[MUSIC PLAYING]

JAGDEESH ULLAL: So I lived in Virginia for almost 17 years and moved to Pittsburgh earlier this year. We landed here on Christmas Day last year. It was the coldest day recorded, at least in last winter. And my wife and I looked at each other and I said, did we make the right decision? Because we lived in Virginia Beach, and this was a little bit of a change.

But so far it's been wonderful. I have wonderful colleagues. Great Fellows and great colleagues here at Presbyterian Hospital Montefiore, so it's been a pleasure so far. I have no disclosures.

What I'd like to do is provide an update with inpatient diabetes management, some diabetes guideline issues, cardiovascular outcomes, some recent medications, update with bone problems, and thyroid problems as well. So let's start with diabetes.

So diabetic ketoacidosis, a topic that's very close to my heart. The panel on the left side is probably a scribbling from a medical student. And you may all realize that you cannot go through your first month of internship without having dealt with diabetic ketoacidosis. It's a very common problem. A very costly one and a very complex one, because this is one of the emergencies that endocrinologists have to deal with.

And really, some of it comes from a lack of preventative programs. It reflects the health care system. It reflects the social system, and there has been a rising trend over decades. It's a hallmark of Type 1 diabetes, but we've begun to see it in type 2 diabetes as well.

We did a study about a year or two ago where we looked at the cost of diabetic ketoacidosis. This was a seven-year span of about 7,000 patients. This was in Virginia, just in our hospital system. Each hospital admission cost about $10,000, and we know that diabetic ketoacidosis is such that people tend to come in over and over. And this is just a snapshot of our findings, but we found that there was a huge racial disparity, a huge socioeconomic disparity, and we're working on publishing this data in the form of a manuscript.

But while I was there, we worked with a software that manages inpatient glucose treatment-- inpatient insulin dosing. The software was called Glucommander. It's available for commercial use, along with several other companies that manufacture software for glucose management. And what we did was, this is actually a decision support tool. So it helps with adjustment of insulin doses.

It was a multi-center study. We looked at 2,600-odd patients. We looked at patients who were on the Glucommander protocol, whose insulin was managed with the software, and patients who were managed with the conventional column-based protocol. I'll show you an example of the conventional protocol.

So what we found was that there was a lower rate of hypoglycemia in patients who had the software utilized for insulin dosing. The length of stay was shorter. Patients achieved better glucose control, achieved faster glucose control, and their acidosis resolved much faster. So it was very surprising. But it was a welcome finding to our hospital system there, which had invested a huge amount of money across probably about 13 or 14 hospitals. So it was well worth the investment.

We also looked at the emergency room utilization in diabetic ketoacidosis. We looked at patients who came in with ketoacidosis, put them on the Glucommander software to dose insulin. Some patients were actually treated in the emergency room and sent home. And of course, the more severe ones were kept in the hospital as observation or as a full admission, so there was some benefit in utilizing the Glucommander software in the emergency department.

In terms of how this actually works, let me spend a few minutes discussing how the Glucommander works. So let me see if my-- yes. So the pointer works here.

So this patient came in with a blood sugar of 500. She was placed on the Glucommander protocol and sure enough, the blood sugars corrected. And all of a sudden, it dropped a little too rapidly, so the software recommends that the blood sugar checks be more frequent. And so it slows down the drip rate, slows down, puts the brakes on, and then the line plateaus a little bit. And then it carries on until the patient reaches goal. The goal here was 100 to 180.

So the patient reached goal. Took some took about four hours, and the patient was maintained within the goal blood sugar range with the insulin dose titration. So this is a typical Glucommander run. Once the IV insulin is done, the patient is transitioned to the Sub-Q module of the Glucommander software.

The insulin doses are recommended. For example, with this patient, they got 40 units of Lantus insulin, 12 units of mealtime insulin. The blood sugars are in range, so it doesn't recommend any correction insulin. If the patient eats, there's a place that the carbs can be entered. Ours was one of the few hospitals that did carb counting across the board.

So it was a 600-bed hospital. All the nurses in the hospital did carb counting. They would go to the patient rooms, count up the carbs that were eaten, enter it into the software, and the software would make dosing mealtime recommendations.

So this is how the dashboard looks like. When the software is opened, it has the initial name, and so forth. The next basal dose. This is the target glucose ranges. This recommends 12 units with each meal. And if the nurse doesn't check the blood sugar in time, this turns red and it starts blinking. So it's a useful tool for analysis.

So after the patient's done with their hospitalization, they're ready to go home. There's a button right here which says Hospital to Home. If this is clicked, these are the recommendations that are thrown at you.

A1C was 9%. Consider the following regimen. Resume home anti-hypoglycemic medications. Add basal insulin. So nice recommendations for those who are not familiar with dosing diabetes medications.

Now this is the column-based method. We still use this at our hospital. When you order insulin in the ICU or on the floor, this is what the nurse prints out, and this is what the nurse follows. And it works. Works really nicely.

However, this is already available to us. Somewhat the rudiments of an electronic glucose management was already available to us at Presbyterian Hospital. How many of you all know about this? Does anybody know about this tool that we have? If not, just email me and I will send you the link.

This works by entering blood sugars-- the previous blood sugar, the current blood sugar, and the current infusion rate. And when you hit Calculate, then it spits out the next infusion rate. So a really nice tool that's already available to us, but not very much utilized.

There's obviously better blood sugar control, so helps the patients. Fewer hypoglycemic episodes, so there's a patient safety benefit. It improves nursing workflow. And for a system like UPMC that has far-flung hospitals across state lines, it really helps distant hospitals without endocrine coverage.

And the next one is meeting hypoglycemia. There's a metric that Medicare is following or will be following, which is the reduction of inpatient hypoglycemia. So using electronic glucose management may actually help with reducing inpatient hypoglycemia.

Now while we are on the topic of inpatient diabetes management, this was a study published a couple of months ago which looked at closed-loop insulin delivery on the inpatient side in non-critical care patients. You all may have heard of Medtronic and the artificial pancreas. It's not a real artificial pancreas, but it's a sensor.

The patient has a sensor. The patient has an insulin pump. The sensor talks to the pump. If the blood sugar is too low, the sensor tells the pump to turn off. If the blood sugar is too high, the sensor directs that the pump comes on and starts bolusing, so it's a closed-loop system. It's available now in the form of a Medtronic pump, but does it have any utility in inpatient diabetes management?

And this study was one of the first that looked at that. And it did show a little bit of benefit in terms of blood sugars. Blood sugars were much better compared to the control group. Fewer hypoglycemia. You can see the lines begin to separate here. The blue line is the conventional insulin delivery, and the red lines are the closed-loop delivery.

So interesting study. Not ready for prime time by any means, but I thought it would be interesting, because I think this might be coming in the future. Maybe 10 years down the line.

Now moving onto the next topic. There was a little bit of a rift between the providers caring for diabetes from the primary care standpoint and the specialty standpoint. This was the ACP guideline for diabetes management. I'm a member of the ACP-- have always been since I was a resident. And when these guidelines came about, endocrinologists read these and felt that some things needed to be different in this.

For example, "Clinicians should pursue goals for glycemic control in patients with type 2 diabetes." OK, that sounds reasonable. "Clinicians should aim to achieve an A1C level between 7% and 8% in most patients with type 2 diabetes." We're going to have to revisit that.

"Clinicians should deintensify pharmacological therapy in patients with type 2 who achieve A1C goals of less than 6.5." Not sure about that too. "Clinicians should treat patients with type 2 diabetes to minimize symptoms related to hypoglycemia and avoid targeting an A1C level in patients with life expectancy less than 10 years or advanced age." That seems reasonable too.

So the endocrine community got together. The diabetologists got together and made a rebuttal to this. Our very own Mary Korytkowski was one of the-- is Mary here by any chance? Mary said she'd be here.

So Mary and her core authors said that when you look at the data that was utilized to come up with the ACP guidelines, it was the ACCORD study. If you all remember in the late 2000s, there were very big blockbuster trials-- the VADT, the ACCORD, and the ADVANCE trial. These were huge, huge trials. And the gist of those trials were intense diabetes control is not necessary.

But the ACP guidelines use the ACCORD trial, which is reasonable. It's a huge study. But the focus of the ACCORD trial was cardiovascular outcomes. So the committee did not review subsequent ACCORD analysis that showed an increased death that occurred in patients who did not achieve a lower A1C goal. And really, the ACCORD trial being a controlled environment, really does not represent the real-world management of diabetes.

So it was also noted that for every 1% absolute increase in A1Cs, there's a 37% increase in severe microvascular endpoints, 21% increase in diabetes-related deaths, and 14% increase in myocardial infarctions. So then this was from the UKPDS study. So therefore, caution was recommended in this paper-- caution that intentional deintensification of therapy makes little sense for patients whose diabetes is well controlled, who have no adverse effects.

For example, I had a patient who was in his 90s-- a really functional person. Wasn't basal bolus insulin. He was doing one shot of basal insulin, one shot of mealtime insulin three times a day. Was really well-controlled. It looked like he had 10 more years to go, maybe even more. So I felt that we didn't need to de-escalate care. So I think de-escalation of therapy needs to be done on a case-to-case basis, based on a number of different things.

For example, this was a publication from 2012, many years ago actually, where they recommended patient attitudes need to be assessed. Patients' social support and resources need to be addressed. So a number of things go into determining what the A1C goal is. There is no one number that's right for everyone.

So I like this picture, and I use it a lot when I teach Fellows and residents and students. Now the American Diabetes Association has its annual guidelines. It puts out an algorithm that has monotherapy, dual therapy, and triple therapy and so forth. This is available in the Standards of Medical Care that's released at the beginning of each year.

But the American Association of Clinical Endocrinology also has interesting guidelines which kind of mirror the American Diabetes Association guidelines. But they are a little bit more pleasing to the eye in that they have these arrows that take you from one to the other-- monotherapy to dual therapy to triple therapy, adding intensification of insulin over here. And these can be very easily downloaded-- aace.com you can go, or Google "AACE diabetes guidelines." You'll get a set of 10 slides. Very nice to look at and use in your patients.

In addition to diabetes management, they also go over obesity management in diabetics. They also go over cardiovascular risk reduction. So please check these guidelines out. They are useful.

So in the year 2018, we now have 12 different groups of medications. These are also in the same set of slides. The green here indicates a favorable benefit.

For example, if your patient comes and says I have hypoglycemia, it's likely that they are on sulfonylureas or glinides, or on insulin. So this shows up as orange, but still available for us. We use insulin all the time. We use sulfonylureas all the time. So we now have 12 different agents. The most recent one is the sulfonylureas that we'll talk about in a short while.

Now this is the Ominous Octet. Have anybody heard about the Ominous Octet? I don't see very many people raising their hands. But the Ominous Octet-- you may ask me why do we need so many diabetes medicines? Why do we need patients to be on multiple therapy?

The reason is because there are eight different defects in diabetes. There's neurotransmitter defect in the brain. There's decreased insulin secretion in the pancreas. There's a paradoxical increase in glucagon secretion in the pancreas.

There's increased hepatic glucose production at the level of the liver. There's decreased incretin effects at the level of the intestine, decreased muscle glucose uptake, increased lipolysis at the level of the fat. And finally, increased glucose re-absorption.

So in diabetes, there's actually a paradoxical increase in glucose reabsorption. The glucose threshold in general is 180 milligrams per deciliter. But in diabetes, type 2 diabetes particularly, the glucose threshold in kidney reabsorption goes maybe up to 220. So this was published by Dr. Defronzo, who is an endocrinologist down in San Antonio, who also happens to be a nephrologist and a leading expert in diabetes and the field of diabetes.

So this is the Ominous Octet. So the Octet is now developing into-- there are 10 pathophysiologic defects. So it's progressing, but this is one of the reasons why we need multiple therapies in diabetes. So let me talk about SGLT2 inhibitors, because I think many of you all use this in practice. And this is the most recent addition to our armamentarium in diabetes.

It's indicated in type 2 diabetes. There is a type 1 indication coming up very, very soon, but not yet. There is a risk of euglycemic diabetic ketoacidosis. These patients come in with ketoacidosis. They have the acidosis. Their anion gap is high. But their blood sugars surprisingly don't tend to be very high.

So typically, diabetic ketoacidosis tend to have sugars in the 400s and 500s. These people may have blood sugars in the 100s or 200s, because they have their kidneys dumping glucose constantly because of the medication. Tends to happen in the insulinopenic patients rather than in patients who are treated with insulin.

There is a weight reduction. So when glucose is leaving, it's minus calories. Patients lose about 300 calories per day. So you keep adding that up, and people lose weight. So there's a weight benefit. Patients lose fluid. On average, they lose about 200 to 400 mL per day, and so that leads to blood pressure lowering.

There's no risk of hypoglycemia. This is not an insulin-mediated mechanism, so there's no hypoglycemia. And now we know that there is actually cardiovascular risk benefit.

So there are four approved SGLT2 inhibitors that are available-- Invokana, Farxiga, Jardiance. So canagliflozin, dapagliflozin, empagliflozin. These have been around for at least four years now. The newest one is ertugliflozin, which is called Steglatro.

They all have a starting dose and a max dose. Everybody starts off at the lower dose and progresses to the higher dose. There is a renal adjustment that needs to be done. If your kidney isn't working, there's no point in giving this medicine because it won't work, because it works through the kidneys.

A1C reduction-- it works. It works better than some of the lower agents, but not very stellar. On average, it reduces A1Cs by 0.7% to 1%. Jardiance, which many of you all may have heard of, in terms of its receptor binding, is the most selective. So there's SGLT2 in the kidneys, and there's SGLT1 in the gut. Both help with absorbing glucose through a sodium-mediated mechanism.

The most recent addition to the warnings in terms of this medicine is necrotizing fasciitis of the perineum, or Fournier gangrene. You may have seen this in men, but maybe about a couple of months ago when I was covering the inpatient service, we saw this in a woman. So necrotizing fasciitis, soon enough-- in fact, I was covering the service in August, and that very month this boxed warning came up.

So there is vaginal yeast infection, urinary tract infection, and obviously with fluid going out, there's increased urination. Hypertension-- if you keep the patients on the same anti-hypertensive treatment and you don't de-escalate treatment, they can have hypertension. Similarly, if you don't de-escalate their treatments with insulin or sulfonylureas, they may have hypoglycemia. There's a bladder cancer thing that showed up.

With canagliflozin, the long-term data showed leg amputations, and it was quite scary. A lot of people called me and said, do I need to come off Invokana? And I briefly took them off Invokana. But then the real world data came. It was presented this year at the American Diabetes Association meeting. The real world is different from controlled studies.

So real world data said no risk of amputation. It's very similar to stories you've heard before. With Rosiglitazone, for example, there was a cardiovascular scare. Everybody came off Rosiglitazone. There was a bladder cancer scare with Pioglitazone. Everybody came off Pioglitazone. But this one, the real world data doesn't show amputation. But it's there.

So now in terms of cardiovascular trials, we have three trials that are available to us-- EMPA-REG, CANVAS. EMPA-REG was empagliflozin. CANVAS is canagliflozin. We still have a number of trials to go, but all of this really came about after the Rosiglitazone scare in the mid to late 2000s when Rosiglitazone was shown to cause bad cardiovascular outcomes.

So the FDA mandated that all diabetes medicines need to be tested for cardiovascular risk. And so here's the whole gamut of cardiovascular outcome trials. We're somewhere in the middle of this right now, but we have several more studies that will come out, and some really good ones.

For example, the EMPA-REG showed cardiovascular risk reduction. It showed really good outcomes with heart failure. And so we now have an indication with Jardiance, empagliflozin, and an indication with liver glutide for cardiovascular risk reduction. So these trials, while very, very expensive, have proven that they are safe. At least, some of the drugs are safe.

Sotagliflozin is a combined SGLT1, SGLT2 inhibitor. It's going to be used in type 1 diabetes. So patients who are on insulin. So can you imagine in a type 1 diabetic who is insulin-dependent, we're going to now recommend a pill for them. So it's going to be a huge change in thinking.

But this was a study that was published last year. It has been accepted by the FDA for consideration for approval, but this study showed a 0.4% reduction in A1Cs and a placebo compared to sotagliflozin. 28% of patients met the outcomes. So more to come on this, but interesting and new promising treatment for type 1 diabetics.

Moving onto diabetes technology-- so the first one is called Eversense. So for a brief, fleeting moment, endocrinologists will become internationalists where we implant this small device in the dermis utilizing these tools. This device sits in the dermis for about three months at a time. Communicates through a transmitter. Transmitter communicates to your smartphone, and you can read the blood sugar continuously. So this is a continuous glucose monitor.

Another one is the Abbott FreeStyle Libre. This patch here is worn on the side of the arm. It's the size of a quarter, and it reads to the device here, but it needs to be flashed over the patch and you can get the blood sugar. No need to prick your finger. An incredibly useful device. I use it quite a lot in my patients.

This has been around for a long time-- Dexcom-- but they've moved up to Generation 6, so Dexcom G6. That's now available. It's a real-time glucose reading device. Extended 10-day sensor wear.

A sensor that's worn on the skin, reads to the glucose monitor or to your smartphone or to one's Apple Watch as well. I have patients who just have their blood glucose all the time on their watches. No calibration needed. Incredibly useful tool. And we use this, again, quite a bit.

So CGM for inpatients-- is there a utility? I know our hospital administrators are rolling their eyes at this right now, but another thing for them to think about is-- so this was five patients. This was glucose telemetry. Can you imagine a person sitting there in front of all these monitors looking at people's glucoses?

So glucose telemetry, just five patients here. May be a thing of the future. But there was a consensus statement put together in terms of inpatient utilization of continuous glucose monitors. It may be useful, but it's costly. Somebody has to interpret the data. So there might be more studies coming out in the near future.

In terms of insulin delivery devices, all of us utilize pens quite a bit. This is the newest addition to pens. I think by now everybody knows about Toujeo, which is U300 insulin. This is the older version. This has been around for a couple of years now. It holds 450 units of insulin.

The newest one is called Toujeo Max, and that holds up to 900 units of insulin, and you can dose up to 160 units at a time. So huge amounts of insulin can be delivered, and patients don't go through pens like peanuts. So that's incredibly useful for the very, very insulin-resistant patients.

Now in terms of insulin patch pumps, we used to use this quite a bit in Virginia. The V-Go basal-bolus delivery device. It comes in 20, 30, and 40 units of basal insulin. There's a small clicker on the side.

You click the clicker and it delivers about two units for a max of 36 units. No electronics. This is disposable. So it's very useful for patients who cannot deal with electronics-- who are relatively not very sophisticated to deal with devices.

The OneTouch Via or the OneTouch Calibra-- we don't know where it stands right now. This is a Johnson & Johnson device. Johnson & Johnson has decided to actively move away from diabetes management. There is a pump called Animus which they are washing their hands of.

So we don't know where this device is, but this device has been bought over by this company. It's a basal-bolus device that lasts for three days with programmable settings. These are all worn on one's skin and delivers insulin subcutaneously. But this is readily available. Somewhat under-utilized, it looks like, in Pittsburgh. But definitely something to think about.

The V-Go device just a little bit more. The max it holds-- the 40 unit one holds about 36. So it holds 40 units for basal insulin, plus 36 units for bolus. So max dose per day is about 76 units. It's peeled off. You peel it off and put it on right here, and there's a clicker that clicks two units at a time.

In terms of medication approval, we had quite many in 2016. A little fewer in-- well, more or less the same, I guess. But Lixisenatide-- a combination of Lixisenatide and insulin. A combination of insulin degludec and liraglutide. Again, semaglutide, which is also from Novo Nordisk. It's a GLP1 agonist.

Here are two flozins-- dapagliflozin and we know ertugliflozin. Right now, sotagliflozin has been accepted by the FDA. We'll have to wait for a final word.

OK, moving on to bone diseases. I think we're OK on time. We're in the doldrums in terms of bone diseases.

Abaloparatide-- this is a slide that I borrowed from Dr. Mahmoud Hussein, because we haven't really progressed very much in terms of approvals for a bone strengthening medication. This was the last approved medicine. This is an anabolic agent-- abaloparatide, also called Tymlos. UPMC insurances prefer this over teriparatide. Obviously it has good data when compared with abaloparatide and teriparatide.

Again, teriparatide has to be used for a total of two years, so if the patients have used teriparatide already for a year, they can use abaloparatide for another year, and that's the max lifetime exposure for the medication. Osteosarcoma in rats, just like teriparatide. Avoid use of in patients with increased risk of osteosarcoma. For example, those who have had radiation exposure for one reason or another.

Vitamin D supplementation-- I think vitamin D has reached the status of wine, alcohol, coffee, and chocolates. In one day and out the next. But this one was interesting in that they looked at 81 randomized controlled trials. This was a meta-analysis that reported fracture, falls, bone mineral densities.

This was routine supplementation, not treatment. So on routine supplementation, vitamin D had no effect on total fractures, does not prevent falls, may aggravate it, and does not have any meaningful impact on bone mineral density. So this was doses greater than 800 international units.

So routine supplementation is probably not recommended. But I use vitamin D all the time for my osteopenia patients, for osteoporosis treatment, for patients on chronic, long-term steroids, for my gastric bypass patients. So I still utilize vitamin D a lot, but I don't put everyone on it.

Now if we've done away with routine supplementation, does it have any other uses? Can it be used in neuropathy? So my mentor, Dr. Arthur Vinik, was a neuropathy specialist, and we looked at every medication and every trial for neuropathy very closely. And this one came about a couple of years ago actually, where they used high doses, like 600,000 units of vitamin D, for neuropathy.

It was a couple of studies-- maybe one. There was a study in Pakistan. But the author was very renowned author-- Rayaz Malik from the United Kingdom. This particular study is from Solomon Tesfaye, who is also a very renowned neuropathy specialist.

So this study showed that there was a difference between vitamin D levels between painless and painful neuropathy. This showed a quality of life improvement over time when over a four-week interval. So maybe some utility in painful neuropathy. We'll have to wait for more data on this.

Now the last one in terms of metabolic bone diseases is burosumab or Crysvita. It's approved for X-linked hypophosphatemic rickets. Now I don't think this is going to be a very common medication that you all prescribe, but nevertheless, the reason I have it here is because I can see pharma slowly steering towards the-- in fact we've heralded already a new era of designer molecules.

So burosumab is an antibody that binds to fibroblast growth factor 23. High levels of FGF23 in X-linked hypophosphatemic rickets causes renal wasting of phosphorus. These patients have low phosphorus levels. These patients also don't have the activation of vitamin D to 1,25.

So these patients are treated with phosphorus replacement and replacement of 1,25 vitamin D. But they do end up getting these bow legs here. It's a small graphic right up here. It's a very bad disease, but we have this antibody now.

But the cost of these molecules are in the tens of thousands per patient per month. So you can only imagine what it does to the health care system. But it's few patients, so this is manageable.

But there are other agents. For example, the PCSK9 inhibitors, which are injectables-- very, very expensive molecules, but incredible results. Cardiovascular results, results on cholesterol with Repatha or evolocumab. So we're now having to deal with very expensive medications and very difficult decisions.

Moving to thyroid. Now this was a paper that came earlier this year. You may think that there's a huge explosion of thyroid cancer incidents, but it's mostly because it's being detected more. Because patients have CTs and they have various other imaging, and they have a small thyroid nodule that needs to be followed.

And so you can see over time here the number of total thyroidectomies have gone up. The number of nodectomies have gone up. So in 2015, there were guidelines for thyroid, well-differentiated thyroid cancers. There was a move towards a less aggressive management, less aggressive surgeries, less aggressive treatments, less aggressive staging as well.

This is a busy slide, but I'd really like to emphasize a couple of points here. When you find thyroid nodules, remember one number-- one centimeter. If they are above a centimeter, please refer them to us. If they are under one centimeter, they can still be monitored. They don't need to be biopsied.

But often we find that one thing leads to another. They end up with a biopsy. They end up with results and we don't know what to do with them. Often the results are atypia or follicular lesion or indeterminate, and then they go to molecular analysis.

Fortunately we are really lucky to have a fantastic group of pathologists here, and we have from the University of Pittsburgh, championed wonderful [INAUDIBLE] analysis pathway of analyzing molecular markers for thyroid cancers. So if you find that you have thyroid nodules, please refer them to us, because we know what to do with atypia and follicular lesion and indeterminate.

As endocrinologists, we understand the molecular markers and how to interpret them. So please don't be stuck with these diagnosis or stuck with the molecular markers and not know what to do with them. Please refer the nodules to us, and we'll be happy to take care of them.

So if you're a hedge fund manager and you have just $1, you can bet your bottom dollar on a spongiform nodule that it's going to be benign. And you will come out a winner. So spongiform nodules-- yeah, it does project OK.

So spongiform nodules are nodules that look like a sponge. So if they look like a sponge, it's good. They will be benign. You don't have to worry about them. If they're a cyst, they're OK. You don't have to worry about them. But if they look like a piece of coal, if they look dark, if they look hypoechoic, if they have irregular borders, if they are hard, if they have these specs called microcalcifications, they need to be biopsied.

But let me just go back to the size, because the size determines a lot. Even if they are high risk, even if they are high suspicion, we still recommend that we wait till it's above a centimeter. Because biopsy in a nodule under a centimeter tends to be technically challenging.

It can be done. I've done it many times. But it can be technically challenging, so please hold onto them until they're over a centimeter. And if they cross a centimeter, we're happy to see them in our clinics. If they are a low suspicion, you can even wait until they are 1.5 centimeters or the SpongeBob types, you can even wait until 2 centimeters. So this is benign to high suspicion.

So we have a fantastic thyroid group at our unit here. All of us biopsy. The top row here, all of us biopsy thyroid nodules. We do our own biopsies. We do our own interpretations.

We have Dr. Mahmud, Hussain and Shannon Johnson are part of our Thyroid Cancer Group. And we manage thyroid cancers-- thyroid nodules. And some of us have added ultrasound certifications, so please don't hesitate to refer patients to us.

You may have heard of subclinical hypothyroidism being favorable in the elderly. If TSHs drift up in the older patients, it may actually be OK. But what about subclinical hyperthyroidism? Subclinical hyperthyroidism is seen when patients have free T4s and T3s that are normal, but the TSH is suppressed. And these patients can be more prone to having atrial fibrillation, heart failure, coronary artery disease, bone loss fractures, and so forth.

So this paper just came out earlier this year, where they have this nice figure that tells you beyond 65 and the TSH is less than one, this patient needs treatment. If they are beyond 65 and the TSH is above 0.1, we probably need treatment based on other clinical factors. But if they are under 65, they can be observed.

Lastly, we heard about the Nobel Prize in Medicine being given to James Allison from MD Anderson and Tasuku Honjo from the University of Kyoto for their work on checkpoint inhibitors in the treatment of cancer.

A quick case that I had last year-- this was a 60, or maybe late 50-year-old patient. He was a construction worker. Very healthy. Nothing else going on. Was in the sun a lot. Ended up with malignant melanoma. Was on pembrolizumab and ended up in the hospital with diabetic ketoacidosis.

It was a little bit of a surprise, but when we dug in a little bit, sure enough, it was the pembrolizumab. It had cured his malignant melanoma. His melanoma was in remission, but he had diabetic ketoacidosis, because the endocrine organs are all cloaked from the immune system.

They are all protected from the immune system. So these checkpoint inhibitors open up the immune system. They increase levels of persisting antibodies or enhanced complement radiated inflammation, for example, in the pituitary.

So if you look at these endocrine disorders over here, you'll find that there's a huge number of endocrinopathies generated from the use of checkpoint inhibitors. And in fact, there's thyroiditis, hypophysitis, adrenal insufficiency, and pancreatitis autoimmune diabetes. So we're having to deal with some of these while their cancer is being treated. So that's all I had for today, and I'll be happy to take questions.

[APPLAUSE]