

Ask the Doctor Session – Teenage and Adult Issues

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Dr. Vellody: I'm very happy to be here for another Ask the Doctor Session. We started having these last year because every time I would end my talk about 'What Families Need to Know', it was always followed by at least a half-hour to an hour of questions from the audience. And so, I thought it would be great to take all of our pooled knowledge – both from the pediatric side and the adult side of what we do – and make a question session for families. We've already have a couple questions that have been texted in so feel free to keep on sending them in and we'll try to get to them. I thought since you guys are formulating what questions you might have right now, we'll introduce ourselves and let you know what our roles are. That way you'll know why certain people are asking certain questions.

I'm Kishore Vellody. I direct the pediatric portion of our Down Syndrome Center in Pittsburgh. We are a very busy clinical practice. This year, we set our yearly record of seeing over 650 patients seen between the pediatric and adult centers together. It means that we are quite busy but it also gives us the opportunity to learn about and gain knowledge of the multitude of issues that come up. So we're happy to be here to share that information with you.

Ms. Cannon: I'm Sheila Cannon. I've been the program coordinator at Children's Hospital, Down Syndrome Center since 1995 – so I've been here for a while. My role is multi-faceted but basically it is to meet with families as the resource person and connect them to whatever resources are best-suited for their individual with Down Syndrome. Whether it is gathering medical or general resources; reviewing IEPs, IFSPs, and then also talking to families who care for an adult, a loved one, making sure that they have those resources as well.

Dr. McCormick: Hello, my name is Dr. McCormick. I work with Kishore in the Pediatric Down Syndrome Center. My training is in internal medicine and pediatrics, so with that, what I bring to the table is that I work with Sheila to create a healthy transitions program for our patients. This program is designed to help our kids transition from adolescence to adulthood. The idea is that we would help them with all of the medical transitions but also with all of the other aspects of life – so we really are trying to be kind of the one-stop shop for our patients.

Dr. Bulova: I'm Peter Bulova. I'm an Associate Professor of General Internal Medicine at the University of Pittsburgh and I've been at this Down Syndrome Center for adults with Down Syndrome for the past 12 years. I also co-run a center for women with physical and intellectual disabilities at another hospital here as well.

Dr. Vellody: Okay so the goal of this session today is for Teenage and Adult-type questions. And Dr. Bulova and Dr. McCormick will definitely help a lot with those. While they are looking at some of the first questions coming in, one question that already came in that I feel I can answer was about Selenium and Magnesium supplementation. What's the role of that in people with Down Syndrome?

That's a great question because certainly there's a lot of vitamin and supplement issues that we run into with our patient population that we're not exactly completely clear on. Selenium is one, Zinc I've seen also, Magnesium – all of these have the mega-supplements for them that are marketed to help replenish those levels. The data is pretty shoddy to be honest with you. There's never really been a study that says, "If you give 100 people with DS this supplement, and a 100 people with DS that supplement, this supplement will work great versus that one." What we really are left with is, really, are a lot of theories but not a lot of data. So at this time, as a whole, we don't endorse any supplements that are out there; data is still waiting to come in for anything that's been of any help.

Audience: [Follow-up question, unintelligible]

Dr. Vellody: Most studies that are going to be done in this era are going to be drug-driven for the most part. A study is going to be done because there's a financial benefit to the company to do that, unfortunately. Selenium, Magnesium, the types of things that you get over the counter – they're all very hard to get people to actually do thorough studies on them.

Dr. Bulova: First question that I have here is, "Any suggestion for a 20 year old female who has showed subtle regression in problem solving abilities in the last 6 months. It is subtle; only Mom sees it and there are no other known health issues."

There are several different things that can cause regression. The most common one, I'll give you an example, tends to be some sort of biopsychosocial issue. I had a patient who was very, very functional who had a pretty significant regression and none of us figured out what it was. And then about three months later, all of a sudden, he was all better, and it turned out that they had done construction on the shower that he usually used. He had to go downstairs to now use the shower, and it just threw off his entire routine. And it was just because of that one little change in his routine that caused him to change every other thing that he would typically get done in that day.

So if it's a small regression, it's often something that often we don't even notice. It's a change that is extremely important to the person, but may not be considered as important to the family. There are a lot of medical issues that can cause regression. The most common one is hypothyroidism. If I were to do a medical work-up which would always be the first thing that I would check. After that, we still look for things like Celiac Disease. We also look for anything that

would cause even subtle types of pain that our patients tend to notice but not complain very much about it. But even that can cause a decline in overall skills.

Now if it's a major regression, I would have more concerns than for subtle ones, because most of the time, those subtle regressions do resolve on their own.

Dr. McCormick: The next question that I saw was, "As we're progressing through adolescence, what is the best way for guys and girls to deal with sexuality."

I think transition, just as we were saying earlier, is a holistic process. That question of sexuality is an extremely important question, but it starts way earlier than when we start having 'the talk', right? What we really start with is, even when our kids are young, is getting them used to our body boundaries and the appropriate ways to express feelings, and also what the private areas of our body are and then progressing as they get older. What we always say when we are talking about sexuality is that we're going to start as early as possible. Talking about those appropriate boundaries, many of our kids with Down Syndrome love to show their emotions with hugs so progressing with that idea as they get older is crucial. Who can we show emotion to? Who can we be hugging? Who can we be kissing?

And then when we're getting to the very specific point of how are we going to be talking about our sexuality as they get older. It's very important to remember that our kids are progressing just as any other normal kids are. They are going to be getting those same emotions, desires, and we need to make sure that we are educating them in an appropriate manner. It's also good to remember that the best way to talk to our kids isn't always through language; it's actually visual. So make sure that whenever you are talking about sexuality, you're doing it in a way that is appropriate for our kids – including those visual aids is a great tool. If you really want to delve into those questions and get a first grasp on the topic of sexuality, there are a couple of great books that Terri Couwenhoven has written for kids. And she's done an amazing job explaining those boundaries and go deeper into that question.

Dr. Vellody: And if you want kind of a brief overview of what is going to be in those books, we did a Podcast with Terry about 6 months ago now that is available on our website. You can take a listen and learn about what the overall message of the book is as well as hear her talk about which books discuss which issues and things of that nature.

Just to give you some background really quick on Terri. She's been one of our clinical coordinators in Wisconsin for quite a while. She also has a child with Down Syndrome and so she has a lot of experience in talking about sexuality and training in sexuality. Very experienced author; does a great job.

Dr. Vellody: The next question, I'm not entirely sure if it's necessarily going to be specific for Down Syndrome or if it can be applied in general, but this is about an eighteen year old, who about three or four times a year has significant vomiting and diarrhea episodes in the middle of the night. Doesn't seem to be in pain, no known food allergies; and again, this occurs only three or four times a year.

I mean, I would think from my perspective, the one thing you would want to make sure of with any child with Down Syndrome that is having GI issues is looking for Celiac Disease. The other things to think about when you have episodic vomiting like that are things like migraines – there can be abdominal migraines. In that case, migraine-type medications can help, but, again, I don't know if this is necessarily something that we see typically with Down Syndrome.

Dr. Bulova: That case in particular wouldn't be specific to the GI system in someone with Down Syndrome. However, what is quite typical for our kids, in specific, is we see that as people get into their twenties, we see a lot of increase in reflux. There's also difficulty in swallowing. It doesn't have to be related to a food allergy but there can be a specific food that tends to get caught and causes this aggressive reaction. We've also seen a lot of chronic constipation that one day, kind of just hits, and the person finally just gets everything out – either from above or below – and then slowly over time it builds up again and the cycle repeats.

The treatment in that case would be to try some sort of bowel regimen, more chronically. And see if it prevents those episodes from happening. The other specific issues that we might see are Achalasia. Achalasia is a narrowing at the bottom of the esophagus. This causes intense difficulties swallowing solids and having no trouble with liquids – and that's how you can tell that things are starting to block further down the esophagus like that. The most common swallowing issue we see is actually the opposite – there is a difficulty swallowing liquids more so than solids because the solids are easier to chew. I think the two hardest foods for our patients to take is Wedding Soup – soups that have a lot of different textures – and hotdogs. People just eat them too fast and they just get stuck. So that's my GI talk of the day!

Audience: [Follow up question, unintelligible]

Dr. Bulova: It's something that tends to occur more after growing has stopped – possibly because of the added weight that every person gets after that period. The metabolism slows down a little bit. It can be all of those things. The achalasia in particular – which is the narrowing at the bottom of the esophagus – is no different in someone with Down Syndrome as it is in someone in the general population. Because of that, you don't have to see any specific gastroenterologist but you probably should go to a good one because anytime you dilate that esophagus, you can develop scar tissue.

Abdominal migraines are brought on pretty much in the same way that headache migraines are brought on. It could be caffeine, dehydration, lack of sleep – but instead of presenting as a headache, it presents as abdominal pain. They're usually associated with nausea, just like a regular migraine. The tricky part with this type of abdominal migraine is that this is visceral pain meaning that it is pain all the way deep down instead of muscular pain so it's extremely nonspecific. It can be the whole belly or it can be just a part of the belly, but it tends to be really, really bad for 24 hours and then go completely away on its own without any intervention.

Dr. McCormick: And there is a spectrum, too, without any disorder called Cyclic Vomiting Syndrome which is on the same range as abdominal migraines. Sometimes our kids have a problem expressing pain, which can be a problem, but there are kids who are vomiting exclusively, granted those are very rare but again, they only last for about 24 hours.

Audience: [Follow up question, unintelligible]

Dr. Bulova: That to me fits the most with chronic constipation and then something out of the ordinary that sort of breaks the camel's back which finally causes the system to clear out.

Dr. McCormick: The next question was related to severe dandruff and if that was related to the process of going through puberty. I'll start by saying in general that puberty causes a lot of changes overall, including our skin and our hair. And so we do see an increase in folliculitis – an infection that occurs around the hair follicle – and dandruff. This can be caused by the changes in sweating, oil production, that is completely normal when going through puberty. So yes, it can be puberty related but not exclusively.

The first thing that you would do to treat this should, obviously being the least invasive one, is to just go ahead and get a really good shampooing such as with Selsun Blue. After that, typically, we have to ask "Is this just dandruff or is this something like psoriasis?" which can be common in our kids. Is it getting to that higher level where now I'm referring the kids and their parents to a dermatologist for a further opinion about it? That is typically what I do.

Dr. Bulova Whenever you're seeing dandruff well and above the normal levels, it's nice to make sure it's not psoriasis. We see lots and lots of skin issues; I think it's mostly because we see a lot of skin turnover. There are a lot of callous formations, things like that. It's just something that we see more often than note, that's for sure. In general, I try to normalize it for my patients – it's not something overwhelmingly concerning as long as it's not causing day-to-day constant problems. Therefore, we rarely go over the normal, standard topical treatments.

Dr. McCormick: I just wanted to jump in here really quick. Probably the most common skin thing I see during puberty is folliculitis and that can be one that is pretty significant – especially in the groin, the buttocks, that area. That’s one that we usually have to treat day-to-day. So when you see an issue that you can treat topically, usually with an antibiotic of some sort. But for on a day-to-day basis, the treatment can involve a specific type of bath, bleach baths. That can definitely help keep the area clean of bacteria. Typically what we do is put about a half a cup of bleach into a whole bathtub of water and have you sit in it for about 10, 15 minutes. It’s kind of like a kid going into a pool: if you notice that your kid tends to have a lot of folliculitis, you might notice that during the summer time it seems to get better. That’s because they’re in the chlorinated pools.

Dr. Vellody: Just to clarify: folliculitis is just a fancy word for infection around the hair follicle. It looks like pimples in those areas. Most commonly you’ll see it in the groin region but also you can see it under the armpits as well.

Audience: [Follow up question, unintelligible]

Dr. Vellody: Yeah, and that’s a real issue because those bacteria live on our skin. It’s a staff bacteria – it lives on our skin naturally. So if you wait until they go in and invade the skin, it’s almost too late. So preventing the bacteria from colonizing in those areas is usually the best prevention. That’s why it’s effective to do those bleach baths. If you do it pretty religiously – 3 times a week – about 10 minutes each, you’ll see a decrease in the folliculitis.

Dr. Bulova: It’s usually a staff infection so the antibiotics that we typically use will be for the ones to treat staff bacterial infections. The most common one is clindamycin – and we prescribe it for the patients to use every single day.

You might end up being on it for years, but at the end of it, it is better to have no infection at all and be on a single antibiotic than it is to become resistant to multiple different antibiotics.

Audience: [Follow up question, unintelligible]

Dr. McCormick: There’s different ways to handle it. One of the ways is bleach baths. Another way is to use those antiseptic soaps to really decolonize the bacteria. I feel like the bleach baths are nice because they’re very easy for the kids. For some kids, they refuse baths – they’ll only do showers – and that’s when you have to go to the other methods. Each treatment, of course, is unique to your kid.

Dr. Vellody: Other things to try to: keeping the nails trimmed because often times it’s the scratching the introduces that bacteria up into that area. Not sharing towels, all those types of things that may potential help spread it.

Hibiclens is another option that was brought up.

Dr. Vellody: The next question for you Dr. Bulova is, “Is there a correlation between Down Syndrome and Epilepsy and if there is, can you elaborate? Is the treatment for Epilepsy still the same as in typical children?”

Dr. Bulova: The typical population has a risk of about 1-5% for Epilepsy; the risk in Down Syndrome is 8-27%. Definitely much higher; very significant association. It tends to have a bimodal distribution meaning that it is much more common in those who are very young and then those who are older (40s, 50s, 60s). Those are the most common times for it to present. The treatment can be exactly the same – there’s nothing specific about the seizures at least not in the adults. There is a really good study from people who were developing the signs and symptoms of Alzheimers that if they had uncontrolled seizures, then they deteriorated very rapidly. If the seizures were controlled, on the other hand, there was less deterioration and they did better. The medicine they used in the study was Kepra so that is what I always use.

Dr. McCormick: As far as children with seizures who have Down Syndrome, as Peter was saying, the most common type that we see are the infantile spasms. Though infantile spasms are a specific type of seizure that occurs in Down Syndrome, it’s a kind of seizure that also happens in the entire population. I’m not a neurologist but it is treated in our patients as other children.

Audience: [Follow up question, unintelligible]

Dr. Bulova: There was a study presented a couple years ago on people that presented with seizure-like activity that were not seizures. So you always have to be careful to watch out for those look-a-like symptoms. Someone might be having reflux and it causes them to jerk because it hurts to have that condition; if you add seizure medicines, nothing will ever change. We had a patient whom we cured all their seizures with Zantac because it was all that irritation.

00:25:19 The other type of condition we look for is the Tachycardia Brady Syndrome. Tachycardia meaning the heart goes very fast. Bradycardia meaning the heart goes very slow. If the heart rate goes into the 30s or below 30s, people can have seizure-like activities as well. There was another comment about a central tremor. I don’t know of any specific association between Down Syndrome and that. The other things that you look for would be autoimmune issues that are more common in the Down Syndrome population – anything that involves the thyroid, for example, can cause a tremor symptom as well. I assume that most of you know, it’s definitely what I know to do, is check the thyroid as the first step whenever I notice a change of any kind, especially if the thyroid hasn’t been checked within the last year or so. Any type of electrolyte abnormality can also cause that fine tremor as well but still, I would do some sort of medical work-up with a patient in this case, because it is not common in people with Down Syndrome.

Dr. Bulova: The next question is, “Are there any hints for helping adults to adjust to the BiPap machine. My daughter is not sleeping. She constantly checks the timer and shuts it off as soon as the targeted time of use is met... down to the minute.”

This is one of the great challenges for working with adults. Just recently, in the Medical Interest Group, we were talking about rates of sleep apnea may be as high as 85%. The literature that I traditionally know of says 30-50%, so we’re seeing this all the time. It is definitely quite a challenge! Because many of our patients just don’t like the sensation of having something on their face, just like the rest of us don’t but even more so. The most common thing that we have found to be helpful is maybe using a sleep medication for a week or two just so the person can get used to it. There are also a few doctors that talk about using positive reinforcement: I know of one doctor that shows his patients the movie ‘Top Gun’ so they get to see Maverick with the mask on his face! Try to build up some sort of positive feeling for it. If your adult has other friends – it’s really nice to get a support group with friends that use it – even if they don’t, they most likely have sleep apnea too and should be using it too! But try to encourage them to get a little bit of peer pressure.

The other thing is to make sure that you start it up very slowly so that you have night where you use the mask with no pressure at all. And then slowly build up to the point where you’re using it and it’s going to be effective.

00:28:27 The next question is about the hypoglossal stimulator. The first article about it came out in 2014 in the New England Journal of Medicine so it is a very new intervention. The hope is that within a couple of years we’re going to find many more treatments for sleep apnea that do not require cooperation. So the hypoglossal nerve stimulator is an implant that detect changes in the lungs and causes the tongue to move forward – it’s an implant so there’s actually a wire that goes up to the hypoglossal nerve so when it’s triggered, it automatically pulls the tongue forward. It’s kind of like a pacemaker. There has been- I know one adult who has had this placed and it seems to work very well. There’s also a recent case study in a child that was presented as one of the top articles of the year. So definitely, it is starting up. Personally, I haven’t started up any of my patients yet because it’s so new, but it may be a nice future treatment.

We’re also seeing some weight loss medications that seem to help. Liraglutine, which is sold as Victoza, the diabetes medication, there are some studies that are coming out that say that it also helps. But in the meantime, BiPab is still the best thing that we have.

Why does Victoza help? One thought is: “Boy, if you lose 20 pounds; that is really going to help!” There’s also a thought that it may be an endocrine issue – that there’s something in the neurotransmitters for central sleep apnea. That should be coming up in the next year about that so keep an eye out. You might know more than your doctors! It probably will continue to only be indicative in

people who are overweight but I think that we have to wait for those studies to come out.

Dr. Vellody: And there is currently a multi-center trial for pediatrics for the hypoglossal nerve stimulator that they're just in the process of enrolling for at the different centers that are participating. It'll be interesting to see where that goes. I know from my experience, I have a lot of patients with sleep apnea who have gone through potential surgical option, won't tolerate the C-Pap, all that stuff, and it would be nice to offer something that actually worked that we could use for these young people.

So I'm going to answer two questions right now, one of which was funny, it was only one word – “gas” – exclamation point. “Particularly disruptive in the school setting,” was the second sentence. We do want to make sure that there is not a medical issue there that results in the gas. One of the big things that we look for, of course, is any type of trigger. Does it happen every time they eat bread, or is it more random and doesn't seem to be related to any food process? If it was related to food, then certainly something like Celiac Disease would be something to think about. The following question was ‘How do you test for Celiac?’ and at this time it's actually a two pronged method. The first is, you send a serum – blood screening – for Celiac and you want to send two labs. One is called IGA and the other is called TTG. The TTG is what gets elevated in somebody with Celiac Disease but the particular type of testing that it is, it requires us to send an IGA. I'd be happy to explain further what that is after the session – but essentially, those are the two labs that you would want to send. Now in about 97-98% of the time, if the person has Celiac Disease, the blood screening would come back indicative of that result. But still, there are cases where people will have Celiac but still not have the blood test come back showing it. Therefore, if you have a strong suspicion ever and the blood test came back negative, it's always a good idea to go to a GI specialist as the next step and they will then do the definitive testing. And the definitive testing is a lot more invasive – it's a scope, in biopsies. Even if the blood test shows Celiac, that's the next step – to confirm it with a biopsy.

00:33:35 Now, going back to the original question, the most common reason that I see for our kids to have gas is that whatever air comes in, has to come out. And a lot of the times, the kids either from a self-made perspective or a behavioral perspective, become air swallows. And the air that gets swallowed either gets belched out or if it goes down the stomach, it comes out the other end as gas. That would be something to look at: is there sometimes that they're either intentionally or unintentionally swallowing some air – that could definitely be a part of where this gassiness is coming from. Drinking soda, that's an example of air swallowing that I was supposed to mention.

Dr. Bulova: Anything that helps with motility that makes it so there is less time for stool and everything to be in the colon won't allow gas to build up. So motility agents, any type of agents that can help everything move at a really good pace, will help the gas problems. Also, our patients don't have the same ability to hold it in as well so if you can do more timed stools – like if you can make sure that they go in the morning each day before school and try to plan a regimen in that way – it will make it so that there is a lot less gas throughout the day.

Dr. McCormick: The next question was 'When is the appropriate time to help our kids transition to adult care?' And I would say, and this may sound like a scary answer, is the ages 14 and sometimes as young as the age of twelve. The reason for that is that "transition" is not the same as "transfer." Transfer is the idea of that is when we physically move from one spot to the other. Transition is the process by which we help our kids get ready for that move, and that's why I said we should start to get our kids ready for it starting at 12 to 14. There is a whole lot of work that needs to go into it. While I am going to be working with you from a medical standpoint saying, "Hey, you have a pediatrician as your primary care doctor. How do we make a decision as to who do you go to for your adult primary care? What about those sub-specialist? How do we actually get all your records from the Children's Hospital over to the adult hospital? How do we know that your kids are ready? What are the ways in which we can check their readiness and then help them build so that they can develop skills of independence?"

It's important to note that transition is not just about health care and that's why we have to start it earlier. It's about "How are my kids going to go from education to employment? What about housing in the future? What about the legal questions – guardianship versus power of attorney? What about Special Needs Trusts and financial issues?" So it's a very complicated system and that's why we want to start out so early. And if someone is not asking you those questions, you need to be asking them those questions so that you can make sure that you have all the things you need to be ready to take that next step. Also, just like Kishore was saying, there are Webinars on the same website as the Podcasts where we post things from our annual Transition Conference to share some more information. We bring people from all areas of transition, we bring lawyers in, people from the financial community, we bring in job coaches, and they all do lectures which we've recorded and posted them up so you can access them at any time. I've also recorded by own personal recommendations about transition in terms of the medical standpoint so we do have a lot of resources. Also, GotTransitions is a great website that has tons of information.

Transfer, when I'm working with people for 6 to 8 years or so, I always make a point to look at each kid individually. When I start the transition process, I make a contract with the family and with the kid and say "My goal is to walk you through this process, and you're going to walk with me so that at 18-21 years of age, we

can get to that transfer process.” Not every transfer is going to happen at this same age as you know. But some of these legal things are going to happen at age eighteen because that’s what the government says – getting that Power of Attorney or guardianship set up by eighteen or else it’s already going to switch over automatically. The health care stuff, I’m going to look at you developmentally, see how complicated their care is, and work with you guys to see what the next step is. It’s a moving target, but like I said, it’s individual for each kid.

Dr. Vellody The next question concerns Alzheimer’s and Peter, this question is for you because I know that you’ve done some research concerning this. “My sister is 34 and Alzheimer’s runs in my family. What can people with Down Syndrome specifically do, eat, et cetera, to help with the onset of Down Syndrome.”

Dr. Bulova This is a great question, glad to have a chance to answer this. So, we’ve never seen a study that shows that having a family history of Alzheimer’s lowers the age of onset when we might see Alzheimer’s in a person with Down Syndrome. We have seen a low risk between 40 and 50 years of age; high risk after 50 years of age; just like in the general population, we don’t have a great way to prevent it. They’ve tried Vitamin E, antioxidants, Memantine and Nemanda, Aricept which is Donepezil, and we haven’t found any studies that have shown that they will change the onset of Alzheimer’s. What I tell patients the most is that avoiding things that create chronic hypoxia can actually help. We try to avoid times when the brain is not getting enough oxygen. I think one of the best things to do is being physically fit – exercise is a great thing to do because it brings a lot of oxygen to the brain. And then avoiding things like sleep apnea – occult sleep apnea is one that I would definitely worry about for hastening the time of Alzheimer’s. But there isn’t any vitamin out there that has shown to make any differences.

Dr. Vellody Peter, could you address – I know this morning when I was doing our talk on Medical Issues one of the things that families asked about was the onset and prevalence of Alzheimer’s – is it in everybody? What do we see now in terms of how frequently it occurs in someone with Down Syndrome?

Dr. Bulova If somebody tells you that your child or young adult has Alzheimer’s and they are under the age of 35, they do not have Alzheimer’s. We just don’t see it before the age of 35. There are lots of things that can cause a decline in skills but it’s not going to be Alzheimer’s and you really have to exhaust all other possibilities first. And really, if you’re seeing a decline before 35, it tends to be some sort of mental health issue. At least that is what latest research has shown.

00:41:08 The risk is up to about 10% between 40 and 50; then it goes up to 25% up into the 50s; and then it can go up as high as 75% after the age of 60. There is a case where somebody was 83 years old who did not have Alzheimer’s – so it’s definitely not a universal problem. I’m hoping that now as our younger, healthier

generations grow up – whom had the great supports early on – that we’re going to see a delay before the onset kicks in. If you look at the brain of someone who has passed away who was over the age of 35 or 40, you will see the plaques and tangles like someone who has Alzheimer’s has. But that does not mean that they would have any clinical signs of it.

We’re doing a study here in Pittsburgh where we’re doing an MRI followed by a PET scan; it’s only for diagnosis. The idea is that hopefully we do a study, find the plaques and tangles, then we find a drug that works, then 5 years later we do another MRI or PET scan and see that the plaques and tangles have gone away. That’s the hope, of course! Or even that we can halt the progression of them. We don’t have a drug that has shown that benefit yet but as soon as we do, I’m sure you’ll hear all about it because it would take over the whole general population too. I think it’s very important to get involved in these studies because that’s the only way that we’re going to have progression. But most of the studies that you are in, are actually going to help future generations because we don’t have anything that can dramatically change the plaques and tangles as of yet.

Ms. Cannon And if you’re interested in the study that is going on currently in Pittsburgh, see me afterwards and I can get you the information.

Dr. Bulova We have another question about a son who is 36 years old who seems to be, in some ways, slowing down – not as interested in doing some of the physical things that he’s done before. The question is what could be going on?

Dr. McCormick: We do see what we call “early aging”. What we’ll see is that people will age up to 20 years faster than they normally would. So you might see someone that is in their late thirties, forties, and fifties and they’re acting like someone in their fifties, seventies, and eighties. One of the recent studies that came out showed a lot of arthritis developing very early – as early as in the thirties. And the way that presents is that they just don’t want to do things that cause pain. Often, I’ll get some x-ray to see if that’s true and after that offer a trial of something like an anti-inflammatory – seeing if that helps. And then always looking for mood-related issues that occur. Often we’ll see, even in younger people in their twenties, there’s transition change, loss of a friend or caregiver, a change in the environment that gets them depressed very easily. And that can certainly take a lot out of a person.

Dr. Vellody: And sometimes that type of change can be very subtle. I mean, we’ve seen in our clinic, this sixteen year old came in with this early diagnosis of onset dementia... at sixteen! And truly, what we ended up finding is that when the older sister moved on to college and everything changed in the household, the routines changed, the way things always were changed – for us, when we go through change, we talk it out and are able to discuss it with somebody else and conceptualize change. But for people with Down Syndrome, it’s very difficult for them to process change – they might perceive something as very dramatic when

we might think of it as not such a big deal. It can actually be a huge deal for somebody with Down Syndrome so it's important to have open communication as much as possible to allow them to express what they are feeling in ways that they are able to do that.

Dr. McCormick: The next question is, "Is it common at 15 to still need ear tubes? And in general, do ear infections, continue into adulthood?"

00:46:16 So what I'd like to start with is saying that the initial need for ear tubes when our kids are younger is anatomic. It's because everything is a little bit smaller, and so their ability to drain the ear liquid in the ear canal is lower. Because of this, it's common to need air tubes. Instead of draining the typical way and pressure-grading the typical way where the fluid goes to the nasal passage and the mouth, they have to do it externally. It isn't a common for a fifteen year old to need that but it's not something that's outside the realm of normal. So I'd say that it's more common when you're younger and then as you get older, those infections become less common and the need for ear tubes become less common as well.

Dr. Bulova: As far as adulthood, I think ear infections become much less common. I see very few ear infections in adults yet we still don't know why that is exactly. The ear canals are still very small, there can be sinus issues, but adults seem to get less of them.

The next question was, are problems with feet typical in people with Down Syndrome? And I wanted to answer this question particularly in terms of gout. Gout is something that can be presented in a behavioral way just in the same way that we were talking about in our 36 year old. Someone who just doesn't want to go dancing anymore doesn't like taking walks – sometimes it's gout. And if you don't look at their feet, sometimes it will go unnoticed because they won't tell you that it's because their foot hurts, it's because they have that big red hot swollen joint. We've had patients that we've even diagnosed over the phone that for years have been complaining of foot pain and decline in activities and it ended up being Gout.

00:48:22 Most people with Down Syndrome have very petite feet that are much smaller but very wide. Flat feet are almost universal, that's why people tend to do much better when you can put an arch in their shoes. We recommend a lot of NewBalance – they seem to have a lot of wide shoes but sometimes not wide enough and that's when you have to get the custom shoes. But plantar fasciitis tends to occur when walking in a shoe that doesn't provide enough support. So again, that can be very common in people with Down Syndrome as well. Achilles Tendonitis itself is not associated with Down Syndrome, however.

Dr. McCormick: I'll answer the next question; "you mentioned a bowel regimen for chronic constipation. What do you suggest that would not limit or alter the body's natural motility?"

Whenever I address constipation in our kids, you're exactly right, we don't want to affect motility but instead only increase water bulk in it to help move it through. There's two ways that you can do that. The first way, I always say, is naturally. A lot of times with our really young babies, I'll say just adding a little bit of juice will help. Juice has a lot of sugar in it; the sugar will stay in the digestive tract and the rest will go into the colon and keep the water in. And the reason why I mention this is because as we get older, my favorite agent to use is Miralax. This is because it is something that is not absorbed from the body – it's only localized – and the reason why it's so helpful is because it is not absorbed and thus only stays in the digestive tract. What it does is it draws water in and it keeps the stool hard and in a huge bulk so water can go in and move their bowels easier. The other thing that's really nice about it is that you can't overdose on Miralax. The reason why is that the worst thing that you can possibly cause is diarrhea. The titrations in our body's always keep us safe.

So when kids are younger, very little, I might start them on half a cap a day – you have to have at least three days to have Miralax take effect. And then after the three days you can see if we're doing a good job or a bad job. If we're doing a good job, we'll stay where we're at; if we're doing a bad job – meaning no stool – then we can increase the amount another half a cap. If we're doing too good of a job, then we can either decrease the amount or space it out like every other day. That's my kind of drug of choice and the important thing to note is that it is not a pro-motility agent. Some of the other drugs you'll see that people will use for constipation like Senna can be a pro-motility agent. The thing about those agents is that they can be good in a short term – like if someone is really backed up and you need something really quick, you can use both to help move it along – but the problem becomes when you use Senna too long, you actually get used to it and it stops working and I think you'll like it to.

Dr. Bulova: The only thing I wanted to add to that is that we've had many patients that seem to have an underactive thirst mechanism. This means that if you don't tell them to drink, they won't drink almost anything. And that is the number one cause of constipation – the body needs water so it pulls it in from the colon and then you have very hard stool because of that. So all I want to say that is if you're having any trouble with bowels, if you're having trouble with gas, try to do the same thing about scheduling and really try to force that water bottle into your family member's hand. Really try to push fluids as best as you can, in a positive way.

Audience: [Follow up question, unintelligible]

Dr. McCormick: What I typically say is, let's say you have a kid who's really, really constipated. Typically when you're really constipated, your colon actually starts to stretch out a little bit and you need to develop a schedule and stay on it for at least a month because you need to keep things moving, emptying the colon, so it goes back to its normal size. Some of our kids will need to be on Miralax for a

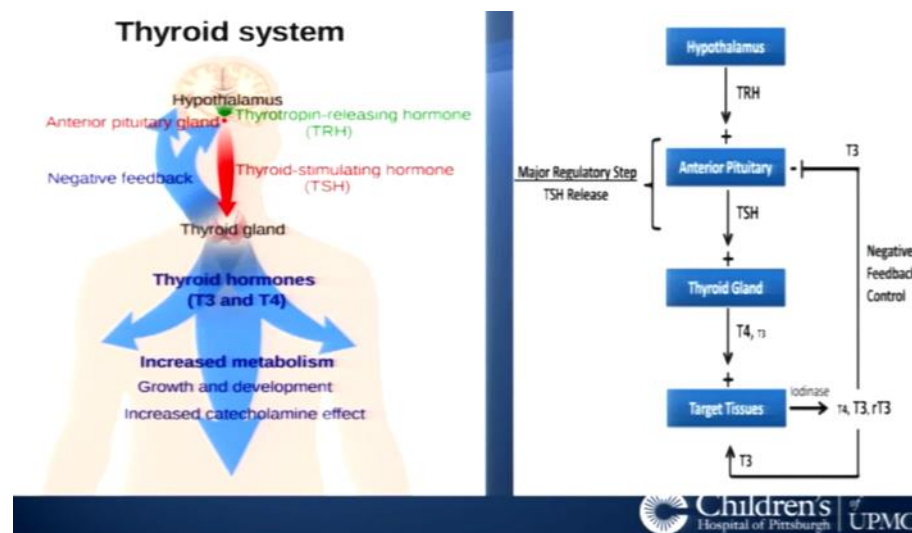
longer period of time. If you're going to do that, you're going to need to go on a stable regimen. I really don't like always playing catch-up with our kids: you'll get your kids cleaned out and then you wait a couple weeks and their constipated again, so you take Miralax again to get cleaned out – this means that you're playing catch-up and you should really be on a stable regimen instead. If you're going to be cleaning your kids out, you're going to need to be on Miralax for a long period of time, but after that, you're going to need to be having them have a bowel movement every day, every other day, and it needs to be soft and not hard – that's when you know you're being successful.

Ms. Cannon: I'll take the next question: "We live in an area that does not have an Adult Down Syndrome Clinic. Is there a process that we can use to connect our internists with a clinic as a resource for her few patients with Down Syndrome?"

There are some resources that are out there. The book written by Dr. Chicoine about Adult Health Care for Individuals with Down Syndrome is a really great resource. Dr. Bulova is currently working with a group on making Adult Care guidelines. There are some things out there as well. Dr. Bulova published a preventive medicine management of adults with Down Syndrome in the British Medical Journal back in 2014 so that can also be used as a great resource for your physician. And I think that if your physician gave us a call or sent us an email, we'd be happy to help.

Dr. Bulova: When we see a new patient, we have a packet that we give them and in them is the review article that we wrote in 2014 that is supposed to be just that: it's supposed to be a how-to guide for internists on what are the most common issues that we see in adults with Down Syndrome. So if you google "BMJ Bulova", you can just pull it up and just give it to your internist and it gives them that checklist in the end of the fifteen most common things that we see.

Dr. Vellody: There's two questions on thyroid which is why I pulled up the slide to go over it.



One question was, “What do you do if the TSH is a little high but all the other thyroid tests are normal?” and the other one was, “What are the normal ranges – are there different normal ranges for somebody with Down Syndrome or not?” So I’ll take the first question from an adult perspective and if any other doctors want to pitch in, that would be great.

00:55:47

So, of course, we want to screen for thyroid issue frequently – the guidelines currently call for annual screenings after that first year of life. The reason for that is that hypothyroidism (underactive thyroid) is the most common thyroid issue that we see and it looks much like symptoms that you see in people with Down Syndrome who don’t have it. There symptoms include constipation, dry skin, maybe fatigue, learning difficulties, things like that which are common in both issues. And so, we really need to be able to test the thyroid in order to know if the symptoms stem from thyroid issues or not.

Thyroid is a little bit complicated because it starts in the brain at the hypothalamus where something called the TRH is released. And then it goes to the pituitary gland when the TSH comes from. So when they test the TSH, they’re testing how much is coming out of that pituitary gland in the brain and then that TSH is actually going to that thyroid gland in the neck and that’s where the T4 comes from. So this is the reason why people check the TSH and T4. Then, just in the beautiful way that works together, when that thyroid hormone reaches the level that it is going to reach, it actually goes back up to the pituitary gland and tells it to stop making the TSH. So it’s kind of like a feedback loop that happens.

If somebody is becoming hypothyroid, the body will start to sense that not enough T4 levels are going to be made and so the TSH levels go up. So it’s kind of odd to think that “hypo-thyroidism” is actually caused when TSH levels are elevated but that’s why. The T4 levels are telling the brain to “Make more! Make more!” and the thyroid gland kind of goes into overtime to make more of it. So what you’ll see, potentially if you catch it early enough, in somebody who is developing hypothyroidism, the T4 may be normal but the TSH start to creep upward. Typically, unless the TSH gets to be above 10, we don’t start treatment because in certain children, the TSH might creep up into that 7 or 8 range and then go back down to normal. In those cases, it’s great, we didn’t start them on a lifetime medication because it was just a moment in time that for some reason, they needed more stimulation to make the thyroid hormone but then it self—resolved.

And so, if the TSH is a little high and the T4 is normal, what we typically do is repeat the labs in about 3 months and then also at the same time, we check for any type of damage in the thyroid with antibodies. The children and adults with Down Syndrome can make antibodies which can start to slightly kill of the thyroid gland. That too is a common cause of hypothyroidism. You might have heard the

word “Hashimoto Thyroiditis” – that’s what’s called when the body itself is trying to kill off its own thyroid gland and it’s causing hypothyroidism. That’s why, in 3 months we would repeat the test, and if everything goes back to normal and those antibodies are negative, we say great – we happened to catch something in a period of time intermittently there but it didn’t end up being hypothyroidism. But in other kids, we check it again and the TSH levels continue to rise or maybe their antibodies are positive, that’s when we get a concern.

00:59:27

A question that has really come up is are there different normal ranges for thyroid hormone levels in people with Down Syndrome, is really driven by some internet information that has been coming out. And the hard part is for parents or caregivers to parce through what’s something more medically-based and what’s something that’s more of somebody’s opinion and we don’t really know where there opinion comes from. The issue with the thyroid levels, and we see this a lot in kids, I don’t know for sure how it is in adults, where they’ve read that we want to keep the TSH levels suppressed further – lower – than what is the normal range. And the problem with that is you’re starting them on a medication when truthfully, they’re body is not needing that extra medication. Now we may run into some additional side-effects and push them hyperthyroidism when that is not our goal. Truly, the normal range is – especially in pediatrics – the normal levels, based on years and years of data, do not have to be treated differently in Down Syndrome versus in someone without it. I don’t know, maybe Peter will be able to give us more insight into how it is in adults.

Dr. Bulova: Yes, and I pretty much agree with everything that Dr. Vellody just said!

All I would say is if we see someone whose TSH levels are a little bit high, then we really just have to watch it but not necessarily treat it. Many people who are already treating it will shoot a little lower on the normal scale which is anywhere from 0.3 to 5.0. So anywhere in that range is normal. Often when we do treat it, we try to get it around 1 – we really don’t want to go below the normal range but rather closer to the lower side. But again, it’s not that big of an issue – like someone with sub-clinical hypothyroidism; it’s not that big of an issue.

Dr. McCormick: And then I’ll just add one thing because it’s a common question that I have related to thyroid for our families as well is this idea between – as Kishore said – hypothyroid and Hashimoto’s Thyroiditis because they are two separate things. So Hashimoto’s is the inflammation of the thyroid and when you have this type of thyroid issue, you don’t have to treat it with medication. Sometimes that clears up on its own and doesn’t lead to the thyroid not functioning. But it does tell us that we need to follow closer so that we see it when it drops. When it drops, and we see the TSH go too high and the T4 go low, that’s when there’s a cause for concern and we’ll start the medication.

The question was, “How do you definitively diagnose SCRD in a Down Syndrome individual who seems to have high pain tolerance and doesn’t express pain well?”

Do you recommend universal screening with EGD, just like we do with sleep studies?" And then the last part will be for Peter: "Is there an increased incidence with Barrett's in adults with Down Syndrome?"

01:03:02

I would say that is a big issue in that with almost anything that we're dealing with in our kids is that sometimes we don't get the specific symptom that we're looking for. "Oh, I have belly pain," but what we can see is a change in some of their other aspects. Maybe we see a change in their behavior but more importantly, maybe we see increased belching, maybe we see an increase in bad breath, maybe we even see some regurgitation that occurs. And those can be symptoms. Also, one of the things that we sometimes do when we're concerned enough, there's two ways of handling the definitive diagnosis. The definitive diagnosis of reflux is either by going down and putting a probe in and measuring the levels of acid, or going in and seeing if we see changes in the mucosa. But, those are both very invasive tests, so another way that we'll often do it is actually by giving an empiric course of antacid medication for four to eight weeks, see if symptoms that we're seeing gets resolved, and that can give us some answers.

One thing I will say about reflux is that Acid Reflux Disease, that's usually something that we see that occurs usually after the age of one, usually after the age of two and can occur all throughout childhood. We see a lot of spitting up that happens in babies with Down Syndrome – and babies in general – but we typically don't treat that because that is usually not an acid producing, injury causing spit up. Usually, I think it's typical in kids around two years old and that's when we actually start to look at it more thoroughly and start to treat the symptoms.

Dr. Bulova: By the way, these are amazing questions! So Barrett's Esophagus is a pre-cancerous irritation of the esophagus that you can see on a biopsy. And the problem with Barrett's is that it is not a problem, but you can see that it can become cancerous in the future. That will always be a concern. The reason why people get Barrett's is through the bathing of the lower part of the esophagus in acid causes chronic changes which can then lead to Barrett's which can then lead to a cancer. In the general population, when somebody is having constant irritation of the esophagus and they're having constant pain, we often talk about having a screening for Barrett's to tell us if we have to be more aggressive in treating the acid reflux. If you have someone who's only having behavioral changes, or someone who won't even tell you they're having reflux, then you might have a concern that they are silently developing Barrett's. If you look at long term studies, how many patients have there been where the cause of death had adenocarcinoma of the esophagus, which is what happens afterwards, I personally have never seen a case and as far as the studies have shown, there is no increase of adenocarcinoma in people with Down Syndrome so I tend to not look for Barrett's unless someone is complaining of daily pain. I just haven't seen increased risk – there have been some large studies in some of the

Scandinavian countries where they have looked at the long term risks of cancer and there really isn't one.

Dr. McCormick: And I would say, I didn't say this directly, but there is no universal guideline for screening with EGD's currently.

Dr. Vellody: So the next question may just be a yes/no type of thing but, "Have you met any gay or lesbian adults with Down Syndrome?" was the question.

Dr. Bulova: I think my short answer is Yes! We have seen gay and lesbian patients with Down Syndrome just as we have in the general population and I don't think we've done anything differently in how we've treated them.

Dr. Vellody: This question is about the possibility of a dual-diagnosis with Down Syndrome and Bipolar Disorder. Do we have any information about that dual-diagnosis? Is this something that we see? Why isn't there more information about that?

Dr. Bulova: Bipolar – we see – well I guess this is a bit controversial because there are studies that say there are lower risks of depression – definitely see both anxiety and depression. Bipolar is when we see a combination of the two in very aggressive forms. There might be periods of mania where someone may stay up for three days in a row, and there might be periods of very low, low. So it's a very severe form of depression with these manic features.

01:01:57 There is no known association with Down Syndrome. It is one that you could see just because it is a problem that we see in the general population so you can see it in people with Down Syndrome as well. It would probably present very differently, however, than you'd see in the general population. I think it would be pretty hard to catch, too. It would also be treated very differently than common depression or anxiety.

Audience: [Follow up question, unintelligible]

Dr. Bulova: I think this is a problem that we're going to see a lot of because Down Syndrome is relatively uncommon. We have somewhere between 250,000 and 350,000 people that have it. You're going to see comorbid conditions where there's an uncommon problem in the Down Syndrome population so it's going to be extremely rare. What I think you do is look for people who have conditions similar to Down Syndrome, so like anyone with any intellectual disability, try to find a psychiatrist that can do both. Look for support group from other people with other intellectual disabilities. I've seen, for example, a patient that has pemphigus, which is a very rare problem, and Down Syndrome, so that's easily 1 in a million or even less.

Audience: Have you ever heard of Intermittent Explosive Disorder?

Dr. Bulova: I have indeed heard of Intermittent Explosive Disorder! I wonder if any of the other doctors have seen it more than I have because it is definitely more common in the pediatric literature.

Dr. McCormick: I think that when we start to talk about a cluster of behavior disorders that happens in certain population of our kids, Intermittent Explosive Disorder, Disorders of defiance, ADD and ADHD, they can be very challenging disorders to manage. I had one patient that had Intermittent Destructive Disorder and it can be a very challenging experience. I think the key for those disorders is getting into really great therapy supports. What we do now is we have a connection in Pittsburgh with one of our clinics, the Merc clinic, that has great behavioral support for kids with intellectual disabilities and psychiatry in the same place and that's what you really need. As a parent, I'm sure it can be extremely challenging. The parents that I've had with this, I've seen how exhausting it can be because it's a continual 24 hour a day process at times. And so, getting as much support as you can, as quick as you can, is what you want to do. Making sure that you have someone specialized in that management, but also a lot of times, there needs to be strong behavioral management provided by people who have had lots of experience with intellectual disability. They are the ones who can help provide that sort of management that will be successful for our kids.

Dr. Bulova: This one is another perfect example of a very uncommon problem that we add on to someone who has Down Syndrome: "Our adult daughter was recently diagnosed with Hemochromatosis. Are there issues associated with Down Syndrome that we should particularly be alerted to in regards to this new diagnosis, especially when it comes to drawing blood to bring down the iron levels?"

01:12:16 Hemochromatosis is an iron over-load syndrome. It is genetic; it is treated by phlebotomy – the way to treat iron levels to prevent them from getting up is by frequent draining of blood. This sometimes needs to happen every few months, every few weeks, whatever it takes to get levels into the normal range. Otherwise, iron levels will build up too much in the liver and eventually cause liver failure.

In terms of specific things for Down Syndrome and how you're going to have to take your adult daughter to have her blood drawn on a relatively frequent basis, is a lot to deal with. One thing I would say is what we find with many of our patients is that if we get them into a groove – as in getting into a routine – they tend to flourish in those routines. So if you have something very positive that is associated with that blood drawn, like if you have something positive that comes right after the blood gets drawn every time, then you can have your adult daughter have that expectation of a positive feeling or association instead of it being such a chore every time.

I would also say that our patients are better exercisers than we are so if you have someone who's in a groove like every day at 9 o'clock they get on the treadmill for 20 minutes, they don't want to get there 'till 9:30 because it's just part of their day, part of their routine.

01:14:19 And if she can't tolerate BiPap well, then you might just want to use nighttime Oxygen which might be a little bit easier for her to tolerate and then she won't have the low Oxygen levels at night. She might still be waking up at night a lot, but she won't be reaching those Oxygen levels that truly drop if she doesn't have any sort of help at night. The other issues that can happen with long term sleep apnea is pulmonary hypertension so you'd want to keep an eye on Echocardiograms to make sure that those levels don't change.

Dr. Vellody: As we're getting towards the end of the session, I just want to remind you guys of the session we're having tomorrow made specifically for the younger age Down Syndrome population 0-12 age. Dr. Bulova won't be there tomorrow but we won't be able to answer the 55 year old questions but certainly, we have another session here tomorrow that we do for parents of younger children.

This next question was, "What can be causing fecal and urinary incontinence after eating carrots, or broth where carrots were cooked?"

Whenever I hear this type of thing in our clinic, something causing gallbladder issues like a vegetable they eat, often I wonder is the vegetable doing what we want it to do – which is softening up the stool – but there's such a large stool mass there because of constipation that it's leaking out and around. And urinary incontinence is also very common in someone with constipation. The reason is that there is only so much space and so if it's full of stool sitting right on top of the bladder, the bladder never really has a chance to empty and eventually just bleed out when it starts to overflow.

01:16:18 So the treatment that we typically find very effective for this combination of fecal and urine incontinence is cleaning out the stool and we've talked about that in an earlier question. Using Miralax, things like that. Carrots, in itself, I can't think of anything that I've ever heard of or seen myself that would cause it outside the possibility that the vegetable effect of making the stool a little bit softer and then those stools coming out around is what I'm thinking.

Dr. Bulova: All I will add is something I talk about in the typical population just as much as I do in the population of people with Down Syndrome, people with Down Syndrome just have a little bit less control so a smaller level of problems can cause significant diarrhea and incontinence. There is something called the FODMAP diet. The FODMAP diet is basically all about foods that can potentially cause bowel problems in some people. And there is a low FODMAP diet and a high FODMAP diet. If you happen to be eating a whole lot of foods that are high in these kinds of issues, they are things like fructose (each of the letters stands

for a different chemical). There's a nice thing from Stanford that explains how people who may have an intolerance to a certain type of chemical can have bad bowel issues as a cause of it.

01:18:08 "Are the typical guidelines for gynecologic concerns and tests for women appropriate for our daughters with Down Syndrome?" Boy, that is a wonderful question! We spent about 4 hours this morning having this debate.

The risk in breast cancer is lower in people with Down Syndrome. And a lot of this research was done by Dr. Brian Chicoine. We probably don't have to be as aggressive. We still don't have any evidence to say that we can treat people to a lower standard so it's hard to say that they don't need mammograms, but they probably aren't going to get the same benefit as the general population.

In terms of PAP Smears, there was a study of 18,000 people in America for over a 17 year period, where not a single one died of cervical cancer. If you look at the studies, the large scale Scandinavian studies, cervical cancer is very rare in people with Down Syndrome. The guideline, still at this point, is to go see your gynecologist – probably getting a PAP Smear every 5 years is okay but it's probably not going to be as beneficial as it is for the general population. We are still arguing and working through how important it is to do. I think that having a gynecologist is a great idea; it's pretty easy to do a PAP Smear, they now even have self-PAP Smears where you don't have to have a pelvic exam, but again, you're not going to see a huge benefit out of them. People with Down Syndrome just don't have the same rates of cancer as the general population does.

Audience: [Question, unintelligible]

Dr. Bulova: In terms of constipation, I've always been a minimalist in terms of giving medical drugs. So if I can get away with not giving our patients drugs, I'm happy to do that if it's safe. If issues can be resolved simply by sticking to a healthy diet, I'll stick with that. I'm not a huge fan of vitamins; I'd rather say to just have a healthy diet.

Audience: [Follow up question, unintelligible]

Dr. Bulova: Yes, I would say a healthy diet, lots of exercise and then you don't need any of that extra stuff.

Audience: [Question, unintelligible]

Dr. Vellody: So the TSH is actually the most important test of thyroid function that in the last pediatric guidelines is exactly what they recommend alone. Then if the TSH is abnormal, then check the T4. That number is quite important. I would not rely just on the T4 mainly because, just as we were talking about earlier, sometimes the TSH may start to rise first before the T4 starts to drop, that's why if you're going to send one of those two, you should send the TSH.

01:21:31 As we're coming down to the end of our time here, I really just wanted to applaud you guys on the fantastic questions. Every time we've done these Ask the Doctors sessions, I'm amazed by the things that are out there that truly are areas which we need to have more information about as a medical team. It's those questions that our family members of people with Down Syndrome may have. Thank you for coming today and I think I speak for all of us. We'll be up here for a little while longer to answer any questions you have for us.

That was awesome!

01:22:09 [End of Recorded Material]