is beyond...

00:13:56.000 --> 00:14:03.000 the current discussion today and again, doesn't seem to be dramatically different than prior.

00:14:03.000 --> 00:14:09.000 So that was viruses and one bacteria I will bring up is something called mycoplasma,...

00:14:09.000 --> 00:14:15.000 which you may have heard of, and it increased in the US last fall and also this past fall, particularly in children and...

00:14:15.000 --> 00:14:20.000 it was the cause of this so-called white lung disease noticed in...



#### 00:14:20.000 --> 00:14:31.000

China, was concerned for maybe another COVID variant, and then places like Ohio and the United States. But it actually is a common bacteria that's a cause of walking pneumonia or a chest cold and spread through droplets and...

00:14:31.000 --> 00:14:36.000

coughing and sneezing like viruses and can be diagnosed kind of in the same way by swabbing your nose or in particular your...

00:14:36.000 --> 00:14:38.000 throat.

00:14:38.000 --> 00:14:47.000

The difference though is that you can treat this with antibiotics. And the classic antibiotic is the Z-pak or azithromycin, which in most cases should be effective.

00:14:47.000 --> 00:14:54.000 Though what is a little notable, as per the CDC, is that there is some increase in resistance to azithromycin...

00:14:54.000 --> 00:14:59.000 so second line antibiotics such as doxycycline or other ones called moxifloxacin or...

00:14:59.000 --> 00:15:04.000 Avelox may be used if people have a known diagnosis of mycoplasma and they're not improving.

00:15:04.000 --> 00:15:13.000 So, there was more of this in the late fall and early winter. It may be a player this winter as well. It's just something to be on the radar.

00:15:13.000 --> 00:15:16.000 Okay, so that is the forecast of the forecast for...

00:15:16.000 --> 00:15:19.000 the winter. And now the reason we're having this...

00:15:19.000 --> 00:15:28.000

webinar is because people with CLL are more likely to get certain infections. And so, we'll talk a little bit about the why of that. Why is that the case?

00:15:28.000 --> 00:15:35.000



Many people with CLL are older, 60s or 70s, with non-CLL medical conditions that can be exacerbated by getting...

00:15:35.000 --> 00:15:43.000

an infection and also contribute to reduced immunity like diabetes or heart or lung disease.

00:15:43.000 --> 00:15:55.000

CLL by its nature does sap the good immune system. A lot of energy is being put into the wrong kind of immune cells and supplies a less functional one in its place, particularly lymphocytes that we'll talk about a little bit later. That's the L...

00:15:55.000 --> 00:15:59.000 in CLL, such as the B cells, which make good antibodies...

00:15:59.000 --> 00:16:02.000 which are less likely to be produced in people with CLL...

00:16:02.000 --> 00:16:06.000 and in particular, people who are on treatments for CLL.

00:16:06.000 --> 00:16:10.000 So, things like steroids or chemotherapy or getting a bone marrow transplant...

00:16:10.000 --> 00:16:16.000 further impair the immune system actually, in an additional way. So other parts, not just the lymphocytes,..

00:16:16.000 --> 00:16:18.000 for example, and that can lead to...

00:16:18.000 --> 00:16:21.000 having it be easier to get an infection...

00:16:21.000 --> 00:16:26.000 harder to fight it off if you get an infection and does unfortunately interfere with some of the...

00:16:26.000 --> 00:16:31.000 impact of preventative vaccines, which are key to keeping us well.

00:16:31.000 --> 00:16:38.000



So, to kind of frame this in a pictographic kind of way, I wanted to show this graphic that I helped develop for a CDC...

00:16:38.000 --> 00:16:45.000 affiliated website to look at COVID-19 as an example, but you could substitute in other viruses here or other infections to kind of create a...

00:16:45.000 --> 00:16:47.000 continuum of risk,..

00:16:47.000 --> 00:16:49.000 from lower risk on the left side to..

00:16:49.000 --> 00:16:56.000 higher risk on the right side. And for COVID in particular, but for many of these viruses, the most important risk factor for getting a severe infection is how old you are.

00:16:56.000 --> 00:17:00.000 And so people, particularly in their 70s, are going to be at higher risk for some of these...

00:17:00.000 --> 00:17:08.000 infections we discussed. Also, not every 70 year old is the same person with respect to their other medical conditions. So as those increase, the potential for...

00:17:08.000 --> 00:17:15.000 infections or maybe complications related to your underlying medical conditions will go up.

00:17:15.000 --> 00:17:23.000 And then one thing that we definitely can change is being vaccinated. So being unvaccinated against whatever disease we're talking about is the highest risk situation versus...

00:17:23.000 --> 00:17:28.000 having a full vaccination and boosting ideally with an updated formulation...

00:17:28.000 --> 00:17:30.000 from last year would be the lowest risk.

00:17:30.000 --> 00:17:37.000

And then there's this big sliding scale of immunosuppression. And in my line of work, I mostly deal with the right side here of people with...



00:17:37.000 --> 00:17:39.000 more intense immunosuppression, organ transplants,...

00:17:39.000 --> 00:17:45.000 people who get lymphodepleting therapies such as rituximab or Obinutuzumab,...

00:17:45.000 --> 00:17:50.000 people who have CLL or stem cell transplants. Those are on the higher end, particularly when the disease is active...

00:17:50.000 --> 00:17:55.000 and being treated. And the issue, as I mentioned, is not only does that make it easier to get infections....

00:17:55.000 --> 00:17:58.000 but they do negatively impact

00:17:58.000 --> 00:18:01.000 some of the benefits of vaccination.

00:18:01.000 --> 00:18:07.000

So, what are some general things that one could do to reduce infections? And some of this sounds like something you learn in school but...

00:18:07.000 --> 00:18:13.000 it's good to review. The one first is wash your hands. And I actually, mentioned that specifically because hand sanitizer is good but not perfect.

00:18:13.000 --> 00:18:17.000 Washing hands for certain viruses actually is important.

00:18:17.000 --> 00:18:22.000 Although there has been controversy in the news and things related to masking,...

00:18:22.000 --> 00:18:27.000 when I go see somebody in the hospital who has influenza, I always wear a mask and...

00:18:27.000 --> 00:18:34.000 eye protection is actually, required. So clearly, if the doctors are doing it, there's probably something good about masking.

00:18:34.000 --> 00:18:41.000



And it's a relatively low risk and inexpensive intervention. And so particularly high quality, well-fitted masks when indoors...

00:18:41.000 --> 00:18:45.000 in high risk situations, so like large groups of people,...

00:18:45.000 --> 00:18:54.000 particularly at times when there are high viral circulation like December, January, February, and a setting that's poorly ventilated would be higher risk. For example, 100 people in a church basement...

00:18:54.000 --> 00:19:00.000 in a choir when everyone's unmasked and the windows are all closed is going to be the highest risk situation versus...

00:19:00.000 --> 00:19:04.000 outside in a fairground with you know 40 people...

00:19:04.000 --> 00:19:07.000 is not going to be high risk at all.

00:19:07.000 --> 00:19:17.000

Another thing that we can do that doesn't affect us but doesn't directly affect us but indirectly helps us is ensuring that close contacts are vaccinated around you,..

00:19:17.000 --> 00:19:26.000

forming this ring of protection. And those people should also let you know if they're not feeling well or ideally asked before gatherings. They are home tested for COVID as well as more recently for influenza.

00:19:26.000 --> 00:19:35.000 And then one that we'll spend a little time on today is what we would call immunoprophylaxis, meaning preventative things that you can do with your immune system, and that would be vaccines,..

00:19:35.000 --> 00:19:38.000 the most common kind, or passive...

00:19:38.000 --> 00:19:43.000 antibody infusions or injections that can help on top of that.

00:19:43.000 --> 00:19:47.000



And we're not going to talk about the use of certain drugs as that would be outside of the scope.

00:19:47.000 --> 00:19:52.000 So I want to talk about how vaccines work as depicted here fighting off...

00:19:52.000 --> 00:19:54.000 cartoon viruses.

00:19:54.000 --> 00:20:00.000 Basically, the whole point of a vaccine is to show you in advance a small important piece of something that could make you sick later.

00:20:00.000 --> 00:20:07.000

You get a head start on it. The things you probably need to be shown it a couple of times before you can really develop full immunity. And that's the sort of concept of...

00:20:07.000 --> 00:20:11.000 priming and then boosting an immune response.

00:20:11.000 --> 00:20:18.000 Relevant to those lymphocytes I mentioned before, one of the main things that vaccines do where they make your B cells make antibodies and they store that memory...

00:20:18.000 --> 00:20:24.000 for a rainy day. If you have a lot of really great antibodies produced and they're very active, they can neutralize...

00:20:24.000 --> 00:20:30.000 the infection, if you have enough of those, you won't get infected. They will block infection altogether.

00:20:30.000 --> 00:20:36.000 The problem is that these will wane over time. And even to begin, there are some people, including people with CLL, who...

00:20:36.000 --> 00:20:41.000 aren't able to produce high and high quality levels of antibody.

00:20:41.000 --> 00:20:47.000

What is arguably as or more important is this concept of T cell memory, another kind of lymphocyte....



00:20:47.000 --> 00:20:50.000 that is important because once the defenses are breached...

00:20:50.000 --> 00:20:53.000 so, you get infected, which happens,...

00:20:53.000 --> 00:20:57.000 those T cells send alarm signals around the body to kind of rally the troops,...

00:20:57.000 --> 00:21:05.000 including antibodies. And certain ones, like killer T cells, are designed to clear and destroy infected cells once the infection begins.

00:21:05.000 --> 00:21:12.000 This is probably most key to prevent severe disease once you get infected, like getting pneumonia from RSV, for example,..

00:21:12.000 --> 00:21:15.000 after infection.

00:21:15.000 --> 00:21:24.000

So the issue and the reason we have this talk here is that if a person either one, doesn't have enough immune cells, you take medicine or you have a cancer that prevents the development of good immune cells;..

00:21:24.000 --> 00:21:29.000 or the cells that you have are weakened or because of medicines you take,...

00:21:29.000 --> 00:21:34.000 vaccine immunity will be diminished. And so the reasons to, rather..

00:21:34.000 --> 00:21:36.000 the ways to...

00:21:36.000 --> 00:21:43.000 reduce some of this deficit is to get potentially more vaccines or vaccines of a different kind, such as those of a higher dose...

00:21:43.000 --> 00:21:46.000 or with an immune booster in it, like an adjuvant.

00:21:46.000 --> 00:21:49.000 Which is a term of art we'll talk about.



#### 00:21:49.000 --> 00:21:56.000

So the complement, meaning the thing that will go along with vaccines, they're important and they will help, but if they're not...

00:21:56.000 --> 00:22:02.000

totally protective, we can provide these sort of passive immunity through antibody infusions, right? And as many people I'm sure on this call are familiar with,..

00:22:02.000 --> 00:22:05.000 there is something called..

00:22:05.000 --> 00:22:12.000

hypogammaglobulinemia, or basically having low antibodies, sometimes referred to as CVID,..

#### 00:22:12.000 --> 00:22:20.000

there's a certain subtype of that. And particularly people with low antibodies and the documentation that vaccine responses are poor, for example, we sometimes test...

00:22:20.000 --> 00:22:23.000 people for like flu antibody after they get a vaccine.

00:22:23.000 --> 00:22:32.000

This can be an issue and puts you at risk for getting infections. And if a person has a history of recurrent sinus infections and is shown to have hypogammaglobulinemia...

00:22:32.000 --> 00:22:38.000 Then, using intravenous immunoglobulin, meaning IV infusions of antibody like IVIG,...

00:22:38.000 --> 00:22:44.000 can help. Usually, it's given every two or four weeks. And it turns out, and these are two graphs here,..

00:22:44.000 --> 00:22:53.000 those antibodies are able to usually recognize and often neutralize common viruses because they're pooled products from everybody in the community. And we've all had flu a bunch of times.

## 00:22:53.000 --> 00:23:08.000

Blood donors tend to be healthy and antibodies tend to be functional. So there is neutralizing antibody against flu in IVIG. And on the right here, this is like the Omicron variant neutralization. And in the sort of circle, open dots, these are people pre-IVIG,.,



00:23:08.000 --> 00:23:12.000 then you get IVIG, and then you're neutralizing antibodies increase...

00:23:12.000 --> 00:23:16.000 for some people to be about, basically similar to the light gray dots, which are healthy people.

00:23:16.000 --> 00:23:18.000 So this is something that can be added on top..

00:23:18.000 --> 00:23:20.000 to vaccination because remember...

00:23:20.000 --> 00:23:25.000 these are just antibodies. There's none of that great T cell stuff that you will also need hopefully,..

00:23:25.000 --> 00:23:28.000 your body will generate to prevent severe disease.

00:23:28.000 --> 00:23:32.000 They work together. All right, so now we're going to talk about...

00:23:32.000 --> 00:23:38.000 a couple of the individual viruses and some of their ins and outs,...

00:23:38.000 --> 00:23:40.000 to be more sort of pointed.

00:23:40.000 --> 00:23:50.000 The first is RSV or respiratory syncytial virus, a common cold virus, but it's actually, despite not getting as much press, it's about as severe as flu in older adults.

00:23:50.000 --> 00:23:54.000 Actually, the lung problems related to RSV tend to be even more serious.

00:23:54.000 --> 00:23:59.000 It is a cause of up to 10,000 deaths per year in adults, typically older adults...

00:23:59.000 --> 00:24:03.000 who are frailer or have chronic lung disease or are immunocompromised.



00:24:03.000 --> 00:24:08.000 And it's the leading cause of hospitalization in young children in the winter.

00:24:08.000 --> 00:24:14.000 So going back a year or so, when there was a national study looking at people with RSV, adults...

00:24:14.000 --> 00:24:22.000 who are older and were in the hospital, the majority of these people were 75 years or older, thinking back to that pictograph with those sort of blue to red risk factors.

00:24:22.000 --> 00:24:26.000 And almost everybody had at least one risk factor for having a...

00:24:26.000 --> 00:24:33.000 severe infection. Five percent of people who are hospitalized died. And then another series, actually, I was part of...

00:24:33.000 --> 00:24:39.000 up to 10% of people who had certain organ transplants, for example, may die after hospitalization for RSV.

00:24:39.000 --> 00:24:41.000 These are generally people who are very old.

00:24:41.000 --> 00:24:50.000 And there are often conversations about using ventilators and stuff like that in that circumstance. So that really just has to be noted.

00:24:50.000 --> 00:24:55.000 Many, many people get RSV, only a certain number get hospitalized and of those...

00:24:55.000 --> 00:25:01.000 a small, you know, a moderate percentage of people can get seriously ill.

00:25:01.000 --> 00:25:05.000 Fortunately, we're in the midst of a revolution, which are RSV vaccines.

00:25:05.000 --> 00:25:10.000 And these are three of the plots from the three landmark studies that show in the blue versus the orange.

00:25:10.000 --> 00:25:15.000



If you didn't have a vaccine versus you did, your risks of getting things like pneumonia from RSV are much, much lower,..

00:25:15.000 --> 00:25:21.000 up to three quarters lower, depending upon the study. And all these vaccines, all...

00:25:21.000 --> 00:25:24.000 create high levels of antibody in healthy adults.

00:25:24.000 --> 00:25:30.000 The three here, Arexy by GSK, Abrysvo by Pfizer, and mRESVIA by Moderna,...

00:25:30.000 --> 00:25:37.000 they appear to be safe. There are rare instances of an autoimmune nerve problem called Guillain-Barre syndrome...

00:25:37.000 --> 00:25:40.000 that are deemed by the CDC to be...

00:25:40.000 --> 00:25:46.000 low risk due to there being less than 10 per 1 million doses administered so far.

00:25:46.000 --> 00:25:52.000 But that means 999,990 people did not have this problem.

00:25:52.000 --> 00:25:59.000 The issue is that there are no published data for people with CLL. There was a Pfizer, there is a Pfizer trial that has yet to be published,..

00:25:59.000 --> 00:26:03.000 some of those data were shown to the CDC that showed that it was safe.

00:26:03.000 --> 00:26:08.000 But we don't have enough information on that.

00:26:08.000 --> 00:26:13.000 So I belabor that. I talk about that because the best treatment for RSV is prevention.

00:26:13.000 --> 00:26:18.000 And the CDC now recommends a single RSV vaccine dose for all adults 75 or older.

00:26:18.000 --> 00:26:23.000 And then for adults 60 to 74 who are at increased risk for severe RSV, and I would



00:26:23.000 --> 00:26:27.000 for intents and purposes, consider that anybody with CLL at this time.

## 00:26:27.000 --> 00:26:39.000

Notably, CDC did not expand the recommendation down below 60, nor did they recommend a second dose, despite some of the data that the vaccine companies provided.

00:26:39.000 --> 00:26:47.000 If you do get sick, tell your doctor because you can get medicine for this. One would be IVIG, which can be given acutely as treatment,..

#### 00:26:47.000 --> 00:26:57.000

especially for someone who we know has low antibodies. There is an antiviral called ribavirin, which can be used for people. The best data are for actually, bone marrow transplant recipients...

00:26:57.000 --> 00:27:03.000 who have basically like the cold version of RSV and preventing the pneumonia version. So, that's the best...

00:27:03.000 --> 00:27:07.000 data for that. In other groups, it's a little bit less well established.

00:27:07.000 --> 00:27:10.000 So talk to your doctor.

00:27:10.000 --> 00:27:16.000 That's RSV, which, as I mentioned, is surging now in the United States. Soon to follow would be influenza...

00:27:16.000 --> 00:27:23.000 which is, I think we're a little bit more familiar with. About one out of 10 people in the US gets flu every year, which is like around 30 million people.

00:27:23.000 --> 00:27:25.000 And of those people,..

# 00:27:25.000 --> 00:27:35.000

about 500,000 or so can be hospitalized and up to 50,000 people may die. And this really varies based upon how many people get vaccinated and how good the vaccine is in terms of matching with...



00:27:35.000 --> 00:27:41.000

what's circulating. And, you know, we know that if you don't see anybody and you don't interact, there will be no flu.

00:27:41.000 --> 00:27:47.000 That's what happened during COVID, but we're back towards basically normal interaction. So there will be flu.

00:27:47.000 --> 00:27:54.000 Now people, similar to RSV, basically the risk of potentially dying if you get hospitalized with flu is relatively high...

00:27:54.000 --> 00:28:05.000

in all comers with blood cancers, particularly more likely in people who are older, as I mentioned, with other major medical problems and very low immune systems. And part of the issue is that people can get a second...

00:28:05.000 --> 00:28:08.000 sort of like a double pneumonia, so to speak,...

00:28:08.000 --> 00:28:13.000 bacteria that normally lives in your lungs can cause problems when your immune

system is focused on fighting off the flu.

00:28:13.000 --> 00:28:20.000

And unfortunately, it is associated with things like heart attacks and strokes. So even more reason to get vaccinated and to get treatment, as we'll talk about...

00:28:20.000 --> 00:28:24.000 if you're ill. So for flu treatment,...

00:28:24.000 --> 00:28:28.000 the main one you're probably familiar with is Tamiflu, or oseltamivir, which...

00:28:28.000 --> 00:28:33.000 can reduce severe disease in high-risk people. So, the combination of being vaccinated and taking Tamiflu if you have flu...

00:28:33.000 --> 00:28:36.000 will definitely reduce your risk of getting very sick.

00:28:36.000 --> 00:28:45.000



Earlier is better with Tamiflu, usually if you give it within the first couple days, that's what the best data are that it can reduce things like getting hospitalized.

00:28:45.000 --> 00:28:50.000 It can cause some stomach upset so, that should be counseled and be aware of that.

00:28:50.000 --> 00:29:00.000 And there are rare cases of resistance of flu to Tamiflu that can emerge over time, but they are, you know, 99% of the time, this is not an issue.

00:29:00.000 --> 00:29:07.000 I think notably and probably less well publicized is that Tamiflu can be given as what we call post-exposure prophylaxis.

00:29:07.000 --> 00:29:13.000 You say, my spouse just came down with the flu two days ago. I feel kind of okay, but we live together.

00:29:13.000 --> 00:29:17.000 That's actually a reason to give Tamiflu if given early on in the...

00:29:17.000 --> 00:29:24.000 disease, even if you don't have a confirmed diagnosis. And that can be, actually, pretty powerful and it works.

00:29:24.000 --> 00:29:36.000 The other drug that's available that actually the WHO recommends as the first line therapy, but that's not quite the case in the United States, is a drug called baloxivir or Xofluza, which is approved for the same things that Tamiflu is, but the benefit of...

00:29:36.000 --> 00:29:42.000 this drug is that it's a single dose. And I particularly like it as an idea for post-exposure prophylaxis...

00:29:42.000 --> 00:29:47.000 because you just take the one pill and that's what's recommended as opposed to maybe taking...

00:29:47.000 --> 00:29:50.000 pills for five to 10 days after exposure.

00:29:50.000 --> 00:29:55.000



The problem is there can be resistance to this drug as well. We have a little bit less experience with it,..

00:29:55.000 --> 00:29:58.000 some have thought that it can be combined with Tamiflu,...

00:29:58.000 --> 00:30:05.000 but it's not clear that that necessarily adds much. So that's not something that's basically typically done. It's usually one or the other.

00:30:05.000 --> 00:30:07.000 But these drugs should be available,...

00:30:07.000 --> 00:30:09.000 if needed.

00:30:09.000 --> 00:30:12.000 Okay, and then the last parts about flu relate to flu shots.

00:30:12.000 --> 00:30:21.000

The most common shot we're probably familiar with. There are many available vaccines. It's a little bit confusing. They all should have some benefit, but the ones I think that are relevant, particularly to older people...

00:30:21.000 --> 00:30:29.000

on the call here are the high dose and adjuvanted vaccines, which are recommended for people 65 and older, because they are, they do create better immune responses.

00:30:29.000 --> 00:30:34.000 The names are listed here if you were to ask at the pharmacy, these should be available to you.

00:30:34.000 --> 00:30:37.000 Don't take a live inhaled vaccine.

00:30:37.000 --> 00:30:39.000 Hopefully you know about that.

#### 00:30:39.000 --> 00:30:48.000

You know, we can't turn back the clock, but it's generally better to give flu shots in late October or early November because the protection for flu shots is the highest in the first three months after you get them.



00:30:48.000 --> 00:30:54.000

Think about the flu peaks in December, January, February, you kind of want those to be when your immune system is...

00:30:54.000 --> 00:30:57.000 feeling really good as opposed to before that time.

00:30:57.000 --> 00:31:00.000 What is important is that you can get a flu shot with any other shot.

00:31:00.000 --> 00:31:07.000 The one kind of caveat is that if you're going to get a shot that has an adjuvant or immune booster in it already, like a COVID shot...

# 00:31:07.000 --> 00:31:16.000

or an RSV shot that has that, they tend to not recommend getting an adjuvanted flu shot at the same time because you may have more side effects. Not necessarily serious, but ones that might be uncomfortable.

#### 00:31:16.000 --> 00:31:26.000

It is important to note that for a flu shot and for all these inactivated vaccines like RSV and COVID, you don't need to time your IVIG dose. Just do it as you're doing it. That shouldn't interfere.

#### 00:31:26.000 --> 00:31:34.000

And one that you might have heard of when you were younger is if you have an egg allergy, you can't get a flu shot. That is not true. You can get any flu shot, including ones that include eggs.

00:31:34.000 --> 00:31:42.000

The only reason would be if you've taken a flu shot before and had a reaction, then the suggestion would be to get a different one than that one.

00:31:42.000 --> 00:31:44.000 Next slide.

00:31:44.000 --> 00:31:49.000 So in CLL and flu, there's not as much information as il kind of wish but...

#### 00:31:49.000 --> 00:31:59.000

kind of like what other vaccines, flu responses are generally poorer. So sometimes as few as maybe a fifth of people will show a boost in their high levels to high levels of antibody...



#### 00:31:59.000 --> 00:32:05.000

but it does reduce severe outcomes. People are less likely to get very sick if you get a flu shot, probably from some of that T cell...

00:32:05.000 --> 00:32:13.000 benefit we talked about before. And as I mentioned, the higher dose in adjuvanted vaccines do improve response, particularly in older persons.

00:32:13.000 --> 00:32:20.000 Now, some medications that many of you may be taking, like the anti-CD20 medicines, rituximab or obinutuzumab...

00:32:20.000 --> 00:32:25.000 or these BTK inhibitors like ibrutinib and Imbruvica or acalabrutinib or

00:32:25.000 --> 00:32:30.000 zanubrutinib, they do really impair antibody responses a little bit more powerfully than some other medicines.

00:32:30.000 --> 00:32:38.000 So, there are recommendations to try to wait a few months from rituximab, for example, to get your shots and wait a couple weeks after the shot before...

00:32:38.000 --> 00:32:45.000 you restart it. But the thing is, you know, time marches on. And so, any vaccine is better than no vaccine in advance of a flu season.

00:32:45.000 --> 00:32:48.000 If that window were to like...

00:32:48.000 --> 00:32:53.000 deep into flu season, it's not worth waiting. You should just get the vaccine before and then readdress...

00:32:53.000 --> 00:32:56.000 later.

00:32:56.000 --> 00:33:02.000 We're not going to talk about vaccination after bone marrow transplant because it's quite complicated and you're basically...

00:33:02.000 --> 00:33:06.000



in a situation where many people say, consider it that you've got no vaccines and restart everything.

00:33:06.000 --> 00:33:08.000 Long story short.

00:33:08.000 --> 00:33:14.000 All right, so that was RSV and flu, and now we'll talk about COVID as the last virus before we do sort of a grab bag.

00:33:14.000 --> 00:33:22.000 You know, we all have a lot of collective trauma here from COVID in the early days if you are immunocompromised or work with people who are immunocompromised...

00:33:22.000 --> 00:33:25.000 with high mortality in the early waves and older adults with...

00:33:25.000 --> 00:33:27.000 immune system issues.

00:33:27.000 --> 00:33:34.000 But the current risk of severe disease is much, much lower. The number of people who are hospitalized has gone down probably...

00:33:34.000 --> 00:33:36.000 you know 20-fold...

00:33:36.000 --> 00:33:46.000 due to a combination of immunity, people getting infections and vaccines, as well as our having a lot of antivirals to treat that we'll discuss. And plus, we know what we're doing, at least on the doctor side.

00:33:46.000 --> 00:33:52.000 The post-COVID condition thing, I'll just mention briefly, like long COVID is not very well understood, unfortunately, still.

00:33:52.000 --> 00:33:59.000

In the early waves, we saw people who were really sick in the ICU and we were familiar with that, that it will take months to get better from that.

00:33:59.000 --> 00:34:02.000 And in the middle wave, something that is still happening a bit...



00:34:02.000 --> 00:34:05.000 some people can get prolonged infections...

00:34:05.000 --> 00:34:08.000 with COVID and not feel normal.

00:34:08.000 --> 00:34:10.000 And that can still happen...

00:34:10.000 --> 00:34:17.000 in the sort of going forward future here of this, I'm not sure what the landscape is. Ideally, if you can avoid getting infected, that would be...

00:34:17.000 --> 00:34:21.000 great. Though you have to live your life.

00:34:21.000 --> 00:34:26.000 Now, as we talked about these variants before with all the numbers and letters, I do think it's worth...

00:34:26.000 --> 00:34:29.000 reiterating why it matters for people with CLL.

00:34:29.000 --> 00:34:36.000

We know at baseline vaccine responses are poorer. And if you look at this plot here from the CDC, the dark blue dots are like how many people...

00:34:36.000 --> 00:34:43.000 showed that they even developed any antibody after the first two COVID shots. And it was 50:50 for some people with CLL...

00:34:43.000 --> 00:34:47.000 as compared to 100% of the average healthy person.

00:34:47.000 --> 00:34:55.000 And if you don't make the antibodies, you can't block the initial infection. And then some proportion of people will develop severe disease or difficult to clear infections, as I just mentioned.

00:34:55.000 --> 00:35:00.000

You know, if I were writing a board exam for infectious disease doctors and I said, who's somebody who's going to have the worst...



00:35:00.000 --> 00:35:03.000 trouble clearing off COVID, uh you know,...

00:35:03.000 --> 00:35:09.000 or SARS-CoV-2 infection, an older person with CLL taking rituximab....

00:35:09.000 --> 00:35:11.000 who hasn't had a ton of vaccines...

00:35:11.000 --> 00:35:14.000 would be a classic case, for a classic case...

00:35:14.000 --> 00:35:16.000 prolonged course with COVID.

00:35:16.000 --> 00:35:19.000 And unfortunately, as the variants change,

00:35:19.000 --> 00:35:22.000 we lost some of our good drugs like these monoclonal antibodies.

00:35:22.000 --> 00:35:26.000 So that does reduce our armamentarium.

00:35:26.000 --> 00:35:29.000 You know, we are in a situation, as I mentioned that...

00:35:29.000 --> 00:35:39.000

the number of people who are getting severe disease is much, much lower, but the relative risk compared to an average person is still 10 to 20 times higher if you're a person, for example, with CLL as compared to a...

00:35:39.000 --> 00:35:44.000 30-year-old person with no medical issues walking around.

00:35:44.000 --> 00:35:50.000 So, with accumulated information about these variants and vaccines, which are very safe,..

00:35:50.000 --> 00:36:02.000

it has been recently recommended by the CDC that people who are greater than 65 or who are immunocompromised receive actually, two vaccines, two doses in a year, as opposed to like this once-a-year flu type of situation.



00:36:02.000 --> 00:36:11.000

They recommend separating by six months. That's actually kind of the upper limit, it can be closer. So somewhere between two and six months is the recommendation. There is flexibility...

00:36:11.000 --> 00:36:15.000 to prevent even additional boosts, for example, people who have had bone marrow transplants.

00:36:15.000 --> 00:36:21.000 There isn't a recommendation for one vaccine over another. Antibody levels tend to be a little bit higher with the Moderna shot,..

00:36:21.000 --> 00:36:27.000 side effects tend to be a little bit lower with the Novavax shot. It's really whatever you're comfortable with and is available.

00:36:27.000 --> 00:36:32.000 There is discussion about whether someone who's had a recent infection should get a vaccine and...

00:36:32.000 --> 00:36:36.000 some people say you can wait a few months after that, kind of thinking of it...

00:36:36.000 --> 00:36:40.000 almost like if it were a vaccine, so to speak and I think...

00:36:40.000 --> 00:36:42.000 one model for vaccination that might work...

00:36:42.000 --> 00:36:46.000 is somebody getting a vaccine in the, uh let's say,

00:36:46.000 --> 00:36:48.000 late summer and then again...

00:36:48.000 --> 00:36:51.000 let's say three or four months later in...

00:36:51.000 --> 00:36:57.000 December to kind of give the coverage for the rest of the winter.

28



00:36:57.000 --> 00:37:03.000

Now, we've talked about IVIG, which can potentially help with all the many different viruses...

00:37:03.000 --> 00:37:09.000 for people who have lower vaccine response. And we've gone through now a couple of...

00:37:09.000 --> 00:37:14.000 monoclonal antibodies as prevention or prophylaxis, some of you may have received this. When these work,..

00:37:14.000 --> 00:37:21.000 these antibodies do reduce severe disease significantly, but the problem is the variants outsmart them. And we're kind of in that pattern yet again.

00:37:21.000 --> 00:37:24.000 The currently available drug called pemivibart or Pemgarda,...

00:37:24.000 --> 00:37:30.000 it's uncertain whether it remains highly active against some of the more recent variants. It depends on who you ask, basically.

00:37:30.000 --> 00:37:37.000 On the left is a study from the New England Journal that showed really significant decrease in neutralization among one of those KP

00:37:37.000 --> 00:37:40.000 variants that gold one there on the right...

00:37:40.000 --> 00:37:45.000 but then the company released information that says on their hands that there should be...

00:37:45.000 --> 00:37:48.000 neutralization of these variants...

00:37:48.000 --> 00:37:52.000 is decreased but not gone.

00:37:52.000 --> 00:37:55.000 And there's actually, another...



00:37:55.000 --> 00:38:03.000

group that found somewhat similar. A lot of reduced neutralization, but not useless, so to speak. So, I would say the jury is out on this.

#### 00:38:03.000 --> 00:38:11.000

The natural history is that variants are smarter than we are. So, I wouldn't be banking on this as the thing that prevents you from getting sick per se as compared to, for example,..

00:38:11.000 --> 00:38:16.000 vaccines and protecting yourself through other means that we discussed.

00:38:16.000 --> 00:38:20.000 All right, so the last part about COVID before we kind of start closing up is...

00:38:20.000 --> 00:38:25.000 treatment for COVID. So, if you're a person who has a lot of things on the right side of that...

00:38:25.000 --> 00:38:31.000 graphic that I showed you, antivirals can reduce the chances of being sick and...

00:38:31.000 --> 00:38:35.000 these are the three in each row that are currently approved. The first one is called remdesivir.

00:38:35.000 --> 00:38:39.000 It's a very good, safe drug that's FDA approved...

00:38:39.000 --> 00:38:44.000 but it's only available in IV. So, some of you may have had this experience, you have to go to an infusion center. It's kind of annoying.

00:38:44.000 --> 00:38:47.000 If you can do it, it's great. But if you can't,...

00:38:47.000 --> 00:38:51.000 you'd be ideally thinking about maybe a pill option if it were available.

00:38:51.000 --> 00:38:55.000 And the one for that that is the most effective is called Paxlovid...

00:38:55.000 --> 00:38:58.000



which is the middle one here, which is an oral pill,...

00:38:58.000 --> 00:39:03.000 twice a day, very effective, but it has a lot of issues that we'll talk about. It's not recommended for people with..

00:39:03.000 --> 00:39:06.000 severe kidney or liver disease and there are a lot of interactions,...

00:39:06.000 --> 00:39:08.000 problems with other medicines you might take...

00:39:08.000 --> 00:39:11.000 that make it less safe.

00:39:11.000 --> 00:39:23.000 And the final drug is something called molnupiravir or Lagevrio, another oral drug twice a day for five days. Very clean in the sense that it doesn't mess with your other medicines. It doesn't sort of matter what your kidney or liver function is, but it doesn't work as well,..

00:39:23.000 --> 00:39:29.000 lower effectiveness. And there are some concerns about creating mutations, either in a person like a..

00:39:29.000 --> 00:39:32.000 pregnant woman or a child, so it's not recommended for those people...

00:39:32.000 --> 00:39:40.000 or in the virus itself. So, when we give it, it's usually either in combination with one of these other drugs or if we don't have any other options.

00:39:40.000 --> 00:39:45.000 But these are available and earlier the better if you're someone who's very high risk.

00:39:45.000 --> 00:39:54.000 Now, I mentioned that thing about the difficulty in using Paxlovid and the main issue is these interactions with other drugs, many of which are listed here, some of whom,...

00:39:54.000 --> 00:40:00.000 some of these you may be taking. And so, what I really recommend is the long story short, is before you're sick...



00:40:00.000 --> 00:40:07.000

talk to your doctor or pharmacist about whether with your current health status and medicines you take, whether you can even take Paxlovid if you were to get ill.

00:40:07.000 --> 00:40:10.000 And there are many resources that you can look at yourself...

00:40:10.000 --> 00:40:14.000 or you can access these online.

00:40:14.000 --> 00:40:20.000 All right. So, with the last five minutes, we do a little bit of what I would call a little bit of an infectious diseases roundup,..

00:40:20.000 --> 00:40:27.000 if we have the time. The first one I do want to talk about is these emerging threats I mentioned. And the main one on my mind has been bird flu...

00:40:27.000 --> 00:40:35.000 which has been in the news. That's another name for this highly pathogenic avian influenza or H5N1 that's widespread...

00:40:35.000 --> 00:40:43.000 in US livestock and in wild birds, presumably other animals as well. And there have been at least 50 cases in people, mostly mild pink eye kind of symptoms, but one...

00:40:43.000 --> 00:40:46.000 person in Canada, a younger person actually, was...

00:40:46.000 --> 00:40:52.000 hospitalized with severe flu in the ICU. And that's a problem because historically these kinds of flus are very deadly,..

00:40:52.000 --> 00:40:59.000 more than half of people have died in the past, and it's not clear why that's different now.

00:40:59.000 --> 00:41:07.000 So, the risk is generally characterized now by the CDC and others as low to the average human, but the sort of existential risk of an outbreak to me...

00:41:07.000 --> 00:41:10.000 is high. So, what can we do?



## 00:41:10.000 --> 00:41:18.000

What you can do is avoid birds. So alive or dead birds, try not to interact with them. If you have a parakeet in your cage you've had for 20 years, that's different,..

00:41:18.000 --> 00:41:20.000 than a bird, a crow you found on your doorstep.

00:41:20.000 --> 00:41:24.000 Also, don't drink raw milk, regardless of what might be...

00:41:24.000 --> 00:41:29.000 stated by government officials. Do get your flu shot. It's unlikely,...

00:41:29.000 --> 00:41:37.000 and including certainly people with CLL, to prevent an infection per se, but it might reduce severity. There's some cross-reactivity between...

00:41:37.000 --> 00:41:41.000 H1N1 that's in the vaccine, the swine flu,,,

00:41:41.000 --> 00:41:47.000 flu strain and H5N1. They share that part. So, there's probably some benefit.

00:41:47.000 --> 00:41:54.000

If you're sick or you're exposed to someone who you know is diagnosed with bird flu or was suspected, early treatments recommended,...

00:41:54.000 --> 00:41:56.000 for example, Tamiflu.

00:41:56.000 --> 00:42:03.000 You really should be talking to an infectious disease doctor about how to manage this if this were truly happening because there's some tricks we might try to do...

00:42:03.000 --> 00:42:08.000 to improve the likelihood that the antivirals work, like combining drugs.

00:42:08.000 --> 00:42:14.000

There are other emerging threats, and I know we're kind of running out of time here, but you're familiar, I think, with the mpox or monkeypox...

00:42:14.000 --> 00:42:18.000



pandemic that swept through the US a couple of years ago.

00:42:18.000 --> 00:42:22.000 This is sort of sporadically happening still in the United States,...

00:42:22.000 --> 00:42:27.000 it's mostly relevant for people with particularly high risk sexual activity,...

00:42:27.000 --> 00:42:32.000 men who have sex with men or exchange sex for payment...

00:42:32.000 --> 00:42:37.000 or someone who had a sort of known exposure. There are vaccines that do work reasonably well...

00:42:37.000 --> 00:42:43.000 and are safe to be given in people with CLL. Unfortunately, antiviral therapy does not work very well.

00:42:43.000 --> 00:42:47.000 The other "M" threat I want to talk about is measles, unfortunately.

00:42:47.000 --> 00:42:51.000 It's an extremely contagious disease that some of you may have had in youth.

00:42:51.000 --> 00:43:00.000 There have been almost 300 cases in the United States in the last year, which is an increase, mostly in children and mostly in the outbreak setting. And things that we can do is make sure that...

00:43:00.000 --> 00:43:04.000 people around you are being appropriately vaccinated, including children.

00:43:04.000 --> 00:43:06.000 Notably, you likely can't get...

00:43:06.000 --> 00:43:11.000 an MMR vaccine safely, you'd have to talk to your doctors about that.

00:43:11.000 --> 00:43:16.000 And medicines like IVIG and rituximab interfere with these vaccines.

00:43:16.000 --> 00:43:21.000



Really, you just want to, similar to other things, prevention is the best type of treatment.

00:43:21.000 --> 00:43:30.000 IVIG can be given to people who are known to be infected or exposed to measles, so that's something you'd have to talk to your doctor about. I think the risk of this is low.

00:43:30.000 --> 00:43:32.000 But if you know there's an outbreak near you...

00:43:32.000 --> 00:43:35.000 that's on the news, that's something to be thinking about.

00:43:35.000 --> 00:43:37.000 All right, the last slide, I believe is about...

00:43:37.000 --> 00:43:39.000 certain drugs you might be taking and certain...

00:43:39.000 --> 00:43:43.000 infections that you might be at higher risk for.

00:43:43.000 --> 00:43:54.000

The first I'll talk about are steroids commonly given to people with CLL. And the rule of thumb here is that essentially they raise the risk of almost any infection, a bacteria infection, a virus infection, a fungus infection.

00:43:54.000 --> 00:43:58.000 And it's a higher risk if you're on a higher dose, particularly when you get above...

00:43:58.000 --> 00:44:01.000 20, 30, 40 milligrams of prednisone.

00:44:01.000 --> 00:44:09.000 What I like to do for people on higher doses of steroids is to give a medicine like acyclovir or Valtrex...

00:44:09.000 --> 00:44:10.000 to prevent things like shingles, in particular.

00:44:10.000 --> 00:44:18.000

It works very well and the drug is very safe. And certain times we give drugs like bactrim to prevent certain opportunistic pneumonias...



00:44:18.000 --> 00:44:22.000 which are uncommon but can be a problem.

00:44:22.000 --> 00:44:32.000

The second group of drugs are these anti-CD20 medicines I mentioned, like rituximab. The highest risk for these things are viral infections and recurrent sort of sinus infections and pneumonias...

00:44:32.000 --> 00:44:37.000 because this also interferes with the antibodies that we typically use to fight off those viruses or...

00:44:37.000 --> 00:44:42.000 or bacteria, I also give Valtrex or acyclovir as prevention.

00:44:42.000 --> 00:44:49.000 IVIG, this is often when people will start to need IVIG for hypogammaglobulinemia.

00:44:49.000 --> 00:44:54.000 It's also just really important that you've had your hepatitis B shots because this is a high risk for hepatitis B...

00:44:54.000 --> 00:45:01.000 problems. And then the last group is these BTK inhibitors that I mentioned, like the Imbruvicas and Calquences and things...

00:45:01.000 --> 00:45:07.000 the somewhat uncommon but more likely if taking BTK...

00:45:07.000 --> 00:45:10.000 i inhibitors are fungal infections like molds.

00:45:10.000 --> 00:45:14.000 And they can be severe and so...

00:45:14.000 --> 00:45:19.000

we need to be aware of that if we're taking care of a person taking these drugs. And some people are put on antifungal drugs if you have a...

00:45:19.000 --> 00:45:28.000

history of having had a mold problem or you have some higher risk features. If you're taking this plus you're taking chemotherapy or plus you're taking steroids, these risks would...



00:45:28.000 --> 00:45:30.000 be increased.

## 00:45:30.000 --> 00:45:38.000

And again, we don't have enough time to really talk about bone marrow transplantation, but the first couple of years after bone marrow transplantation are going to be the highest risk for basically all these things.

00:45:38.000 --> 00:45:45.000 All right, so with that whirlwind, thank you for your attention. I want to do a brief summary, which is...

00:45:45.000 --> 00:45:54.000

just making sure everyone knows it is respiratory infection season. RSV now, flu shortly, and COVID, a little bit harder to predict, but probably in the next month.

### 00:45:54.000 --> 00:46:05.000

There are risks for serious infections that relate to your age, your medical conditions, and your immunosuppression. We talked about some of the specific drugs here and how their combination would...

00:46:05.000 --> 00:46:07.000 be a highest risk situation.

### 00:46:07.000 --> 00:46:15.000

Basically of everything I talked about, prevention is the best treatment for these things. So we have drugs, we have antiviral drugs when you get treated, but really vaccines are the most important thing.

00:46:15.000 --> 00:46:20.000 Vaccine immunity is lower in people with CLL, but it's imperfect, but it's important.

# 00:46:20.000 --> 00:46:26.000

And the time to get vaccinated is now for any of the things I just mentioned. If you're eligible and you haven't gotten these shots, you should be getting it.

00:46:26.000 --> 00:46:33.000

And you can complement these with IVIG if you meet the criteria that I mentioned and your doctor thinks that it's appropriate.

00:46:33.000 --> 00:46:38.000

There are several emerging threats that I am worried about, most particularly H5N1,...



#### 00:46:38.000 --> 00:46:46.000

and this just reinforces the importance of vaccines and having an expert treatment team like an infectious disease doctor who's familiar with cancer patients...

00:46:46.000 --> 00:46:48.000 if this ends up coming up...

00:46:48.000 --> 00:46:50.000 which I hope it does not, but...

00:46:50.000 --> 00:46:52.000 better safe than sorry.

00:46:52.000 --> 00:46:57.000 All right, so with that, I want to thank my colleagues at Johns Hopkins. I work in our Transplant Research Center...

00:46:57.000 --> 00:47:00.000 running kind of our epidemiology side of things...

00:47:00.000 --> 00:47:07.000 And then of relevance to this talk, is I also run a study called the Emerging Pathogens of Concern in Immunocompromised Persons, or EPOC study...

00:47:07.000 --> 00:47:11.000 at Hopkins, and this is our study team. If you're interested in knowing more about that,...

00:47:11.000 --> 00:47:14.000 here's our website. We basically study the vaccines...

00:47:14.000 --> 00:47:20.000 that were in people who were not included in trials, such as people with CLL.

00:47:20.000 --> 00:47:32.000 All right, well, thanks for your attention and I'm looking forward to taking your questions.

00:47:32.000 --> 00:47:37.000 Dr. Werbel, thanks so much for that incredible...

00:47:37.000 --> 00:47:42.000 presentation. I mean, there was so much covered in that and so much important material...

38



00:47:42.000 --> 00:47:48.000 and I'm deeply appreciative of that last sentence...

00:47:48.000 --> 00:47:53.000 that you were studying vaccines in people who don't get studied in...

00:47:53.000 --> 00:48:01.000 vaccines. We were excluded from the original COVID trials in an effort to get them over the finish line quicker.

00:48:01.000 --> 00:48:06.000 If you could just comment on that general area of...

00:48:06.000 --> 00:48:10.000 how we respond. I know you touched on this...

00:48:10.000 --> 00:48:21.000 but how different vaccines are, because there's a lot of data-free zones here, isn't there, in terms of how well we do. And the early data suggests it's not so great.

00:48:21.000 --> 00:48:29.000 So, if you could just comment on that area and how patients and clinicians might work together to improve understanding of how vaccines...

00:48:29.000 --> 00:48:33.000 work in the immunocompromised.

00:48:33.000 --> 00:48:36.000 Thanks, Dr. Koffman, and thanks for the invitation again to speak.

00:48:36.000 --> 00:48:38.000 Yeah, you know,..

00:48:38.000 --> 00:48:42.000 there is a knowledge gap,..

00:48:42.000 --> 00:48:44.000 we have these general senses...

00:48:44.000 --> 00:48:49.000 the degree to which people respond to vaccines or don't, depending on their...



00:48:49.000 --> 00:49:00.000

immune status, so to speak, their immune system. But I think what's honestly one of the biggest takeaways is that it's not like a monolith. There are significant differences among people depending upon...

00:49:00.000 --> 00:49:03.000 a lot of the factors that we've talked about, including age,...

00:49:03.000 --> 00:49:09.000 the type of cancer somebody might have and whether or not you're on therapy and what that therapy is.

00:49:09.000 --> 00:49:15.000 It's pretty safe to say that on balance for most like typical vaccines, the immune response is going to be lower...

00:49:15.000 --> 00:49:17.000 but it's going to be something.

00:49:17.000 --> 00:49:26.000

And so that's one of these key takeaways that the vaccines, are vaccines, all these vaccines are going to be important. They're likely to reduce the likelihood in particular, of getting severely ill,

00:49:26.000 --> 00:49:28.000 many of the things we talked about.

00:49:28.000 --> 00:49:36.000 But the ability to create these high levels of like antibody, for example, those neutralizing antibodies that block you from being infected, period,..

00:49:36.000 --> 00:49:41.000 that's hard to achieve for a lot of people with CLL, particularly because of the medicines and...

00:49:41.000 --> 00:49:49.000 the combination. And there's a need, you know, and as we actually had a separate conversation about, there's a significant interest...

00:49:49.000 --> 00:49:54.000 to have dedicated trials in people with CLL or other immunocompromising conditions because...



00:49:54.000 --> 00:50:01.000

we're getting to the point here where enough is a little bit of enough, where you know we got to have like gold standard information on people...

00:50:01.000 --> 00:50:08.000

and from then, we can really be prepared for what's the best regimen to improve immunity,..

00:50:08.000 --> 00:50:11.000 doing vaccines more frequently or higher doses,...

00:50:11.000 --> 00:50:13.000 you know, et cetera.

00:50:13.000 --> 00:50:20.000 So let me follow up on the vaccines because there's a ton of questions on that. And you made an interesting statement, which, and...

00:50:20.000 --> 00:50:30.000 which was, don't worry about the IVIG dosing. Like if I just got my IVIG, I thought, I better not get my vaccine because...

00:50:30.000 --> 00:50:37.000 the body's lazy if it already has some antibodies, it's not going to make more. But you're saying that I can get them...

00:50:37.000 --> 00:50:40.000 close to each other, it really doesn't matter.

00:50:40.000 --> 00:50:42.000 Yeah, you know, I mean, certainly for these...

00:50:42.000 --> 00:50:46.000 longstanding inactivated vaccines like the flu shot...

00:50:46.000 --> 00:50:49.000 there is data that shows that there is data that shows that there is data that shows that...

00:50:49.000 --> 00:50:52.000 you can get the vaccine close to IVIG.

00:50:52.000 --> 00:50:57.000 For live vaccines or live attenuated vaccines, like the older shingles shot,...



00:50:57.000 --> 00:51:03.000 MMR, those shots, you can't get them anywhere near IVIG because of the reasons you just said.

00:51:03.000 --> 00:51:09.000 There was a bit of a grey zone with mRNA vaccines, they weren't studied very well,...

00:51:09.000 --> 00:51:12.000 and for a time we were pretty...

00:51:12.000 --> 00:51:15.000 clear that it was not recommended to get IVIG surrounding them.

00:51:15.000 --> 00:51:19.000 The guidance has changed to say that it can be done,...

00:51:19.000 --> 00:51:21.000 you know uh, so I think...

00:51:21.000 --> 00:51:24.000 in even if there wasn't amazing...

00:51:24.000 --> 00:51:27.000 precise data on that it was more that,...

00:51:27.000 --> 00:51:29.000 these vaccines are important.

00:51:29.000 --> 00:51:36.000 Even if there's like a gray zone here, the benefits of getting them and not also interfering with the other thing that's keeping you kind of...

00:51:36.000 --> 00:51:38.000 stable and healthy,..

00:51:38.000 --> 00:51:41.000 you know, it's not worth...

00:51:41.000 --> 00:51:44.000 switching all these things around for this sort of uncertainty.

00:51:44.000 --> 00:51:50.000



So let's push a little bit more on that, in the era where we had good pre-exposure prophylaxis,..

00:51:50.000 --> 00:51:56.000 they often recommended trying to get vaccinated before you got Evusheld and I wonder if the same stuff...

00:51:56.000 --> 00:52:02.000 Is true with Pemgarda. I know that the company that makes that has another product in development that's supposed to...

00:52:02.000 --> 00:52:05.000 you know, stay more ahead of this.

00:52:05.000 --> 00:52:09.000 What do you advise your patients in terms of that?

00:52:09.000 --> 00:52:17.000 Yeah, I guess I don't want to talk out of both sides of my mouth here, but maybe a little bit of a difference is when you're giving a high dose of a monoclonal antibody...

00:52:17.000 --> 00:52:20.000 that's specifically designed...

00:52:20.000 --> 00:52:23.000 for a particular bug, so to speak,...

00:52:23.000 --> 00:52:27.000 that might, particularly in the first few days, lead to some...

00:52:27.000 --> 00:52:30.000 reduction of sort of being exposed to this...

00:52:30.000 --> 00:52:32.000 antigen, the foreign particle.

00:52:32.000 --> 00:52:35.000 But it shouldn't have any impact on...

00:52:35.000 --> 00:52:37.000 a different vaccine, for example.

00:52:37.000 --> 00:52:46.000



So we do, you know, and it's in the packaging as well to recommend spacing things by like two weeks or so.

00:52:46.000 --> 00:52:51.000 Get your vaccine and then you can get your antibody two weeks after that, for example.

00:52:51.000 --> 00:52:55.000 So I think we do tend to kind of still say that. But again, it shouldn't interfere with...

00:52:55.000 --> 00:53:00.000 a vaccine that's not the exact product we're talking about, like your RSV vaccine and your...

00:53:00.000 --> 00:53:03.000 Pemgarda or whatever.

00:53:03.000 --> 00:53:09.000 And talk to me a little bit about one of the decisions a lot of us have to make as we're in treatment...

00:53:09.000 --> 00:53:15.000 and these vaccines aren't going to work as well for us. And especially if we're on treatments...

00:53:15.000 --> 00:53:20.000 with monoclonal antibodies which stick around for months and months after in studies from...

00:53:20.000 --> 00:53:26.000 LLS have shown that you just don't respond the same even a year after for some people...

00:53:26.000 --> 00:53:28.000 with rituximab or obinutuzumab.

00:53:28.000 --> 00:53:38.000 So the timing of the vaccine, especially, I mean, it's kind of a no-brainer to me. You get the flu shot because it's flu time and some benefit is better than none.

00:53:38.000 --> 00:53:45.000 But some of the shots like RSV is a one-off shot or the pneumonia shots you can't, aren't annual shots.



00:53:45.000 --> 00:53:49.000 So should we wait on those or I mean,...

00:53:49.000 --> 00:53:55.000 how do you work that out with your patients? And I'm sure consultation with the hematologist too, but it's,..

00:53:55.000 --> 00:54:05.000 these are difficult decisions for patients about you only get one shot at the RSV vaccine, at least as of now. Should you wait till you're off treatment or just get it and that's it?

00:54:05.000 --> 00:54:06.000 What do you tell people?

00:54:06.000 --> 00:54:08.000 That's a really good question,...

00:54:08.000 --> 00:54:11.000 I'm going to pass the buck a little that it's case by case.

00:54:11.000 --> 00:54:12.000 Okay.

00:54:12.000 --> 00:54:16.000 If the drug you're talking about, like rituximab is critical to keeping...

00:54:16.000 --> 00:54:21.000 lymphoma under control, et cetera. You don't want to mess with that cycle your six cycles of

00:54:21.000 --> 00:54:24.000 R-CHOP or these, you know, type of things,...

00:54:24.000 --> 00:54:27.000 you know that, that takes precedence.

00:54:27.000 --> 00:54:37.000

There are these ideals where it's an ideal to wait like, let's say six months, after a dose of rituximab to achieve like maximal antibody protection from a...

00:54:37.000 --> 00:54:44.000 vaccination. That's the ideal. And to then again, lag the next dose by about two weeks after you've...



00:54:44.000 --> 00:54:48.000 received the vaccine. That's the ideal. But life doesn't always line up...

00:54:48.000 --> 00:54:52.000 perfectly. If someone's a very high risk person for getting a severe disease,...

00:54:52.000 --> 00:54:57.000 let's call it, let's say like RSV, you know, a person, 75 year old person with...

00:54:57.000 --> 00:55:06.000 bad asthma, CLL on rituximab, you know, obinutuzumab or venetoclax and whatever it may be,...

00:55:06.000 --> 00:55:11.000 you know, being in advance of the RSV season and getting your vaccine

00:55:11.000 --> 00:55:17.000 is going to be just what we're going to say to do. Even though we just have to be aware that...

00:55:17.000 --> 00:55:21.000 there's going to likely be a ceiling on the level of at least antibody production.

00:55:21.000 --> 00:55:24.000 The nice part, I will say, is that, as I said, vaccines...

00:55:24.000 --> 00:55:27.000 produce immunity in several ways,

00:55:27.000 --> 00:55:29.000 things like T cell immunity...

00:55:29.000 --> 00:55:34.000 aren't really that affected by rituximab. It's a B cell drug, an antibody drug. And in other...

00:55:34.000 --> 00:55:40.000 like people with MS, it's been shown that you can have pretty good T cell responses against something like COVID, even though you've received...

00:55:40.000 --> 00:55:44.000 rituximab and don't have great antibodies.



00:55:44.000 --> 00:55:45.000 Case-by-case.

00:55:45.000 --> 00:55:46.000 I don't understand how,..

00:55:46.000 --> 00:55:52.000 you don't have B cells how you present, but I guess other cells can present the antigen it's,..

00:55:52.000 --> 00:55:57.000 it's complicated. A couple other questions on the timing of the vaccines.

00:55:57.000 --> 00:55:59.000 One is, what about...

00:55:59.000 --> 00:56:08.000 we had these childhood vaccines. Some of us had the childhood illnesses. Are we protected into some of the treatments we have wiped out the protections?

00:56:08.000 --> 00:56:16.000 It's not very common, but some of us have had transplants. Some of us had CAR-T therapy. A lot of us have had antibodies.

00:56:16.000 --> 00:56:25.000 Do we need to get our childhood vaccines again? I know this is an area, again, that seems to be changing the approach to this.

00:56:25.000 --> 00:56:29.000 What do you recommend in those cases?

00:56:29.000 --> 00:56:34.000 Yeah, I mean, I think the general rule of thumb, and it is complex with bone marrow transplants, is that with...

00:56:34.000 --> 00:56:38.000 allogeneic bone marrow transplants that are completely ablative,...

00:56:38.000 --> 00:56:42.000 whole body radiation and high doses of chemotherapy...

00:56:42.000 --> 00:56:43.000



you...

00:56:43.000 --> 00:56:47.000 and in somebody else's immune system, not your own, which is the only way it's done in CLL.

00:56:47.000 --> 00:56:50.000 Yes.

00:56:50.000 --> 00:56:52.000 We still consider people as...

00:56:52.000 --> 00:56:55.000 we can't bank on the immune system of the donor.

00:56:55.000 --> 00:57:01.000 Therefore, you should be revaccinated as if you haven't had vaccines and CAR\_T would be similar.

00:57:01.000 --> 00:57:04.000 Um, you know,..

00:57:04.000 --> 00:57:09.000 I believe that there is some residual immunity...

00:57:09.000 --> 00:57:13.000 from your donor, but...

00:57:13.000 --> 00:57:18.000 need, you know, this whole concept of priming and then boosting that up, you know, still needs to be...

00:57:18.000 --> 00:57:21.000 given like you still are going to need some oomph...

00:57:21.000 --> 00:57:24.000 to the cells that are taking time to totally reconstitute, it takes...

00:57:24.000 --> 00:57:26.000 oftentimes like two...

00:57:26.000 --> 00:57:31.000



for the whole immune system to really get back. And that's presuming you don't have issues like...

00:57:31.000 --> 00:57:37.000 graft versus host disease requiring high doses of steroids or obviously relapse of disease so...

00:57:37.000 --> 00:57:41.000 better safe than sorry on that one too. We say really just restart that...

00:57:41.000 --> 00:57:45.000 even though there may be some residual immunity from your donor.

00:57:45.000 --> 00:57:47.000 Let's boost that up.

00:57:47.000 --> 00:58:00.000

But the drugs like obinutuzumab, rituximab, the BTKis, venetoclax, they don't affect the childhood immunity or the immunity you've had from getting the illnesses. I mean, they affect your ability to fight it when you've got it, but you'll still...

00:58:00.000 --> 00:58:08.000 have that immunity preserved or do you need to get revaccinated? Because almost all of us have had some of that if we're not treatment naive. Yeah,..

00:58:08.000 --> 00:58:11.000 right, I guess...

00:58:11.000 --> 00:58:13.000 an example of that, let's say, would be something like...

00:58:13.000 --> 00:58:15.000 the hepatitis b problem.

00:58:15.000 --> 00:58:22.000 It's a little bit different, but like hepatitis B, if you have an infection with hepatitis B and your body makes antibodies, it kind of locks it all away.

00:58:22.000 --> 00:58:26.000 And then you get something like rituximab, the risk of that reactivating is very high.

00:58:26.000 --> 00:58:33.000



So even though you had some immunity, it can be explicitly depleted by something like rituximab. And you can lose things...

00:58:33.000 --> 00:58:37.000 in the blood like your measles antibody.

00:58:37.000 --> 00:58:40.000 But it's not likely in that latter case...

00:58:40.000 --> 00:58:46.000 unlike hepatitis B, it's not likely that your immunity to measles has been totally evaporated.

00:58:46.000 --> 00:58:50.000 It is possible that, you know, the totally sterilizing...

00:58:50.000 --> 00:58:53.000 beautiful immunity from the...

00:58:53.000 --> 00:58:56.000 series is decreased.

00:58:56.000 --> 00:59:03.000 And that is one of the reasons why people will be on things like IVIG, which contains lots of antibody against measles,..

00:59:03.000 --> 00:59:07.000 for example. So it's one of these things where there will be a decrease in that...

00:59:07.000 --> 00:59:11.000 original childhood immunity but not, uh, immunity,...

00:59:11.000 --> 00:59:15.000 total elimination.

00:59:15.000 --> 00:59:16.000 So...

00:59:16.000 --> 00:59:19.000 like for polio stuff like that, you know, like you don't get, you know,...

00:59:19.000 --> 00:59:20.000 that's not gone.



00:59:20.000 --> 00:59:22.000 Yeah.

00:59:22.000 --> 00:59:31.000 There's a lot of questions about IVIG and let's start with just base. Does it matter whether it's subcutaneous or IVIG or do they both provide similar protection?

00:59:31.000 --> 00:59:40.000 Yeah, and the docs who prescribe this can help tune it to like the right dose for the right person at the right frequency, but they should be equally effective...

00:59:40.000 --> 00:59:42.000 as long as you're sort of following up their...

00:59:42.000 --> 00:59:44.000 effect.

00:59:44.000 --> 00:59:48.000 And you did cover this a little bit, but for some, other some questions about,...

00:59:48.000 --> 00:59:52.000 the difference like immunoglobulin is a...

00:59:52.000 --> 01:00:03.000 passive immunity whereas vaccines are an active immunity. So just remind us how IVIG works compared to a vaccine. I know you covered this a little bit, but there were some questions about it.

01:00:03.000 --> 01:00:11.000 Yeah, I mean, as sort of noted, the IVIG is just antibody and it's a pooled product donated by healthy donors...

01:00:11.000 --> 01:00:13.000 so it's the most effective at...

01:00:13.000 --> 01:00:17.000 preventing infections for very common things:...

01:00:17.000 --> 01:00:23.000

common bacterial or viral infections that all of us who could potentially be a blood donor have had...



01:00:23.000 --> 01:00:29.000 10 times in their life. Like I've probably had RSV 10 times in my life or six times in my life.

01:00:29.000 --> 01:00:32.000 And if I donate my antibody, it's pooled with many different donors,...

01:00:32.000 --> 01:00:35.000 you get that immunity passively.

01:00:35.000 --> 01:00:39.000 It will rise up, particularly if you dose it appropriately to a level that hopefully...

01:00:39.000 --> 01:00:44.000 reduces your risk of getting infected in the first place by, let's say RSV or flu...

01:00:44.000 --> 01:00:47.000 or even these bacterial pneumonias.

01:00:47.000 --> 01:00:49.000 The problem is there's waning in that...

01:00:49.000 --> 01:00:52.000 and that's the need for repeat dosing...

01:00:52.000 --> 01:00:57.000 and they're not perfect. You know, there's variation between the batches of IVIG and...

01:00:57.000 --> 01:01:11.000 there's variation in the different strains of things that are circulating, like COVID, as we talked about. So the defenses can be breached even if you're taking IVIG. Hopefully less will get through the fences because some are kind of gummed up by the antibody that...

01:01:11.000 --> 01:01:15.000 you've received. And then you're reliant upon the rest of your immune system...

01:01:15.000 --> 01:01:19.000 which tends to take a couple of days to kick in.

01:01:19.000 --> 01:01:21.000 So, the T cell immunity...



01:01:21.000 --> 01:01:25.000 generation of your own antibodies from your stored memory...

01:01:25.000 --> 01:01:29.000 to kind of clean up the mess, prevent dissemination of an infection...

01:01:29.000 --> 01:01:32.000 from like a cold to a pneumonia,.. 01:01:32.000 --> 01:01:34.000 that's kind of how they would work together.

01:01:34.000 --> 01:01:44.000 In the IVIG, I always tell people it's usually a year old, so it's not on top of the latest flu or the latest COVID variant and stuff like that because it takes...

01:01:44.000 --> 01:01:46.000 a long time to process it.

01:01:46.000 --> 01:01:50.000 It's pooled from thousands and thousands of donors and I'm,...

01:01:50.000 --> 01:01:54.000 but it's always a little bit out of date.

01:01:54.000 --> 01:02:01.000 A common question is about sinuses. Sinus infections seem to be a real problem.

01:02:01.000 --> 01:02:04.000 Nobody dies of them, but they sure make people miserable.

01:02:04.000 --> 01:02:11.000 Any advice on how to avoid them, how to treat them? Chronic sinusitis seems to be a big issue...

01:02:11.000 --> 01:02:20.000 in CLL, are there any tips you have for people, any ways to prevent them or treat them when they get them other than

01:02:20.000 --> 01:02:21.000 what we've talked about?

01:02:21.000 --> 01:02:25.000 Yeah, you know, when I think of sinus infections, I think of two components:...



01:02:25.000 --> 01:02:28.000 One, maybe the one maybe,..

01:02:28.000 --> 01:02:31.000 more simple one is structural. Obviously, we're all different in here.

01:02:31.000 --> 01:02:34.000 There are people who are going to be more predisposed depending on their anatomy.

01:02:34.000 --> 01:02:39.000 That part, I am not that expert in and that's an ENT problem, so to speak.

01:02:39.000 --> 01:02:40.000 So let's put that.

01:02:40.000 --> 01:02:46.000 I always say the Lord in his wisdom put the drain in the roof in our sinuses. It's just they're poorly designed.

01:02:46.000 --> 01:02:47.000 You know, and nobody,...

01:02:47.000 --> 01:02:49.000 they're more designed to keep your head light. Honestly, that's the historical...

01:02:49.000 --> 01:02:51.000 That's right.

01:02:51.000 --> 01:02:53.000 background.

01:02:53.000 --> 01:02:54.000 Yeah.

01:02:54.000 --> 01:03:03.000 But anyway, that's the part that you can't fix that easily, but should be evaluated if you have recurrent sinus infections. But then the cause of these tend to tend to be a virus.

01:03:03.000 --> 01:03:11.000

And then occasionally, you'll have a bacterial sort of super infection on top of that while your body has spent time kind of trying to fight off the virus that caused the sinus infection.



01:03:11.000 --> 01:03:16.000 Classic for that would be you have this sinus type symptoms for seven to 10 days.

01:03:16.000 --> 01:03:20.000 They kind of got better and then they acutely worsened. You have worsening pain,...

01:03:20.000 --> 01:03:25.000 Fever, potentially greenish drainage, that sort of second phase might suggest a bacterial infection.

01:03:25.000 --> 01:03:29.000 As mentioned in the IVIG part of the talk,...

01:03:29.000 --> 01:03:33.000 people with a current sinus infection should be screened for hypogammaglobulinemia...

01:03:33.000 --> 01:03:41.000 in addition to the structural stuff. And that's where IVIG is one of the indications. Like if you look at the NCCN guidelines, cancer guidelines for CLL,..

01:03:41.000 --> 01:03:49.000 there's a whole, there's a line in there that talks about recurrent infections, particularly in the context of total IgG antibody in the blood less than...

01:03:49.000 --> 01:03:51.000 somewhere in the four to 600 range,...

01:03:51.000 --> 01:03:54.000 that's a reason to consider IVIG to reduce that.

01:03:54.000 --> 01:03:56.000 Otherwise, it's um,..

01:03:56.000 --> 01:04:03.000 you know, just like any infection prevention, if they tend to be caused by viruses, things we do to reduce viruses would...

01:04:03.000 --> 01:04:08.000 likely reduce the downstream problems like sinus infection. So, washing your hands and

01:04:08.000 --> 01:04:11.000 wearing a mask, etc.



01:04:11.000 --> 01:04:14.000 And what about the saline irrigations and things like that?

have the structural problems, the anatomy problems...

01:04:14.000 --> 01:04:25.000 Although I'm not an ENT, sterile washes and things, particularly again with people who

01:04:25.000 --> 01:04:29.000 can be helpful. If you don't have those structural problems, the issue is probably not...

01:04:29.000 --> 01:04:32.000 going to necessarily be fixed by...

01:04:32.000 --> 01:04:35.000 sinus rinses. It's more fixing your...

01:04:35.000 --> 01:04:38.000 immune system, so to speak, or lifting that up.

01:04:38.000 --> 01:04:45.000 So I'm going to leave respiratory for a minute and ask about some GI issues.

01:04:45.000 --> 01:04:47.000 Norovirus, both acute and chronic.

01:04:47.000 --> 01:04:48.000 Yeah.

01:04:48.000 --> 01:04:54.000 Are there any tips on that, ways to get rid of a chronic norovirus infection?

01:04:54.000 --> 01:05:00.000 Remind the people who don't know what a norovirus is and why that is a risk for CLL patients.

01:05:00.000 --> 01:05:04.000 Yeah, it is. Norovirus is very annoying.

01:05:04.000 --> 01:05:13.000

It's a virus that is commonly known as like the cruise ship virus when you see 500 people on a cruise ship throwing up and having diarrhea, it's usually from norovirus. It's very contagious.



01:05:13.000 --> 01:05:18.000 It circulates year-round with some spikes in the summer and some in the winter.

01:05:18.000 --> 01:05:23.000 It is one of those things by the way, for which hand sanitizer is not that great.

01:05:23.000 --> 01:05:27.000 So that's one of the handwashing viruses, similar to the common cold,...

01:05:27.000 --> 01:05:30.000 spread through drops and stuff like that.

01:05:30.000 --> 01:05:32.000 In terms of...

01:05:32.000 --> 01:05:36.000 so, that's the general prevention side of things and the epidemiology.

01:05:36.000 --> 01:05:38.000 Fixing norovirus, we do not have great...

01:05:38.000 --> 01:05:44.000 therapies so I'll just say that there have been multiple trials looking at different things and how to fix that...

01:05:44.000 --> 01:05:50.000 and they're not great. Some will use things like IVIG because again, most of us have had norovirus a bunch of times.

01:05:50.000 --> 01:05:53.000 The issue is that when you get IVIG,...

01:05:53.000 --> 01:06:01.000 injected or intravenous, it doesn't necessarily get into the gut that well, the gut lining. So, some people in severe protracted cases, like we've done this,...

01:06:01.000 --> 01:06:04.000 can occasionally get what they call enteral IG like a...

01:06:04.000 --> 01:06:07.000 nose tube and that that puts...



01:06:07.000 --> 01:06:10.000 the antibody in the gut. That's for very refractory cases.

01:06:10.000 --> 01:06:14.000 And the issue with norovirus is that it can be up and down.

01:06:14.000 --> 01:06:18.000 People can have diarrhea for a few weeks and it goes away and...

01:06:18.000 --> 01:06:22.000 you know it's hard to diagnose. So those are some options that again require...

01:06:22.000 --> 01:06:25.000 GI doctors and infectious disease doctors.

01:06:25.000 --> 01:06:29.000 There is technically an antibiotic that is used...

01:06:29.000 --> 01:06:32.000 called nitazoxanide or Alinia, I believe.

01:06:32.000 --> 01:06:36.000 Uncertain how well it works, we do sometimes use it,...

01:06:36.000 --> 01:06:41.000 it's available. It's used for intestinal parasites also.

01:06:41.000 --> 01:06:44.000 So that is an option, but the data are a little bit, uh,...

01:06:44.000 --> 01:06:46.000 weak.

01:06:46.000 --> 01:06:53.000 Here's one that I've never seen as a family doc, but maybe you have intestinal spirochetosis,...

01:06:53.000 --> 01:06:55.000 is a gastric infection common in CLL.

01:06:55.000 --> 01:06:56.000 Tell us.



01:06:56.000 --> 01:07:03.000

I don't think, it's very not very common in the United States. It is common in immigrant populations. It's actually a demographic thing.

01:07:03.000 --> 01:07:05.000 Spirochetes are just a kind of bacteria.

01:07:05.000 --> 01:07:12.000 Lyme disease that's caused by spirochetes, syphilis is caused by a spirochete. They're kind of like, tricky.

01:07:12.000 --> 01:07:17.000 Intestinal spirochetosis is something you can make on a colonoscopy biopsy.

01:07:17.000 --> 01:07:20.000 It's more common in sub-Saharan Africa, certain parts of Asia.

01:07:20.000 --> 01:07:23.000 It's usually asymptomatic and doesn't cause an issue but...

01:07:23.000 --> 01:07:28.000 we're talking about people with different immune systems and the potential that it could contribute to...

01:07:28.000 --> 01:07:31.000 Gl upset is possible.

01:07:31.000 --> 01:07:38.000 Seems a little bit complicated, again, this is like a GI doctor or ID doctor issue. Sometimes people give like penicillin a la...

01:07:38.000 --> 01:07:45.000 syphilis or doxycycline a la Lyme disease.

01:07:45.000 --> 01:07:52.000 So while we're on the gut, the microbiome, which seems to be the really hot item, is there any...

01:07:52.000 --> 01:08:03.000

things that's different in a CLL patient in terms of their microbiome, anything we can do to ensure a healthy microbiome? Is there enough attention, too much attention being paid to this?



01:08:03.000 --> 01:08:11.000

The CLL Society is actually doing research where we're funding a research project on the microbiome in CLL.

01:08:11.000 --> 01:08:14.000 Yeah, and I wouldn't call myself a microbiome...

01:08:14.000 --> 01:08:16.000 expert. I think...

01:08:16.000 --> 01:08:20.000 it's one of these things that's probably integrated with a lot of...

01:08:20.000 --> 01:08:25.000 diseases, but the integration is very hard to parse out...

01:08:25.000 --> 01:08:30.000 And I think right now we're kind of a little bit more at, and I don't want to be offensive, but let's just say...

01:08:30.000 --> 01:08:34.000 the promise and reality are not at the same spot right now like,...

01:08:34.000 --> 01:08:39.000 we have a lot of things we wanted you to like look at the microbiome or potentially enhance it but...

01:08:39.000 --> 01:08:44.000 the bedside version of how we can do that has not really been realized. I will say things like...

01:08:44.000 --> 01:08:49.000 there's a question, I think, in the chat about like kefir and certain yogurts and things like that.

01:08:49.000 --> 01:08:51.000 Those are one of the few things that we know...

01:08:51.000 --> 01:08:55.000 can help with certain things like antibiotic associated diarrheas.

01:08:55.000 --> 01:08:59.000 We just have to be a little bit careful if you have a very low immune system,...



01:08:59.000 --> 01:09:04.000 certain things like probiotics can occasionally cause real disease.

01:09:04.000 --> 01:09:06.000 The classic being like lactobacillus,...

01:09:06.000 --> 01:09:11.000 something you've probably seen on the, lactobacillus is like in these dietary supplements, and so...

01:09:11.000 --> 01:09:15.000 people with really low immune systems, we tend to not recommend they take high doses of the...

01:09:15.000 --> 01:09:17.000 probiotics because the probiotics,...

01:09:17.000 --> 01:09:24.000 certain strains of them, can be a lot. They're alive and they could cause issues so that's a question to run by your doctors for sure.

01:09:24.000 --> 01:09:27.000 Sorry, I don't have too much more on the microbiome.

01:09:27.000 --> 01:09:31.000 All right. Urinary tract infections is that...

01:09:31.000 --> 01:09:37.000 It seems to me I've seen that a lot in CLL. Any thoughts on that?

01:09:37.000 --> 01:09:42.000 I know that as a family doc, I sometimes prescribe prophylaxis if they're related to...

01:09:42.000 --> 01:09:48.000 sexual activity and stuff like that. And I know men with prostatism can get...

01:09:48.000 --> 01:09:54.000 more urinary tract issues. Any thoughts on that? Is that a problem you see as an ID doc with CLL?

01:09:54.000 --> 01:10:05.000



Yeah, well, I certainly see UTI problems in general a lot. It's not a classic association with CLL because the lymphocyte compartment of your immune system tends to not be the thing you need to control...

01:10:05.000 --> 01:10:08.000 UTIs., that's more the...

01:10:08.000 --> 01:10:15.000 other infection fighting cells. If you are on something like steroids, the risks goes up because the risk for everything goes up if you're on steroids.

01:10:15.000 --> 01:10:18.000 Additionally,..

01:10:18.000 --> 01:10:25.000 diabetes, particularly if you have poor diabetes control, that is a risk factor for recurrent UTIs.

01:10:25.000 --> 01:10:30.000 I do, though, I don't necessarily think about CLL with too much of a different...

01:10:30.000 --> 01:10:33.000 patch than I do for the average person...

01:10:33.000 --> 01:10:39.000 with UTIs, it's usually these other factors, like I mentioned, diabetes, post-menopause,

01:10:39.000 --> 01:10:48.000 sometimes sexual practice and occasionally, again, anatomy because that definitely can vary.

01:10:48.000 --> 01:10:57.000 Airplane flights, the whole issue, and you and I spent some time talking about this before, is how do you strike the balance?

01:10:57.000 --> 01:11:04.000 They have things that they want to go to, but airplane flights can be dangerous or has that overstated the danger on those?

01:11:04.000 --> 01:11:09.000 What do you recommend for your CLL patients? Let's be specific,...

01:11:09.000 --> 01:11:14.000



who want to fly because there's a family wedding on the other coast...

01:11:14.000 --> 01:11:22.000 or they haven't taken a vacation because of COVID. Is it safe for them to go to an airport? Is it safe for them to go...

01:11:22.000 --> 01:11:31.000 on a plane? Is it safe for them to eat at a restaurant? Talk to us a little bit about that and maybe spend a little time about making it as safe as possible, especially on the plane.

01:11:31.000 --> 01:11:34.000 Yeah, you know, if you think back to that,...

01:11:34.000 --> 01:11:36.000 that's your graphic I made with the red...

01:11:36.000 --> 01:11:38.000 you know, lines and stuff,..

01:11:38.000 --> 01:11:42.000 you know, a person can...

01:11:42.000 --> 01:11:50.000 hopefully have a, be empowered to have a sense of what their individual risk is going to be for something like COVID or another virus infection based upon how you map out.

01:11:50.000 --> 01:11:53.000 Someone who's 75 with...

01:11:53.000 --> 01:11:56.000 very bad heart failure or kidney disease...

01:11:56.000 --> 01:12:01.000 who has CLL and is on rituximab and...

01:12:01.000 --> 01:12:04.000 ibrutinib and highly, you know, very treatment experienced...

01:12:04.000 --> 01:12:07.000 that is a person who's more likely to get infections and they,...

01:12:07.000 --> 01:12:12.000 if you get infections, they are more likely to be serious.



#### 01:12:12.000 --> 01:12:22.000

That said, you know, we only live once, right? So, I mean, if there are things that are situationally important, then it becomes this matter of risk tolerance. You need to first know your own risk...

01:12:22.000 --> 01:12:28.000 and then think about your tolerance relative to whatever event or travel you want to do.

01:12:28.000 --> 01:12:30.000 You know, we rarely tell...

01:12:30.000 --> 01:12:32.000 anybody like you can't travel.

01:12:32.000 --> 01:12:35.000 I think we tend to give recommendations that are like in very highly...

01:12:35.000 --> 01:12:37.000 immune suppressed...

01:12:37.000 --> 01:12:42.000 parts of your life, like the first couple of months after a bone marrow transplant,...

01:12:42.000 --> 01:12:45.000 not a great time to travel because it's your

01:12:45.000 --> 01:12:49.000 small, you're just more vulnerable unless it's something really critical.

01:12:49.000 --> 01:12:54.000 And, you know, particularly in those situations, your vaccine immunity and stuff is just not going to...

01:12:54.000 --> 01:12:58.000 get you there. But for average people who are kind of at their steady state in life,...

01:12:58.000 --> 01:13:04.000 things that are important are important. And what you can do is optimize things like the passive or...

01:13:04.000 --> 01:13:10.000



active immunoprophylaxis to be at least two to four weeks before some event you're going to do and when you...

01:13:10.000 --> 01:13:16.000 go through airports and airplanes, actually, I think the biggest risk times are

01:13:16.000 --> 01:13:23.000 are some of the like densely packed groups when you're waiting in line to go through customs or whatever...

01:13:23.000 --> 01:13:26.000 when airplanes are actually not in the air.

01:13:26.000 --> 01:13:31.000

So, when you're planning or deplaning, those are higher risk. When you're in the air, the air is circulating, to be honest, and unless you're sitting...

01:13:31.000 --> 01:13:39.000 And it's going through HEPA filters and it's the takeoff and the landing that are the risk to your life and to infections.

01:13:39.000 --> 01:13:47.000 Yes, exactly right. So, I mean, I do recommend you wear masks for sure for those sort of high risk points. And then in between, it's really a risk tolerance...

01:13:47.000 --> 01:13:50.000 Thing. Generally worth it because masks are annoying but...

01:13:50.000 --> 01:13:56.000 there are worse things in life, you know, and who wants to get a cold, right?

01:13:56.000 --> 01:14:08.000 Now, CLL is a very heterogeneous disease and some of us are in active surveillance or what we used to call watch and wait all our time. Others are in deep remissions and others are on active therapy.

01:14:08.000 --> 01:14:16.000 So I tell patients they're immune compromised no matter where they are, regardless of their treatment. It's just a degree...

01:14:16.000 --> 01:14:21.000 of how immune compromised there are. Is there any granularity...



01:14:21.000 --> 01:14:26.000

you want to add to that in terms of where patients are at? I push people,..

01:14:26.000 --> 01:14:34.000

the minute you're diagnosed, catch up on your vaccines because your immunity is going to be worse in a year from now than it is now in all likelihood.

01:14:34.000 --> 01:14:44.000 Talk to us about, because there's a lot of questions, about how immunocompromised am I. Also, this is an immunologist question about testing for immunity.

01:14:44.000 --> 01:14:47.000 And there are some things the immunologists do or are there things that...

01:14:47.000 --> 01:14:52.000 you recommend that patient consider or do they really make a difference?

01:14:52.000 --> 01:14:56.000 Yes, these are good and complicated questions. They're individualized.

01:14:56.000 --> 01:14:58.000 I agree with you,..

01:14:58.000 --> 01:15:00.000 the combination of like...

01:15:00.000 --> 01:15:03.000 active CLL, meaning you either have...

01:15:03.000 --> 01:15:10.000 very high lymphocyte counts or very high CLL counts and with lower...

01:15:10.000 --> 01:15:13.000 blood counts of the other blood counts.

01:15:13.000 --> 01:15:18.000 In particular, that plus getting treatments continuously are going to be the higher risk states.

01:15:18.000 --> 01:15:24.000 Obviously, that's even higher if you start having bone marrow transplants in the first couple years after that or CAR-T therapy.



01:15:24.000 --> 01:15:27.000 So that's kind of that sliding scale...

01:15:27.000 --> 01:15:30.000 from the watchful waiting or ...

01:15:30.000 --> 01:15:34.000 with sort of low disease activity tests, you start going up in the different stages and...

01:15:34.000 --> 01:15:36.000 you know,..

01:15:36.000 --> 01:15:39.000 that is something that your hematologist should be...

01:15:39.000 --> 01:15:42.000 able to tell you where you are on that spectrum.

01:15:42.000 --> 01:15:48.000 I do and when I see patients and I look at their medical charts, I mean, you can...

01:15:48.000 --> 01:15:53.000 there are some lab tests that are helpful for quantifying some of that.

01:15:53.000 --> 01:15:58.000 We talked about some of them. You can get total immunoglobulin levels. 01:15:58.000 --> 01:16:01.000 If you haven't had that done, a little trick is if you look at your...

01:16:01.000 --> 01:16:06.000 liver test, if you ever get that, and you just subtract the albumin from your total protein...

01:16:06.000 --> 01:16:09.000 the rest is mostly immunoglobulin. If that's less than two,...

01:16:09.000 --> 01:16:12.000 I'm like, you're probably hypergammaglobulinemic. That's like an inside thing.

01:16:12.000 --> 01:16:13.000 Yep.

01:16:13.000 --> 01:16:16.000 You could always just test that though. Also, the lymphocyte count itself...



01:16:16.000 --> 01:16:20.000 That's part of most chemistry panels. We did a chem 20 or whatever. It's there, yeah.

01:16:20.000 --> 01:16:25.000 Right. It's there. You know, obviously you have your white cell counts. If your neutrophil count is low,..

01:16:25.000 --> 01:16:29.000 less than a thousand, particularly less than 500,...

01:16:29.000 --> 01:16:34.000 that's going to be a high risk state for several infections. And for lymphocyte counts, obviously it's a little bit difficult to interpret with CLL...

01:16:34.000 --> 01:16:39.000 sometimes, but people can send like...

01:16:39.000 --> 01:16:44.000 CD4 counts like these T cell subtyping. And I look at that as like this part of this...

01:16:44.000 --> 01:16:52.000 picture of someone's immune system. How much antibody can they produce, how good are their infection fighting cells? How many T cells are available?

01:16:52.000 --> 01:16:57.000 And you can kind of, at least, put people in like low, medium, high risk states...

01:16:57.000 --> 01:17:03.000 particularly informed by a blood doctor who's like, okay, your CLL is this active. We put you on these medicines,..

01:17:03.000 --> 01:17:06.000 you're in the red zone with respect to these certain...

01:17:06.000 --> 01:17:12.000 diseases. And this is definitely a really big sliding scale that requires...

01:17:12.000 --> 01:17:15.000 people to be expert in CLL.

01:17:15.000 --> 01:17:20.000 And you can do like we do with HIV patients, CD4 counts, CD8 counts, and ratios.



01:17:20.000 --> 01:17:22.000 Okay.

01:17:22.000 --> 01:17:24.000 The other thing that I. Go ahead.

01:17:24.000 --> 01:17:30.000 I was going to say, and also, as I think someone mentioned in the chat, and I mentioned in the talk, people do sometimes check for like...

01:17:30.000 --> 01:17:38.000 flu antibody or after you get a vaccine as a marker of how kind of reactive your immune system is. If those are very kind of mute,..

01:17:38.000 --> 01:17:41.000 don't really go up with a vaccine,...

01:17:41.000 --> 01:17:47.000 that means you're pretty immunocompromised. They should go up.

01:17:47.000 --> 01:17:56.000 And what we know, for example, with the COVID vaccine is that most people, I was talking to a doctor from Australia, do eventually respond...

01:17:56.000 --> 01:17:58.000 to the COVID vaccine, never as robust.

01:17:58.000 --> 01:18:04.000 But we're not going to get there with one shot or two shots. It's often multiple shots and that's why...

01:18:04.000 --> 01:18:06.000 the twice a year recommendation.

01:18:06.000 --> 01:18:13.000 What he said, at least in Australia, maybe they have different blood in Australia, 80% of people were getting...

01:18:13.000 --> 01:18:17.000 adequate antibody response, but it took multiple doses...

01:18:17.000 --> 01:18:18.000



of the vaccine to get there.

01:18:18.000 --> 01:18:23.000 Yeah, that's about right. And there always is going to be a subset of probably five to 10% of people who really...

01:18:23.000 --> 01:18:27.000 struggle and that's usually people who are taking...

01:18:27.000 --> 01:18:29.000 rituximab or obinutuzumab,..

01:18:29.000 --> 01:18:32.000 recent bone marrow transplant, those like very sort of intense...

01:18:32.000 --> 01:18:34.000 periods.

01:18:34.000 --> 01:18:36.000 And we know those people do have T cell response.

01:18:36.000 --> 01:18:37.000 Yep.

01:18:37.000 --> 01:18:40.000 At least some of them do have the T cell response.

01:18:40.000 --> 01:18:46.000 And one of the other things that I've seen done is if you're going to get a vaccine like n pneumonia vaccine, which is...

01:18:46.000 --> 01:18:51.000 like Prevnar 20, which covers 20 different subtypes of pneumonia,...

01:18:51.000 --> 01:18:57.000 you can then test your antibodies before and after and see how they go up...

01:18:57.000 --> 01:19:04.000 and that can be extremely helpful because it's not just how many soldiers you have, it's how good they are at fighting, you know, how weaponized they are.

01:19:04.000 --> 01:19:10.000



Some specific questions I'm going to put you on the spot on. Is there a preference for an immune compromised...

01:19:10.000 --> 01:19:12.000 patient in terms of which...

01:19:12.000 --> 01:19:17.000 RSV vaccine to get? And you did mention there's a couple preferred...

01:19:17.000 --> 01:19:22.000 flu vaccines adjuvant versus the high dose?

01:19:22.000 --> 01:19:24.000 Help us understand when we're...

01:19:24.000 --> 01:19:28.000 choosing because we don't know which vaccine should we get.

01:19:28.000 --> 01:19:33.000 Right. You know, and the party line always has to be whatever vaccine is available and you're willing to get,..

01:19:33.000 --> 01:19:38.000 you should get. But if you have the option of time and you know,...

01:19:38.000 --> 01:19:43.000 you're selecting among them, there may be some differences in immune response...

01:19:43.000 --> 01:19:47.000 for people who are heavily immunocompromised.

01:19:47.000 --> 01:19:49.000 For flu, we just talked about...

01:19:49.000 --> 01:19:54.000 particularly older persons, higher dose or adjuvanted flu vaccines do increase...

01:19:54.000 --> 01:19:58.000 immune response. That's true. That's why they're recommended for older people.

01:19:58.000 --> 01:20:04.000 Being able to get those if you're someone under 65 is complicated, there's insurance issues...



01:20:04.000 --> 01:20:09.000 and you usually need like a doctor's note and stuff like that so...

01:20:09.000 --> 01:20:11.000 I can't, you know, I can't...

01:20:11.000 --> 01:20:16.000 recommends, but some people do do that.

01:20:16.000 --> 01:20:21.000 Additionally, and it was one of these questions just speaking about flu,...

01:20:21.000 --> 01:20:23.000 there are some...

01:20:23.000 --> 01:20:28.000 populations for whom their data to get a second flu shot if you're, let's say a...

01:20:28.000 --> 01:20:31.000 48-year-old lung transplant recipient,...

01:20:31.000 --> 01:20:39.000 there have been data that show if you get a second flu shot like three months later, the risk of flu in the second part of the season is lower. It is a booster...

01:20:39.000 --> 01:20:41.000 but that also runs into insurance issues...

01:20:41.000 --> 01:20:46.000 and needs notes and stuff. And so, these are not things that are recommended by the CDC, but there are data for that.

01:20:46.000 --> 01:20:52.000 In terms of RSV, as I mentioned, the data on immunocompromised people is very scant.

01:20:52.000 --> 01:20:55.000 I happened to run a study that studies this in...

01:20:55.000 --> 01:21:00.000 immunocompromised populations so I have some inside knowledge of this and...



01:21:00.000 --> 01:21:05.000 I will say in our hands, we feel that an adjuvanted vaccine,...

01:21:05.000 --> 01:21:10.000 similar to the flu vaccine is probably more likely to at least get high levels of antibody.

01:21:10.000 --> 01:21:17.000 So, the GSK vaccine does have an adjuvant. The Pfizer vaccine does not.

01:21:17.000 --> 01:21:21.000 And the mRNA vaccine is like a different technology for which there's almost no information...

01:21:21.000 --> 01:21:26.000 in immunocompromised people. I have only a few people in my study who've gotten that and I don't have an idea.

01:21:26.000 --> 01:21:33.000 So in our hands, we have tended to recommend the GSK vaccine.

01:21:33.000 --> 01:21:36.000 It does cause some more reactions,...

01:21:36.000 --> 01:21:38.000 you know, because it's like an adjuvant...

01:21:38.000 --> 01:21:40.000 so it's kind of some personal preference there.

01:21:40.000 --> 01:21:43.000 But I'll go back to the first thing I said, which is...

01:21:43.000 --> 01:21:45.000 they're all likely to be beneficial.

01:21:45.000 --> 01:21:48.000 Whatever one you're comfortable with, is the one you should get.

01:21:48.000 --> 01:21:51.000 And then in terms of COVID shots,...

01:21:51.000 --> 01:21:58.000



there's a little bit more information. I mean, in our hands and in other studies, the Moderna vaccine does seem to increase...

01:21:58.000 --> 01:22:02.000 antibody levels at least a little more than the Pfizer vaccine.

01:22:02.000 --> 01:22:06.000 It's probably because there's a bit of a higher dose in there...

01:22:06.000 --> 01:22:14.000 but that tends to only really be seen when people are in the highest immunocompromised state.

01:22:14.000 --> 01:22:18.000 In terms of the Novavax vaccine, there's very scant information.

01:22:18.000 --> 01:22:27.000 We're just getting our own info together on that. It is adjuvanted, which would make you think maybe there's a potential to lead to better immune responses...

01:22:27.000 --> 01:22:33.000 but there's almost no information that would support that. And in fact, most of the information in healthy people...

01:22:33.000 --> 01:22:39.000 shows that antibody levels tend to be a little bit lower than the mRNA vaccines, particularly the Moderna vaccine,..

01:22:39.000 --> 01:22:44.000 just in head-to-head studies in healthy populations. So, the jury is definitely out.

01:22:44.000 --> 01:22:48.000 There do tend to be fewer side effects with the Novavax vaccine...

01:22:48.000 --> 01:22:52.000 for reasons that are probably just related to not having the mRNA,...

01:22:52.000 --> 01:22:55.000 the lipid thing that's in the mRNA.

01:22:55.000 --> 01:23:01.000 But, it's not clear that that corresponds to how well they work.



01:23:01.000 --> 01:23:06.000 Talk about most of us with CLL are older and have other things...

01:23:06.000 --> 01:23:13.000 happening to us and sometimes other things in our body like dental implants or cochlear implants or...

01:23:13.000 --> 01:23:21.000 total joint replacements, anything special about that in terms of infection management?

01:23:21.000 --> 01:23:24.000 If there is a cochlear implant, a dental implant,...

01:23:24.000 --> 01:23:26.000 a knee or hip that's replaced...

01:23:26.000 --> 01:23:29.000 that you think about as an ID doc?

01:23:29.000 --> 01:23:35.000 I will say that most guidelines do not recommend changing what you do...

01:23:35.000 --> 01:23:40.000 vis-a-vis dental work for joint replacements, particularly if they're not new.

01:23:40.000 --> 01:23:47.000 Like brand new. Brand new, we can talk about it.

01:23:47.000 --> 01:23:52.000 The cochlear implant thing is very interesting. I've not actually run into that issue, but that is a concern to me.

01:23:52.000 --> 01:23:57.000 Cochlear implants are associated with higher risks of invasive strep infections in particular.

01:23:57.000 --> 01:24:01.000 They go in the area in the ear canal and things that...

01:24:01.000 --> 01:24:03.000 are colonized with these streps that we all have that can,...

01:24:03.000 --> 01:24:07.000



cause pneumonia and sometimes can cause things like meningitis...

01:24:07.000 --> 01:24:11.000 or serious like brain infections. The combination of that with someone with CLL...

01:24:11.000 --> 01:24:14.000 is high risk for that.

01:24:14.000 --> 01:24:19.000 Definitely optimizing vaccination, testing the IgG antibodies to see if you need IVIG,...

01:24:19.000 --> 01:24:25.000 and in rare cases, people actually do prophylaxis. And I would have to see somebody's individual...

01:24:25.000 --> 01:24:28.000 situation to the side about prophylaxis with a drug like amoxicillin...

01:24:28.000 --> 01:24:32.000 against strep for people with a cochlear implant. So that's actually a very...

01:24:32.000 --> 01:24:34.000 important situation to discuss with your...

01:24:34.000 --> 01:24:38.000 Doctor, that intersection.

01:24:38.000 --> 01:24:43.000 So if we're having, if we're sick,...

01:24:43.000 --> 01:24:51.000 who do we call? Do we call with an infection? Do we call you? Do we need an infectious disease? Do we call our hematologist?

01:24:51.000 --> 01:25:00.000 And where do you fit in in the care? I don't think most of us have an infectious disease doc on our team.

01:25:00.000 --> 01:25:04.000 And I think of you mostly in the hospital setting, and I'm sure that's...

01:25:04.000 --> 01:25:09.000 a characterization that isn't completely accurate but...

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01:25:09.000 --> 01:25:13.000 help us understand what we do now. I got the flu. I'm coughing and I've...

01:25:13.000 --> 01:25:19.000 got my Tamiflu, but I'm not getting better you know who's my next call to?

01:25:19.000 --> 01:25:22.000 Yeah, I think in the vast majority of cases of the...

01:25:22.000 --> 01:25:26.000 people on the call, infectious disease doctors are not going to be involved in your care.

01:25:26.000 --> 01:25:35.000 They may not be available. There's some states where there are barely any infectious disease doctors, you know. It really depends on your health center and where you live.

01:25:35.000 --> 01:25:40.000 It's only when things get complicated. Yes, typically if you end up in the hospital or repeated sort of...

01:25:40.000 --> 01:25:42.000 courses of therapy for something that don't...

01:25:42.000 --> 01:25:45.000 seem to be helping.

01:25:45.000 --> 01:25:50.000 The best case scenario is that either a primary care doctor or your primary...

01:25:50.000 --> 01:25:53.000 blood cancer team, uh are uh,...

01:25:53.000 --> 01:25:55.000 on the speed dial for you if you need them...

01:25:55.000 --> 01:25:59.000 and that they're educated and empowered,

01:25:59.000 --> 01:26:05.000

potentially informed by a colleague who's an infectious disease doctor about what to do for most of these scenarios. Like at Hopkins, we develop...



01:26:05.000 --> 01:26:09.000 protocols, let's say that we give to all the transplant...

## 01:26:09.000 --> 01:26:21.000

nurses and things for what do we do in the setting of RSV or what do we do in the setting of flu? Just kind of like spread that knowledge and understand that 95% of the problems are going to be channeled through...

01:26:21.000 --> 01:26:24.000 doctors or nurse teams who know you best.

01:26:24.000 --> 01:26:26.000 So, um,..

01:26:26.000 --> 01:26:30.000 you know, there aren't that many infectious disease doctors and...

01:26:30.000 --> 01:26:33.000 can't be everywhere at once and many,...

01:26:33.000 --> 01:26:39.000 like I said, 95% of the time, your team should be able to sort of manage these things, particularly if they have reference materials...

01:26:39.000 --> 01:26:42.000 that are, you know, up to speed.

01:26:42.000 --> 01:26:47.000 Could you give us that back of the napkin, you caused a lot of excitement about this way to...

01:26:47.000 --> 01:26:50.000 rough calculation of IgG with total protein.

01:26:50.000 --> 01:26:54.000 Oh, yes. You know, that's like me as I look through patient charts,...

01:26:54.000 --> 01:26:56.000 if you haven't had it tested,...

01:26:56.000 --> 01:26:59.000 you know, which you just should to be honest if like...



01:26:59.000 --> 01:27:02.000 that's part of what your concerns are because it's an...

01:27:02.000 --> 01:27:09.000 inexpensive test done by like every lab. But if you have the albumin on your, um,...

01:27:09.000 --> 01:27:15.000 chem panel, chemistry panel, and you have the total protein on your chemistry panel,...

01:27:15.000 --> 01:27:20.000 you just subtract the albumin from the total protein. The rest of that is usually...

01:27:20.000 --> 01:27:23.000 immunoglobulin. And so albumin...

01:27:23.000 --> 01:27:30.000 tends to be like, you know, three and a half to five or so in total protein tends to be...

01:27:30.000 --> 01:27:33.000 you know, five and a half to...

01:27:33.000 --> 01:27:36.000 seven and a half, it can depend on a person...

01:27:36.000 --> 01:27:41.000 and so if that ends up being less than two, that tends to be associated with hypogammaglobulinemia.

01:27:41.000 --> 01:27:47.000 But you should just check it. You don't have to do your own math. Also, there are some chem panels that'll say something called like globulin.

01:27:47.000 --> 01:27:53.000 They'll just calculate it for you. And you can just look at that. You don't have to do your calculation, but it'll be almost exactly the same as...

01:27:53.000 --> 01:27:56.000 that little...

01:27:56.000 --> 01:28:02.000 chem panel trick.

01:28:02.000 --> 01:28:03.000



Yeah, yeah.

01:28:03.000 --> 01:28:05.000 Right. But the test is a really inexpensive, simple test. And it also tells your IgA, IgM, and IgG.

01:28:05.000 --> 01:28:07.000 Right.

01:28:07.000 --> 01:28:08.000 Right,..

01:28:08.000 --> 01:28:13.000 which are important and may qualify you if you've had recurrent infections to get the supplement.

01:28:13.000 --> 01:28:24.000 There's a lot of questions about Lyme's disease and if that's been treated. Is it more of a risk in CLL? Any comments on that?

01:28:24.000 --> 01:28:32.000 You know, I've never seen that to my, I mean, maybe there's one out there, like a study of Lyme disease in people with CLL, and maybe there's a Google of one.

01:28:32.000 --> 01:28:36.000 It is not one of these infections that I necessarily think are...

01:28:36.000 --> 01:28:39.000 more common or dramatically worse in people with CLL...

01:28:39.000 --> 01:28:43.000 per se. To be honest, the biggest risk factor for Lyme disease is an exposure thing.

01:28:43.000 --> 01:28:47.000 I, you know, I grew up in sort of...

01:28:47.000 --> 01:28:55.000

suburban New York, and I'm sure I've had Lyme disease. And if you tested me, I would have antibodies positive for having been exposed to Lyme.

01:28:55.000 --> 01:29:01.000 It's not something that we really think like reactivates necessarily when your immune system goes.



01:29:01.000 --> 01:29:03.000 It's just...

01:29:03.000 --> 01:29:05.000 an exposure thing and I wouldn't...

01:29:05.000 --> 01:29:07.000 go hunting probably,..

01:29:07.000 --> 01:29:10.000 no pun intended, I meant more like looking for it...

01:29:10.000 --> 01:29:19.000 as the cause of problems, unless you're someone who's got very high exposure risk.

01:29:19.000 --> 01:29:20.000 Yeah.

01:29:20.000 --> 01:29:21.000 You use the word adjuvant several times, but I know you...

01:29:21.000 --> 01:29:24.000 explained it a little bit, but could you re-explain it, please?

01:29:24.000 --> 01:29:26.000 Yeah, so...

01:29:26.000 --> 01:29:31.000 there are these, I'll tell you almost like a story about it.

01:29:31.000 --> 01:29:39.000 Adjuvants are a type of immune stimulator, an immune booster, and there are many kinds.

01:29:39.000 --> 01:29:48.000 Some of the vaccines that people get that are particularly, that cause like particularly arm reactions, for example, tend to have adjuvants in them like...

01:29:48.000 --> 01:29:50.000 the shingles shot, if anyone's had that.

01:29:50.000 --> 01:29:59.000



About one out of 10 people have a pretty sore arm or pretty red arm, and that's because of the adjuvant. It tends to be some sort of chemical that is broadly reactive in most people.

01:29:59.000 --> 01:30:09.000 And some of the classic stories are that they're like these trees in the Amazon that someone like, rub against and their arm swells up hugely. And so people have like found the tree bark and sap from that,..

01:30:09.000 --> 01:30:12.000 found the chemical structure of it and created it as an adjuvant...

01:30:12.000 --> 01:30:17.000 that will recruit immune cells to the site of something like an infection kind of...

01:30:17.000 --> 01:30:19.000 alarm your immune system to this...

01:30:19.000 --> 01:30:22.000 otherwise harmless you know, uh, piece of...

01:30:22.000 --> 01:30:26.000 flu shot, you know, and then that kind of is almost like a...

01:30:26.000 --> 01:30:28.000 off-target effect in a way to...

01:30:28.000 --> 01:30:32.000 recruit parts of your immune system to be like, hey, I remember flu. I'm going to make some...

01:30:32.000 --> 01:30:36.000 flu immunity now.

01:30:36.000 --> 01:30:37.000 So...

01:30:37.000 --> 01:30:40.000 So adjuvant, that's one strategy to improve immune response.

01:30:40.000 --> 01:30:44.000 So, we seem we answer one question, we get more on this just...



## 01:30:44.000 --> 01:30:53.000

somebody who's going to have a total joint replacement, anything special, somebody who's going to have a valve replaced or a pacemaker or anything special about those?

01:30:53.000 --> 01:30:55.000 In someone who has CLL?

01:30:55.000 --> 01:30:57.000 Oh, yeah, these are CLL patients.

01:30:57.000 --> 01:31:02.000 Yeah, you know, it's going to be case by case. I think if you're people who are on a lot of steroids in particular,...

01:31:02.000 --> 01:31:06.000 that's a high risk for having a surgical site infection.

01:31:06.000 --> 01:31:11.000 And, you know, as we know, steroids can sometimes cause bone problems and then you need to get a joint replacement so...

01:31:11.000 --> 01:31:14.000 those are situations where you have to be,

01:31:14.000 --> 01:31:18.000 the surgical team needs to be aware of that and...

01:31:18.000 --> 01:31:25.000 understand that there may be a higher risk of getting a bacterial infection around the operative site.

01:31:25.000 --> 01:31:30.000 We don't tend to do much different apart from trying to lower the steroid dose if we can...

01:31:30.000 --> 01:31:33.000 around the surgery to kind of let wound healing improve.

01:31:33.000 --> 01:31:36.000 There's some other drugs like sirolimus,...

01:31:36.000 --> 01:31:42.000



Rapamun, that people take after bone marrow transplant that are also associated with poor wound healing.

01:31:42.000 --> 01:31:46.000 So those are other high risk situations. But CLL, again, is sort of a baseline problem is...

01:31:46.000 --> 01:31:51.000 the bacterial issues or skin issues tend to be a little bit lower...

01:31:51.000 --> 01:31:59.000 with the exception of very significant hypogammaglobulinemia. So IVIG can help a little with that.

01:31:59.000 --> 01:32:06.000 So let me run through a couple things here because we're coming in. I'm going to ask you in a minute here just to kind of summarize or any takeaway points you have.

01:32:06.000 --> 01:32:13.000 There was a couple questions specifically on CLL. Didn't CLL cause hair loss and some of the treatments can, but it's rare.

01:32:13.000 --> 01:32:16.000 The CLL usually does not cause hair loss.

01:32:16.000 --> 01:32:24.000 Does taking iron prevent you from getting anemia with CLL? Not unless you're iron deficient. It's not going to prevent it. Most of the anemia in CLL,..

01:32:24.000 --> 01:32:30.000 the CLL itself can either crowd out the bone marrow or suppress the activity

01:32:30.000 --> 01:32:35.000 of the healthy cells so anemia is common. There's also autoimmune conditions.

01:32:35.000 --> 01:32:42.000 So you have to know what kind of anemia, and there are many different kinds of anemia. An iron deficiency anemia,..

01:32:42.000 --> 01:32:50.000

if you have that, then it's not the CLL and you want to see if they're, you know, in younger women, that can be menstrual, but in the people...

01:32:50.000 --> 01:32:56.000



older, we worry about GI bleeding, colon cancer, peptic ulcer disease. There's all kinds of things,...

01:32:56.000 --> 01:33:04.000 that's not a trivial diagnosis in iron deficiency anemia needs to be figured out why you're iron deficient. It can be diet, but that's...

01:33:04.000 --> 01:33:11.000 pretty rare. People ask the difference between IgA, IgM, and IgG. They're different...

01:33:11.000 --> 01:33:17.000 antibodies, the only one we can replace is IgG, and that's in the immune globulin...

01:33:17.000 --> 01:33:23.000 and it's the workhorse to really oversimplify. The IgA is on the mucosal membranes...

01:33:23.000 --> 01:33:34.000 so it lines the ENT track, but also the gut tract. And the IgM is kind of the fast acting bigger antibody. I mean, that's incredibly oversimplifying it.

01:33:34.000 --> 01:33:37.000 D and E, which are beyond the scope of...

01:33:37.000 --> 01:33:43.000 getting into this, but the only one we can place is IgG.

01:33:43.000 --> 01:33:45.000 I think...

01:33:45.000 --> 01:33:51.000 we have a lot more questions. Skin infections, they are more common in CLL.

01:33:51.000 --> 01:33:57.000 All infections are more common in CLL. That's the bottom line. Eye infections are more common.

01:33:57.000 --> 01:34:02.000 I did want to ask you one question before you do the summary.

01:34:02.000 --> 01:34:11.000 Gardening. And if you're on a BTKi and you're working in the dirt and fungal and these things aren't a pathogen and...



01:34:11.000 --> 01:34:20.000

your partner can be digging up the garden. Should we be masking when we're working in the garden, especially if we're on a BTKi or something else like that? That's a question.

01:34:20.000 --> 01:34:21.000 Okay.

01:34:21.000 --> 01:34:28.000 It's a great question. It hasn't been like directly studied, but I think of it a little bit like, again, people who are very soon after an organ transplant.

01:34:28.000 --> 01:34:35.000 Usually after the first three months or so, I do recommend wearing gloves in consideration of a mask if you're doing things like...

01:34:35.000 --> 01:34:40.000 renovations, gardening, you're like a big woodworker, stuff like that.

01:34:40.000 --> 01:34:44.000 The likelihood of these infections is generally relatively low...

01:34:44.000 --> 01:34:48.000 but they are increased...

01:34:48.000 --> 01:34:52.000 In the use of things like the BTK inhibitors, high doses of steroids,...

01:34:52.000 --> 01:34:57.000 in early after stem cell transplant. So those are situations where I do recommend that,...

01:34:57.000 --> 01:35:00.000 if it doesn't cramp your style too much.

01:35:00.000 --> 01:35:03.000 So...

01:35:03.000 --> 01:35:08.000 any takeaway thoughts in a couple minutes here of what you think that's really important for patients to know.

01:35:08.000 --> 01:35:12.000 Yes. I mean, I think one, and we talked about this before too is...



01:35:12.000 --> 01:35:17.000 to your point, almost all of these infection things are going to be higher,...

01:35:17.000 --> 01:35:21.000 on balance, if you have a diagnosis of CLL, but it's a sliding scale

01:35:21.000 --> 01:35:26.000 depending on how immunosuppressed you are. There are some things we can do, right? We can...

01:35:26.000 --> 01:35:30.000 get vaccinations, we can make sure our friends and family are vaccinated,...

01:35:30.000 --> 01:35:35.000 IVIG if we need. And then all those things I mentioned that are not...

01:35:35.000 --> 01:35:37.000 drugs but reduce risk like...

01:35:37.000 --> 01:35:42.000 washing your hands and wearing a mask in these high risk situations.

01:35:42.000 --> 01:35:45.000 That said, again, we only have...

01:35:45.000 --> 01:35:49.000 one life. And we really want to, I would really want to emphasize that...

01:35:49.000 --> 01:35:59.000 despite increased risks, this doesn't mean never leave your house, right? If you never leave your house, you're probably not going to get an infection, but your quality of life is not going to be great. So, it's more about making smart choices...

01:35:59.000 --> 01:36:01.000 to reduce your risk, both in terms of...

01:36:01.000 --> 01:36:05.000 these interventions we talked about as well as situationally you know,...

01:36:05.000 --> 01:36:09.000 particularly at high levels of respiratory virus circulation,...



01:36:09.000 --> 01:36:12.000 if you know you're very immunosuppressed...

01:36:12.000 --> 01:36:20.000 that's just not particularly a great combination to be doing things that are going to be like

big groups of people. If you have to do it because it's a really important thing, it's a funeral,..

01:36:20.000 --> 01:36:22.000 well, it's a wedding, it's a you know, a...

01:36:22.000 --> 01:36:25.000 Pilgrimage, you know,..

01:36:25.000 --> 01:36:28.000 boost yourself up before that, wear a mask,...

01:36:28.000 --> 01:36:32.000 wash your hands and the risks will be lower. It's just going to be higher than if you sat in your...

01:36:32.000 --> 01:36:34.000 chair in your living room.

01:36:34.000 --> 01:36:40.000 It's all a balance, risk-benefit, missing a family event, something is worth taking the risk.

01:36:40.000 --> 01:36:48.000 We didn't get to all the questions, but we have a way. Thank you for great questions. Dr. Werbel, thank you for making this...

01:36:48.000 --> 01:36:51.000 really a great...

01:36:51.000 --> 01:36:53.000 I think, very granular and impactful...

01:36:53.000 --> 01:36:57.000 kind of presentation. If we didn't get to your questions,...

01:36:57.000 --> 01:37:01.000 email us at Ask the Expert address after this event.



01:37:01.000 --> 01:37:06.000 And we'll share that email address in these closing slides.

01:37:06.000 --> 01:37:09.000 We do want to thank our,..

01:37:09.000 --> 01:37:12.000 our generous donors who made this program possible.

01:37:12.000 --> 01:37:23.000 Big thanks to everyone for joining us. Dr. Werbel, just really great. I want to have you back and I want to interview you about some of this research that you've been doing.

01:37:23.000 --> 01:37:29.000 Please complete our event survey. It's really important to us. It really helps us.

01:37:29.000 --> 01:37:34.000 We listen to your feedback. We read it. We review it as a team and we make changes based on it.

01:37:34.000 --> 01:37:41.000 This event was recorded. It'll be available on our website with the slide deck and a written transcript. People asked about that.

01:37:41.000 --> 01:37:52.000 Usually takes about a week. Your questions, asktheexpert@cllsociety.org, all one word, askthexpert at CLLSociety.org. You can see it there.

01:37:52.000 --> 01:38:05.000 Join us for our next webinar, which will be from ASH 2024. And there's a ton of great stuff there. Dr. Nitin Jain is doing it with us. I'll be one of the speakers there. That's on January 9th.

01:38:05.000 --> 01:38:15.000 And finally, this is the season of giving. Please remember the CLL Society. We're a nonprofit. Any donation is fully tax deductible.

01:38:15.000 --> 01:38:21.000 We're invested in your long life. If you can invest in the long life of the CLL Society,...

01:38:21.000 --> 01:38:24.000 by supporting our work, we'd be so grateful!



01:38:24.000 --> 01:38:32.000 Stay strong. We are all in this together. Thank you for your attention.