*(PLEASE NOTE: Transcribed automatically by Vimeo, mistakes are possible/likely. Our apologies.)*

## TRANSCRIPT - GR 01 28 22 *"*Transplant Endocrinology*"* – Meg Stumpf, MD from the University of Virginia

* 00:16:56Okay, everyone, welcome to grand rounds.
* 00:17:00And to get started with the introduction and hand it over to Dr Stumpf so welcome to grand rounds, here we have documented stone from our division of endocrinology diabetes and metabolism.
* 00:17:10to lead us on a review of transplant endocrinology, including our own transplant endocrinology program and how.
* 00:17:16immunosuppressive medications impact the endocrine system, among other topics so Dr Stumpf.
* 00:17:21received her medical degree from suny downstate medical university and then completed her combined medicine and pediatric residency.
* 00:17:27And chief residency at the University of Tennessee health science Center in memphis Tennessee.
* 00:17:32Dr something came uva to complete her fellowship training in endocrinology and then later joined our endocrinology division 2018.
* 00:17:40Dr Stumpf has been recognized as a brilliant clinician, as evidenced by her department of medicine excellence in clinical care Ward and her 2021 you the experience and patient.
* 00:17:51uva experience and patient experience award Dr Stumpf is the principal investigative for two studies for the Center for diabetes technology.
* 00:17:59Well, the one of those focusing on the use of closed loop insulin delivery systems for glucose control and patients with insulin dependent diabetes after kidney transplantation.
* 00:18:08As we all care for more and more transplant recipients through the health system, it is vital that we have a more complete understanding the medical problems they face after transplant.
* 00:18:15The protein effects of their immune suppressive regiments with that I’ll hand the MIC over to Dr Stumpf.

**Meg Stumpf, MD**

00:18:25hi everybody can you hear me.

* 00:18:29Alright, so I want to first of all say thank you so much for inviting me to speak about transplant undergrad ology.
* 00:18:37I gave this talk essentially to my undergrad division this past fall, it was really well received and I appreciate the opportunity to sort of introduced the idea of transplant underground you to a more broad audience and internal medicine in general.
* 00:18:52I have a lot of fun with it, I really like what I do, and so I hope that you'll enjoy this as well.
* 00:19:01let's see.
* 00:19:04a hard time advancing my slides I apologize, here we go, so my disclosures I don't have any financial disclosures.
* 00:19:12I don't plan on discussing any non FDA approved use for medications or devices, however, some of this some of this conversation might sort of.
* 00:19:21broach the subject so I’ll do my best to to give you a heads up if we're going off of off labels, so to speak.
* 00:19:29And I’ll give you some disclaimers as well, I really do intend for this to be more of a broad overview, there will be, I think.
* 00:19:36topics that you'll find interesting that are worthy of more in depth discussions later, but for the purposes of this talk I’ll probably be going quickly so save some questions for the end.
* 00:19:46I also recognized as I was putting these slides together that the data that I’m presenting is probably heavily skewed towards the abdominal organ groups because that's the program that I’m primarily embedded in so.
* 00:19:57I want to give my apologies to the heart and lung group which might be a little neglected and you deserve better so I’ll do better next time.
* 00:20:05And then I also wanted to just put out there because it's a question that comes up sometimes transplant endocrinology does not have its own fellowship training.
* 00:20:14Like some of the other transplant sub specialties, so I would say that my expertise and development, and this particular nisha sort of been a little bit more baptism by fire, so this is me.
* 00:20:27My objectives today are to just give you a broad description of the transplant endocrinology and our clinical Program.
* 00:20:35I want to essentially walk you through that program talk about my role of transplant undercurrent for the pre transplant evaluation and pre op assessment.
* 00:20:46That will bring us into evaluation of patients who are being considered for beta cell replacement therapy pancras islet transplant for consideration.
* 00:20:56And then, after that we'll kind of move towards the bar post post operative and long term post transplant care, I think the bulk of the top will be in this beta cell replacement category.
* 00:21:09So a question that I sometimes get is what is transplant endocrinology and it's a fair question.
* 00:21:15But this is sort of the definition that I would put forward, which is that I serve in a collaborative role I love that it's multi disciplinary.
* 00:21:24niche we're providing care for patients who are undergoing EVAL peri operative management and post operative care.
* 00:21:30Currently at uva I’m embedded into the abdominal organ transplant group, although I do work as a smith with the heart and lung group.
* 00:21:39I provide Inpatient glucose and undercurrent management for patients admitted to the abdominal transplant surgery service and then outpatient care as well.
* 00:21:47And then that setting I’m trying to provide endocrine focused expertise for evaluations for pancreas and islands.
* 00:21:54i'm trying to medically optimize patients with endocrine disorders for transplant surgery my goal is also to improve the transition of care from the Inpatient and outpatient environment.
* 00:22:06One of my goals is to increase and improve access for patients to diabetes technology and to provide some sub specialty expertise in terms of medication management for patients, particularly diabetes management for transplant specific group.
* 00:22:23Sometimes get a question that surprises me, but I wanted to say what I don't do, which is that I don't do pancreas or islet transplant surgery.
* 00:22:31These pictures, are the most graphic that you'll ever get in a talk from me, I don't like looking at people's insides so much respect for my surgical colleagues.
* 00:22:39that's not part of my job, thank goodness, and I also don't do immunosuppression therapy that's not part of my formal training.
* 00:22:49and actually there was a consensus group for post-transplant diabetes that met I believe in Europe and Austrian around 2014.
* 00:22:58And they actually put forward some commandments for endocrinologist and the first commandment was thou shalt not change immunosuppression therapy, to avoid diabetes, so I don't change prednisone attacker Linus doses to make diabetes management easier so stop asking me.
* 00:23:15I wanted to give you a schematic of what my transplant group what my workflow sort of looks like because I’m a visual person so.
* 00:23:24Essentially, here is kind of a scheme of how patients go through transplant evaluation and then for the surgery face.
* 00:23:31And my entry into this is generally after a patient has been referred, and that, with the medical specialist in the search can surgical specialist for the various worker and group that they're being.
* 00:23:43referred to, usually what will happen is a patient, as identified as having some kind of undercurrent issue that maybe needs to be looked at further maybe there's concerns it's not optimally manage before they can go forward surgery.
* 00:23:55Maybe it's a patient who has diabetes and a question comes up about whether they would benefit from a pancreas transplant as well, and so, at that point that's usually, when i'm entered into the into the patient's care.
* 00:24:09i'm also involved, of course I view this more as a parallel pathway.
* 00:24:14So, particularly about pancreas transplant since we'll talk about that a lot today I don't view this as.
* 00:24:22You know, a referral to me, means that we stopped going through transplant EVAL workup It means that I will continue to assess their diabetes and hopefully optimize care try and clarify diagnoses as the patient continues to go forward.
* 00:24:36So that you're not really delaying their process through optimization and listing and all that stuff.
* 00:24:45Once in Oregon once a patient has been listed and then, once patients active on a list, and they have an organ available that.
* 00:24:52transplant and so I’m also involved in the Inpatient therapy, as I mentioned, and then wants their discharge I’m able to provide post operative follow up appointments, as well as long term continuity of care appointment so.
* 00:25:05That to have my endocrine fingers all over the medical charts and multiple touch points through the process and I think that helps me to provide more continuity of care that way.
* 00:25:16So we're cruising along we've already finished the first objective the next is to discuss the preamp EVAL phase.
* 00:25:25So primarily I’m focusing on bone disease and diabetes and I’m putting bone disease on one slide my apologies to my bone specialist colleagues.
* 00:25:36Essentially, in my group, particularly with working in the abdominal world the things that we see most frequently are related to chronic kidney disease and.
* 00:25:46hepatic asked you a dystrophy so talking about the kidneys first metabolic bone disease in the context of chronic kidney disease.
* 00:25:54is a really difficult area of endocrinology with not a lot of great interventions from an endocrinology standpoint.
* 00:26:02So the primary focus of bone disease for kidney patients is comin is nephrology To be honest, until that's really looking at regulating the issues of secondary hyperparathyroidism.
* 00:26:14And I was looking I did a literature review on to prepare for this on trying to see has there been any more progress in evaluating some of the medications we have for.
* 00:26:25osteoporosis, in the context of kidney patients and there was a review that was published this this 2021 nice hooray and I read it.
* 00:26:36And it said basically there's low quality evidence and no convincing evidence for use of any of our osteoporosis medications in this population so.
* 00:26:45I didn't know if I should laugh or cry, but it makes it a very short period of this conversation so it's difficult basically we're looking at managing the calcium, phosphorus vitamin D access there.
* 00:26:58On the liver side a little bit more interesting give you a little bit of an idea of what we're looking at so hepatic kostya dystrophy and bone disease in the context of cirrhosis is pretty common.
* 00:27:09Particularly in those who are suffering with goalie static disease there can be coexisting inflammatory bowel disease and all of these things are kind of pointing towards issues with absorption and vitamin D deficiency.
* 00:27:22Other things that are sort of interesting about patients with cirrhosis they we have demonstrated that low IGF one levels and high uncomplicated bilirubin levels can inhibit osu blast activity.
* 00:27:36Hypo gonads ISM is very common in this patient population which is not good for bone disease, and then there are some lifestyle factors, there can be alcohol use malnutrition sedentary lifestyle and all of those can contribute to worsening bone disease.
* 00:27:52Generally speaking, the treatment, for that is going to be bisphosphonates and patients generally tend to respond very well to bisphosphonate therapy.
* 00:28:00And then, of course I can't not include glucose quarter quite related bone disease, which can be seen in any organ group, particularly our pre op evaluations for lung transplant.
* 00:28:12Those folks can sometimes have a pretty high rate of exposure and duration of exposure to pregnant zone, and so, then we generally treat with as possible, as for them as well and it's important to assess this.
* 00:28:26bone health pre transplant, because the risk of fractures and worsening bone disease is happens really quickly after the transplant phase and so patients are at high risk of developing fractures pretty quickly.
* 00:28:39Until you want to try and get ahead of that fracture risk as much as you can.
* 00:28:45Then we will move towards diabetes, which is the bulk of what I do and the bulk of this talk so.
* 00:28:52I put in here, diabetes and its many forms, I think that the longer that I’m doing diabetes management, the more than convinced that it's a spectrum and actually diagnosis can sometimes seem marquee.
* 00:29:04And so I can sometimes get a referral for a patient, for instance, who has end stage renal disease.
* 00:29:10And they are insulin dependent and the team as well would this be a good candidate for a pancreas transplant.
* 00:29:18Sometimes patients have been told that they have type one diabetes and sometimes they've been told they have type two diabetes, and so the question comes up what's going on, really.
* 00:29:27Also, this is the acronym for post transplant diabetes, technically, this is reserved for a patient who you were confident did not have diabetes before transplant, and then they were diagnosed after.
* 00:29:41But it's it should be noted that sometimes that's not necessarily clear whether or not diabetes was preexisting and cystic fibrosis related diabetes, we also deal with, but although, of course, the diagnosis there shouldn't be marky.
* 00:29:54Another thing that makes my job tricky is that a once he can actually be deceiving, particularly in my abdominal group population.
* 00:30:02I gave you a reference here that specific to kidney disease but it's also true for other groups hemoglobin a one sees obviously dependent on hemoglobin and so various hemoglobin off of these can affect your accuracy of your agency.
* 00:30:18End stage renal disease in particular party patients who are being treated with ECO, for instance, can have high turnover.
* 00:30:25And that can make the Agency inaccurate also some of my patients in the liver group as well seem to have artificially low hemoglobin anyone see perhaps from their sport and medically and sequestration.
* 00:30:38So it's a difficult world being a diabetes doctor and not knowing if you can trust your agency as an assessment, and so my goal is always, of course, to try and clarify how welcome fooled is this patient.
* 00:30:52And so.
* 00:30:53That can be an interesting part of my job and going towards assessing control anyone see being just a number that supposed to correlate with your average glucose doesn't really give you a good idea of risk of hypoglycemia or risk of hyper variability in glucose control and so.
* 00:31:16We have other strategies for that, and in that case you know I would be talking about continuous glucose monitoring and the Ada this year actually got a little bit more specific about using cgm as an assessment.
* 00:31:27When I’m looking at pre transplant patients as well, and particularly their diabetes and trying to optimize management I’m also have an eye towards healthy weight.
* 00:31:36And some of my patients might be coming in and struggling with overweight or obesity, which can increase risk of certain surgical complications, then I have other patients who are coming in, are actually pretty malnourished and you've been hectic and so.
* 00:31:50That healthy weight can go either direction and it's important to have an eye towards optimal nutrition therapy when you're trying to manage their diabetes.
* 00:31:59And essentially I’m trying to take all that information and give my transplant colleagues and assessment of where I think there, they are and where we can go.
* 00:32:07And then, to try and communicate goals for both the transplant team and the patient in terms of what should we be aiming for here.
* 00:32:16This graph I find helpful to illustrate that point it's been in the standards of care for it from the Ada for many years now.
* 00:32:24And of course it's using a one see as your standard which I just told you might be questionable.
* 00:32:29Essentially, this is trying to illustrate the point that an agency of 7% is generally a safe goal for most folks, but it should be individualized and there are a lot of different factors that might influence you to say this.
* 00:32:43This patient should be aiming for stricter control or might be a better idea to aim for less strict control because of their risk of complications, and so this is just to illustrate that it should be individualized and so.
* 00:32:58So, think about that.
* 00:33:01um so that's essentially my spiel on what I would do for an evaluation for a pre op candidate.
* 00:33:10And now we're going to go into specifically the question about what about pancreas or island transplant what options are there, who should be a candidate.
* 00:33:19When you're hearing about all this diabetes that's existing in my pre transplant group, you might ask well if they have diabetes and they're going for an organ transplant can't you give them a pink and the answer could be definitely maybe.
* 00:33:35Okay, so here is a little information about beta cell replacement transplant.
* 00:33:41So pinker's transplantation alone is reserved for type one diabetes simultaneous pancreas kidney which is abbreviated SDK or pancreas after kidney transplant is available for patients either Type one or Type two.
* 00:33:57Currently islet cell transplant therapy is exclusively for patients with type one diabetes allergenic islet cell transplants in the US are only in clinical research protocols that's not true in Canada and Europe and Australia, where they're actually approved.
* 00:34:14For us, and autologous islet cell transplant, so our FDA approved in the United States, and we do total pinker techniques with autologous islet transplants team that's here at uva.
* 00:34:25i'm Dr Rao and I and Dr Friedman, who I’m going to shout out at the end collaborated on trying to sort of talk about how pancreas transplant selection has evolved over the years and I learned a lot to these give you kind of some ideas of how.
* 00:34:41The transplant network has looked at criteria for pancreas transplant for various patients, and you can see that there's a C peptide threshold that they recommend so a C peptide less than two with no BMI threshold was proposed versus C peptide greater than two.
* 00:35:00They could be considered for pancreas transplant only if there'd be a mine was 28 or less.
* 00:35:07That that evolved in the BMI thresholds were dropped there's always should be an asterisk whenever we're talking about C peptide levels.
* 00:35:15Because, as my colleagues and endocrinology taught me, and we know well, is that these levels are really dependent on where your glucose is and difficult to interpret.
* 00:35:26So that being said in 2018 there were about 15% of patients whitelisted who had type two diabetes and recipients so that's kind of been evolving over the years.
* 00:35:40Just to give you a little bit of an idea as well about well doesn't make sense to give a pancreas transplant patient has type two diabetes I pulled in this slide from a colleague that I’ve borrowed from a colleague Dr Baron.
* 00:35:53That, I think, does a great job of giving you a picture of.
* 00:35:57How beta cells reserve essentially changes through the diagnosis, through the evolution of type two diabetes so on the top graph you can see.
* 00:36:08This stands for impaired glucose tolerance which is sort of the pre diabetes kind of World Diabetes which is diagnosed when fasting sugars so fasting glucose and purple here is over 126 months time zero and a random glucose over 200.
* 00:36:26And then, this is trying to show what the beta cell reserve is for patients with type two diabetes.
* 00:36:33where you can see that, in the context of insulin resistance, there can be plenty of beta cell activity, but then as patient develops over in clinically apparent diabetes than their beta cell.
* 00:36:45reserve will decline and so eventually many years out a patient will certainly be insulin dependent.
* 00:36:51And so, for many of my patients that I’m evaluating who've had diabetes, for decades, and now have end stage renal disease, they very well may have poor beta cell function and be insulin dependent.
* 00:37:03So what does the Ada say about criteria for pancreas transplant.
* 00:37:08So, generally, they say, it should be considered an acceptable therapeutic alternative to insulin therapy and diabetic patients they don't specify one or two.
* 00:37:16who have end stage renal disease and we plan to have a kidney transplant, and this is based on literature review that the successful addition of a pancreas doesn't jeopardize patient survival.
* 00:37:25And may improve the survival of the kidney graft itself and restore glucose normal glucose so that's a positive.
* 00:37:34For patients with type one diabetes, though it's a little bit more murky.
* 00:37:39Here is a scheme that Dr brown I tried to put together for how to evaluate a patient with type one diabetes, who is coming forward to say, can I get a pancreas transplant.
* 00:37:49And so it really branches off on a lot with their degree of kidney disease, so you can see if they have advanced critical chronic kidney disease or end stage they have two options, one would be going towards a living donor versus.
* 00:38:05going for the deceased donor and so, if a living donor for a kidney transplant is not available then they would be going towards a simultaneous pancreas kidney as pk.
* 00:38:16If they do have a living donor available, then they would they could be transplanted with the living donor kidney and then listed for a pancreas afterwards we did include the islands in here too, for those countries where it's available.
* 00:38:30In the moderate ck do category gets a little tricky so for some folks they may be.
* 00:38:36If they have a living donor who could come forward, then you know they may be available to arrange that and then be listed for the pink Greece after if they don't.
* 00:38:44Then it really comes down to this whole engine here of hype in documenting hyper liability and hypoglycemia So these are absolutely necessary to establish that the patient has exhausted all therapies, to try and.
* 00:38:59limit this affecting their life before you go through with a pancreas transplant it alone.
* 00:39:06So this is this is where it comes down to So what does the Ada say about that, how do we find define hypermobility and hypoglycemia.
* 00:39:14So this was in my colleagues who have seen this talk now a couple times you're going to be tired of clicking on these headlines but.
* 00:39:21I think that it's worth pointing out that they're a little bit difficult to interpret really so without having an indication for kidney transplant.
* 00:39:30You should consider a pancreas transplant along this situation so history of frequent acute severe metabolic complications, including hypos market hypoglycemia and keto os doses.
* 00:39:41clinical and emotional problems with exactness and some therapy that are so severe as to be incapacitating or consistent failure of insulin based management to prevent up to complications.
* 00:39:53And so I have said before, and I agree that when you read this It seems pretty straightforward you get a sense that this should definitely be a last resort, and you kind of have this sense that, when you meet this patient you'll know it when you see it.
* 00:40:07But the issues when you are actually faced with trying to decide if a patient qualifies or not, is that these are actually not very objective terms.
* 00:40:15And so what what is the frequency how market should your market hypoglycemia be what does incapacitating look like to you as a clinician versus the patient.
* 00:40:28And what so we're clear about if we can't prevent acute complications with our insulin based management, but what about those who are failing to prevent chronic complications from their diabetes kind of a question.
* 00:40:43So the Ada says absolutely if this is happening, you should refer for them to be looked at by a multidisciplinary group.
* 00:40:51And transplant centers are expert at multi-disciplinary evaluations they're highly regulated and they're very good at it there's excellent access to social workers financial people nutrition therapy.
* 00:41:04Who can really kind of help give a multi-disciplinary approach to helping the patient deal with these issues.
* 00:41:12And sometimes even if they don't qualify for transplant it's beneficial to have them come to the Center and some of these resources can help them deal with other things.
* 00:41:22um the crux of this is how we documented consistent failure of our endocrine therapies and so that's where I feel like I can be helpful, which is.
* 00:41:35You know what, how do we define failure of a therapy and I feel that there's sometimes room for interpretation.
* 00:41:41When these patients are coming to us there could be variable perspectives between what does endocrinology consider a failure of medical treatment versus, how does the transplant group look at this.
* 00:41:52And so, this kind of becomes the wild card, and one of the things that I’ve noticed in my clinical program here is that a lot of my.
* 00:42:01A lot of the patients I’m assessing haven't actually been seen by specialists in quite a long time, sometimes they can have type one diabetes and not been seen by an endocrinologist in decades, or maybe not since they were in pediatric here.
* 00:42:14This is actually a picture that I just got yesterday that's This is my own patient population geographic area which just completely overlaps with our transplant catchment area, and so you can see that there's a lot of folks who are coming from.
* 00:42:26A wide area and may not have access to specialty care till they're here.
* 00:42:32So just to make sure we define hypoglycemia.
* 00:42:36And there's a difference, sometimes in when you're looking in this literature between what's referred to as problematic hypoglycemia versus defined severe hypoglycemia so I just wanted to tease that out a bit so there's a paper that I’ve borrowed from.
* 00:42:54by Dr Shaw audrey who is looking at trying to define.
* 00:42:57These things to give objective criteria for pancreas transplant, and he puts forward that a definition for problematic hypoglycemia would include two or more episodes per year of documented severe Hypo or even just one episode associated with impaired awareness.
* 00:43:15And so, essentially what we come down to is that if you have a patient who has hypoglycemia on awareness they're unable to treat themselves and require the assistance of others or Ms then you've got a potentially dangerous situation.
* 00:43:29Severe hypoglycemia we have more concrete definition of the triple triad so i'm sure you recognize this symbol from your harrison's textbook of internal medicine i'm just kidding it's from Harry Potter.
* 00:43:42But anyway, so that's what pulls triad and that's how we define hypoglycemia and you can assess it by the Clark or gold scores, which have been validated.
* 00:43:50So if you have then my role as an endocrinologist is first to do a sweep of what I would call low hanging fruit.
* 00:43:58If the patient has come to you and they're struggling with hypos you want to make sure that you've rolled out the major players, what type of insulin are they using regular and mph insulins have kind of more delete peak in activity until they can make hypoglycemia bit unpredictable.
* 00:44:17How are they dosing their insulin inappropriate balance between bazell and bolts Joe, so this is something that we discover all the time when we're evaluating new patients.
* 00:44:27They may be not timing their insulin appropriately, etc, how are they administering insulin.
* 00:44:34lipo hypertrophy is something that we commonly you know sort of gloss over, but essentially if patients are injecting insulin into the same subcutaneous space over and over again.
* 00:44:43Just like what hypertrophy can occur, and then, when they're injecting into that space absorption of insolence very unpredictable that same thing if they're injecting it into their muscle actually so you want to be assessing how they're actually delivering their insulin.
* 00:44:58And then the psychological and psychosocial things are really common also really difficult to deal with, but.
* 00:45:04um but very real, sometimes we have patients who are struggling with lows and we discover that.
* 00:45:10they're terrified to develop the complications associated with diabetes, that they are preferring to target a glucose of maybe 7200 because they're terrified of developing complications and that tight control they're imposing on themselves as increasing the risk of lows.
* 00:45:28I am the authors put in here denial and it's something that we deal with a lot and I just like to point out that denial is very normal part of a grief reaction.
* 00:45:37And you know, whenever anybody has a diagnosis of diabetes, they will go through a grief reaction and it's very normal part of it.
* 00:45:46And I think we're all familiar with how you know grief reactions can sort of pop up on person anytime.
* 00:45:53Also, depression and diabetes burnout very real and should be addressed and cognitive impairment of course can impact somebody's ability to adhere to their prescribed bedroom.
* 00:46:05So here is where the low hanging fruit is gone and now we've advanced into kind of more advanced endocrine care to try and prevent severe hypoglycemia and a patient with type one diabetes, so this is a schematic.
* 00:46:16And so here, I was laughing because I was thinking that transplant under transplant group have more acronyms than anybody, but I think, maybe we do.
* 00:46:26So here are the different stages that you go through to try and optimize diabetes care for patients struggling with hypos so of course first line therapy should be structured diabetes education.
* 00:46:39This would be you'd start out with a patient who was on multiple daily injections and self-monitoring their blood glucose and you want to make sure that's concurrent with hypoglycemia specific education.
* 00:46:50Assuming that you have done that, and they're still struggling with lows then second line therapy will generally be to introduce some diabetes technology and so.
* 00:47:01This stands for continuous subcutaneous insulin infusion also called this insulin pump therapy, and so this was a paper from 2015 so it's outdated by likes to graphic so and keeping it.
* 00:47:14But essentially this group was saying is we have Level one to two evidence for using pump therapy, first with self-monitoring finger stick.
* 00:47:22And I would just like to make the disclaimer and be transparent, that in my clinical practice I tend to introduce real time continuous glucose monitoring, first with alarm features, but essentially you're trying to assist the patient have more.
* 00:47:40More information about what their glucose patterns are alarm features that will warn them if their glucose is dropping and for pump therapy, then you can you know suspend even on the oldest pump models, you can suspend insulin.
* 00:47:55which gives you a little bit more control over risk of lows.
* 00:47:59moving into third line is what I would call kind of more advanced pump therapy, this is already outdated technology, but I would substitute it here, for this is sensor augmented pump.
* 00:48:12Meaning you're using a cgm and an insulin pump but they don't necessarily talk to one another.
* 00:48:17And once they once you're using a pump with algorithm capability and a sensor that can talk to a pump.
* 00:48:23They can use low glucose to spend, although that's been replaced now with suspend before low because we have predictive algorithms that can tell the pump to stop insulin delivery.
* 00:48:34before your low by a low is predicted and then, this in fact would be replaced now in recent times with hybrid closed loop insulin therapy, which can do suspend before low, as well as conservative correction doses vince one with predictive hypoglycemia.
* 00:48:52And then, if they fail all of those advanced therapies, then the fourth one would be considered the beta cell therapy with eyelid or pancreas transplant.
* 00:49:02So the question would be with all of our recent advances and diabetes technology, and I believe you all have had some recent grand rounds as well from some of my colleagues who are particularly expert in this.
* 00:49:14The question sort of remains will anybody actually fail those therapies didn't quite effective and so who would be left looking at this fourth line.
* 00:49:23So, Dr overholt here and I actually went to our colleagues at the Center for diabetes technology, the cdt here at uva to kind of ask do we have any data that actually looks at this.
* 00:49:35And so, these are some published trials that look at various insulin pump algorithm based insulin delivery.
* 00:49:46For patients with type one diabetes and between these trials, you know, we were able to look at about 370 subjects and they were looking at the continuous glucose monitoring data for those folks.
* 00:49:58And when querying who's who's spending greater than 5% of their time with central glucose less than 70 despite the algorithm being turned on there were about 40 subjects who were still having quite a bit of time in the low range so I’m not trying to say that I would.
* 00:50:17necessarily define hypoglycemia on pump therapy, as you know, I’m not sure that this definition is exactly perfect, is what I need to say but it's a starting point to sort of assess how frequent are we having hypoglycemia despite this tech.
* 00:50:33And so it's still out there.
* 00:50:37And so, then the next question might be who are those patients who are still failing therapy and what you're left with often is.
* 00:50:45A group of patients who you would expect to be really difficult to manage, despite these advanced therapies.
* 00:50:51So this so called other causes are things that we went into an endocrinology that are really tough, so this stands for hypoglycemia hypoglycemia associated autonomic failure gastroparesis which can make timing of insulin delivery to the glucose absorption from the meal really problematic.
* 00:51:14mal absorption conditions of course celiac and extra credit insufficiency you can have somebody who has adrenal insufficiency Hypo Pitt hypothyroidism can cause hypoglycemia fictitious disorder can be out there and really difficult to manage misuse of insulin.
* 00:51:33Alcohol access can also contribute to hypoglycemia.
* 00:51:37And in insulin autoimmune syndrome is a real thing and can sometimes a curl rare usually more associated with folks who had been exposed to more bovine or porcine.
* 00:51:47For sign derived insolence but can happen in other situations, the idea here is that the insulin can be sort of bound up by antibodies and then unpredictably released causing lows.
* 00:51:59And then metabolic con causes renal failure and hepatic failure which sort of the world that I live in in the transplant group can contribute as well to problematic hypoglycemia.
* 00:52:13So I wanted to give you a case study just that I think just this was a particular case that I had good data to present and sort of illustrated, while the various aspects of my transplant endocrinology program and so.
* 00:52:28I had a patient who was referred, who had a diagnosis of autoimmune hepatitis and was has developed cirrhosis related to that and also had been diagnosed, three years after that, with type what was treated as type one diabetes, although.
* 00:52:47This patient handed detectable C peptide when they were first diagnosed presented in diabetic keto acid Josias like Type one managed like Type one.
* 00:52:57But it has three years of exposure to tackle Linus related to the hepatitis and so kind of compounded the diagnosis, a little bit there, so when I say diagnosis can work, this is kind of one of the examples.
* 00:53:09Her measured a month see was consistently lower than where her serum glucose is we're coming back and, in fact, when we started to use continuous glucose monitoring, we found out that for absolutely they once he was under under estimating glucose control.
* 00:53:25So this gives you, you know some data that we were able to obtain when we put continuous glucose monitoring on this patient very high insulin requirements for patient her size.
* 00:53:40i'll also note that, for full disclosure do last time was tried, although you know the the medication label will say you know use caution for hepatic condition.
* 00:53:51pathetic insufficiency we were trying to address some of the insulin resistance issues that were going on with this patient and she was having a very hard time hearing to mealtime insulin.
* 00:54:04So we were struggling with actually quite a bit of hypoglycemia as well as pronounced hypoglycemia and only in target 27% of the time.
* 00:54:14consistently going into diabetic keto acid Josias from this poor control and unable to be sort of stabilized from a medical standpoint for listing.
* 00:54:25The transplant group was looking at this situation of course for a liver transplant, but then the question arose could this person also get a simultaneous liver pancreas transplant they do exist it's uncommon.
* 00:54:37What should the diagnosis be should it be listed under Type one, is it not Type one, how would we classify this um so there was there were interesting questions there and then but can we actually stabilize this patient to be safe for transplant.
* 00:54:55So we actually was able, we were able to prescribing and train this patient on the control IQ algorithm pump, which is a hybrid closed loop option.
* 00:55:07That gives automated correction doses of insulin as well as insulin suspend here when there's risk of hypoglycemia.
* 00:55:14And we were all very relieved and thankful and I’m going to shout out my amazing coordinators and pump trainers in a second, but we were able to.
* 00:55:25improve this patient glucose control significantly so that she was more medically stable unable to be transplanted.
* 00:55:32And then you can see that her glucose control got even better after receiving the pink Chris and I will say, of course, you don't notice the average glucose here's 150 instead of 90 to 100 as you'd expect after a pancreas transplant but.
* 00:55:44This patient was also still on higher doses of prednisone at this stage in the post transplant period so not terribly surprising, but this is on going from about one unit per kg per day of insulin to nothing, no expansionist insulin so success.
* 00:56:05Right, so now moving on towards the end think we're doing okay.
* 00:56:10So post transplant management.
* 00:56:13I really enjoyed this part of my job, because I think the patients feel you know really quite grateful for having the second chance to feeling better.
* 00:56:23They can kind of feel more and will usually have better energy levels, they are more able to eat the way they want to exercise the way they want to, and I sort of view this as.
* 00:56:33An opportunity to tell the patient you you're allowed to be healthy now, and so, for our pancreas transplant patients who I was just mentioning one example, my follow up.
* 00:56:46can be pretty straightforward actually but you do have to monitor for hypoglycemia which can recur, sometimes in the setting of.
* 00:56:53High dose steroids for rejection therapy, you need to assess for post transplant diabetes, which can occur for a patient who's received a pancreas.
* 00:57:02Which more of an insulin resistance sort of picture versus actually is could there be recurrence of autoimmunity causing diabetes again, and this is another area where you could go on a deep dive super interesting studies that came out of Miami looking at that.
* 00:57:18For our organ recipients heart lung liver, kidney everybody you're doing ongoing maybe not kidney ongoing assessment of bone disease to reduce risk of fracture.
* 00:57:31we're looking at aiming to tailor your endocrine and diabetes approach to mitigate some of the risk factors of metabolic problems that post transplant patients suffer with.
* 00:57:43We want to try and reduce the rates of obesity, we want to reduce the risk of recurrence of Nash, for the liver patients we're trying to avoid recurrence of neuropathy.
* 00:57:52we're giving attention to risk for a KPI or urinary tract infections or immunosuppressed patients they're on call Center and inhibitors which can make a little tricky to to treat their kidneys well in the post operative phase.
* 00:58:07And whenever I feel that, when one of my goals as a transplant endocrine person is to try and optimize the use of insulin but also non insulin agents for these folks and increase access to tech for our patients who are continuing to need to manage diabetes post-operatively.
* 00:58:25most commonly continuous glucose monitors, which are quite helpful.
* 00:58:31This is just a little slide that I have from another talk on the incidence of diabetes and particularly post transplant diabetes and the organ recipients so.
* 00:58:39This is the percent of patients with diabetes on the kidney liver and heart lists pre op who of course still have diabetes post on.
* 00:58:49And then, this is the rate for post transplant diabetes, for those who have gone through organ transplant.
* 00:58:56And so you can see, this pretty high rates of developing post transplant diabetes after organ transplant and then That being said, post transplant diabetes doesn't really have an end point anytime after transplant you could be diagnosed with this even decades later so.
* 00:59:14You know these rates could potentially become higher.
* 00:59:19um here's my slide on prednisone this mean was actually sent to me by one of my transplant nephrology colleagues said so.
* 00:59:27I said you do know what you're doing so Satan stick tax on there, but basically steroids, is the world that I live in and so obviously these cause a lot of problems, particularly for folks with diabetes, but also problems with bone health.
* 00:59:42They increase the risk of waking post transplant they have immediate issues with causing insulin resistance, but also disrupt insulin secretion.
* 00:59:56coulson earn inhibitors are very interesting medication so here's just one slide, but it has a nice graphic, so this is looking at the.
* 01:00:05Data cell toxicity that is evidence and evidence in patients who have been exposed to coulson earn inhibitors, this is the healthy control and then these are folks who have fear, who were found post more don't have various.
* 01:00:19beta cell damage after being exposed to a cycle sport and tackle I mess, and this is not necessarily that cyclists born cause more damage we're tackling this per se, but this just examples of what you might see.
* 01:00:32So the calcium iron inhibitors you know can cause sort of insulin resistance, they can cause.
* 01:00:39Also insulin deficiency patterns, what I tend to see in my practice is that in the beginning post-operatively we're dealing with the predominated effects of steroids and insulin resistance.
* 01:00:50But as the patient becomes more and more removed from their transplant event their diabetes seems to have.
* 01:00:56More likelihood to have insulin deficiency as well, and so you have to have that in the back of your mind if you need a lower threshold to start insulin therapy for that patient who's had a long time of exposure to counselor and have a nurse.
* 01:01:08And towards as well, I need to find a good picture to put on to this group, but this is less less commonly used in my abdominal organs population that I’m my use I see most commonly.
* 01:01:19But they can cause problems with insulin response and release you might see them and also in.
* 01:01:29Patients who you know, for instance, are being treated for breast cancer using our Linus in my practice I’m tending to think of hyper leukemia as the thing to watch out for for patients exposed to these meds.
* 01:01:43What treatment options do you have for patients who have diabetes, but have also have an organ transplant, and that can sometimes if a patient providers, a lot of anxiety about what safe to use and what isn't.
* 01:01:57This this table is also starting to get outdated, but I liked the table, so I kept it essentially you've got your old familiars you've got sulphonylurea is you've got republican i'd you've got metformin.
* 01:02:11you've got pioglitazone DPP four and hammers and insulin course.
* 01:02:17I would say that in my practice i'm trying to always reduce the risk of hypoglycemia trying to choose agents that are not going to be week game, promoting.
* 01:02:25And so I put in here, this was out of out of our January just this month standard of care from Ada, and this was already starting to be writing on the wall last year as well.
* 01:02:38But essentially the Ada says for patients with diabetes you're trying to use agents that are going to try and reduce the risk of developing or furthering atherosclerotic and cardiovascular disease, as well as heart failure and CBD and that's basically all of my patients.
* 01:02:56And so, notably absent or these agents have gop one receptor Agnes and Estelle to two inhibitors, and so the question remains, you know.
* 01:03:07What kind of safety data will we be seeing that specific to the transplant recipients they're small studies.
* 01:03:15And so I tried to kind of summarize some of the points from some of the more recent studies that have come out looking at the safety of gop ones and SG lt two inhibitors, and these are coming out, mostly in the kidney patients, not surprisingly it's the largest group of transplant recipients.
* 01:03:34And so I think that we're going to see an increase in use of sgt two inhibitors and G lps because of these beneficial.
* 01:03:45Because they're beneficial for patients with these kinds of risk factors, but it should be noted that they can that they're not as extensively studied in the transplant group, of course.
* 01:03:58And that risk of urinary tract infections and my chronic infection should be looked at seriously and patients who are on Anti rejection medications.
* 01:04:08And, as well as considering risk of like dehydration gop ones can cause sometimes some pretty significant najah and for PL intake which could increase your risk of having.
* 01:04:21Patients develop a kiss or other issues and the SG lt two inhibitors, of course, as well across diarrhea Rhesus and so you have to be quite careful.
* 01:04:30anecdotally what we're noticing is that for patients who are having these agents introduced to try and mitigate risk of heart failure and other things is that we're having to be quite careful about reviewing the antihypertensive medication list as well, to avoid issues.
* 01:04:48So more on that to come i'm quite sure and, that being said, we made it through the learning objectives hooray.
* 01:04:57I need to give big shout outs, I want to make sure that, first and foremost I shout out my nursing care coordinators, that I work with in my two endocrine clinics.
* 01:05:08Jennifer pinata who's at 14 and ELISE mariner who's at my pan tops location my locations, as if I don't share them with all my colleagues, but diabetes management.
* 01:05:20is complex, some of our new agents, I was just talking about including insulin are effective, but quite costly access to technology is can be.
* 01:05:30Really burdensome and I could not offer my patients the best care without their support, and so they deserve huge round of applause and I appreciate them so much.
* 01:05:42I want to thank all of my undergrad colleagues who of course see transplant patients as well, and not the only one, and they taught me so much.
* 01:05:50And, and then I want to thank my colleagues at the transplant Center who welcomed me into their fold Dr overhauled Sir who's the division chief and quite expert and pancreas and islet transplant.
* 01:06:00Dr braman who's the surgical director of the kidney and pancreas group.
* 01:06:04program Dr Doyle is the medical director for the pancreas program but also passing on the reins to Dr Rao another transplant nephrologist very soon.
* 01:06:14So I appreciate all that they taught me, and I also wanted to thank the group at the Center for diabetes technology as well who've helped to support some of my interest in cgm use in this group and.
* 01:06:26and have shared with us some of their data about risk of hypoglycemia so I really appreciate all of you, and thanks so much for having me.

**Izzy Budnick**

01:06:40Okay, thanks that was great.

* 01:06:44We asked folks to drop their questions in the chat or asked to be unmuted and.
* 01:06:51i'll just start off with one, though I you know you mentioned most of your work isn't the kind of abdominal transparent world but does seem like maybe some of the post transplant diabetes is you know impacted by the superior immunosuppression.
* 01:07:05From my kind of basic understanding like.
* 01:07:08part, especially the lung transplant just have much more intensive immune suppression regimens it involves involved at all with them and see kind of more difficult to control, diabetes, or other endocrinology.

**Meg Stumpf, MD**

01:07:20mm hmm yeah so the lung transplant population, I have to give a big shout out to my colleagues who are more embedded embedded into the cardiovascular.

* 01:07:32surgical Center and the Cardio metabolic clinics and they see the majority of the heart and lung transplants and actually their program existed before I came in in 2018.
* 01:07:43you're right that the lung transplant patients receive a lot of immune suppression, they tend to be on higher doses of group record equates for longer.
* 01:07:51I think that we see a lot more insulin dependence for a larger amount of time before we can wean them to other therapies.
* 01:08:01Essentially, the management strategies, though aren't too dissimilar you know, in terms of the agents that we have available to treat the glucose excursions.
* 01:08:11But that's why it's so helpful, I think, to have somebody who's really embedded in the program and can easily communicate with the transplant team about how the anti-rejection mentor are changing.
* 01:08:22so that you can make nimble adjustments, particularly for insulin dependent patients and many of our Google quarter quaid heavy patients are are on mph and human long, for instance, to deal with that.

**Izzy Budnick**

01:08:38Great thanks so much.

* 01:08:42we've got a message from Dr route so thanks to mag for next month review we go your own transplant any tips on how to promote referrals for pancreas islet cell transplant.

**Meg Stumpf, MD**

01:08:55yeah it's a it's a great question Dr allison Thank you so much um I think that.

* 01:09:04I think that in you know it's interesting for as endocrinologist and I think that you know sort of sort of the exposure that we get through our medical training is that.
* 01:09:13we're medical doctors and we want to use all of the tools that we have to give our patients the best medical management and we often don't think of the surgical option as quickly and so.
* 01:09:27I guess one of my goals by introducing this topic to to all of internal medicine into internist and primary care doc's who might be managing diabetes, as well as that it's okay to think about this earlier.
* 01:09:39And and just because you're you may personally be feeling dubious that a patient is a good candidate for transplant surgery doesn't mean that they're not a good candidate for a referral and evaluation, so I was trying to.
* 01:09:53to sort of point out that the Multi disciplinary EVAL that happens in the transplant centers can benefit our patients.
* 01:10:00Even if they're, even if we find that actually we could offer different medical management, but I think outreach is going to be the answer to that.

**Izzy Budnic**

01:10:14Great thanks so much.

* 01:10:24Well Darren any other questions, I want to thank you again, Dr some really fantastic talk and thanks for everyone for joining us here on Friday and hope to run this very weekend.

**Meg Stumpf, MD**

01:10:36Thanks so much.