



## Strategies for Diabetes Management: Case Presentations

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### Introduction

Dr. Ellen Habas, an endocrinologist with the Indian Health Service, Cherokee Service Unit in Cherokee, North Carolina, presents treatment options for 4 patients with diabetes. Each case presents several options for treatment and Dr. Habas discusses her approach based on her years of clinical experience.

Case 1 - Mr. A is an elderly gentleman with long standing type 2 diabetes, poor compliance, poor glycemic control but expressed a renewed interest in managing his diabetes.

Case 2 - Mr. B is a middle-aged man diagnosed with type 2 diabetes when he is admitted to the hospital for an emergent cholecystectomy.

The third patient provides discussion of another typical scenario but perhaps more complicated. Ms. C is a young woman who had gestational diabetes treated with insulin. A year later, she is treated with oral agents and a healthy lifestyle. In spite of great compliance with all that's been recommended, she has not been able to achieve consistently good blood sugars.

The 4<sup>th</sup> case is about Dr. Habas' work with an obese adolescent girl (D.D.), who is already having medical complications, because of her weight and diabetes. Dr. Habas provides discussion of a number of treatment considerations including: the child's sleep apnea, research regarding the efficacy of bariatric surgery in patients such as D. D., and also the need for beginning care for D.D.'s younger sister G.G.

I am Jo Ellen Habas; I work with the Cherokee Diabetes Program in Cherokee, North Carolina. I'm an endocrinologist. I'd like to talk with you about some of my patients, some of the things that they have taught me about taking care of diabetes.

### Case Study A

So let's start with Mr. A. He is a 69-year-old man diagnosed with diabetes, Type 2, 13 years ago. You have been seeing him for six years. We had all kinds of reasons to cancel or postpone his visit. In general, A1Cs range from 10 to greater than 14. He takes NPH 35 at bedtime and Regular 15 BID. He has proliferative retinopathy, that is now fortunately stable; also stable CKD with a GFR of 28 and he has a distal sensory neuropathy but takes real good care of his feet. His sister recently started dialysis and he is starting to think more about his diabetes. So he called to make an appointment to see me to talk about what we could do about that. So when he calls, what do you say to him?

- A. Congratulate him on his commitment to improve his diabetes control. Suggest that he start exercising, follow a diet, visit with the nutritionist and take his insulin exactly as prescribed.
- B. Order labs, make an appointment for him to see the eye doctor and nutritionist, and ask him to check his sugars various times during the day and to take his medications exactly the way he's been doing.
- C. Tell him to have labs drawn that were previously ordered, make an appointment for him to see the eye doctor and nutritionist and ask him how he is really taking his meds.

You know that in the past he has been sedentary, he has not been eating in a healthy manner and just judging by when he comes in for refills, you know he doesn't take his medications regularly. If he suddenly does everything that he is supposed to be doing, he will be at a serious risk for hypoglycemia. If he looks at the insulin bottles and sees what has been prescribed, and that's not exactly what he has been taking, if he suddenly does take it, he really could be in big trouble. So you have to prod and try and figure out what exactly he's been doing and then work from there.

The other thing is you don't want to improve his diabetes control right this second because of his proliferative retinopathy. Too rapid control has been associated with worsening of proliferative retinopathy. Also certain kinds of exercise, especially those that include the valsalva maneuver. My favorite thing to give patients is those stretchy bands to exercise with and that actually is not good for someone with proliferative retinopathy. And if you're not sure, check with his eye doctor.

And lastly here, tight control in patients with established microvascular complications, heart disease, who have had diabetes for a long time, are elderly, or at high risk for low sugars, or have no complications, it might be okay for us to actually lower their targets. The A1C of 7, we're finally admitting may not apply to everybody, and I think as practitioners, we've known this all along. We've had elderly, very fragile patients come in with A1C of 7.4 or 7.5, and we've just said we're not going to hurt them by pushing the meds.

So that's what I would say about Mr. A. Talk to him, figure out what he is doing, move slowly, give him a refresher course in eating and just work from there, trying to get him as well-controlled as you safely can, without risking low sugars.

### **Case Study B**

Okay, Mr. B. Mr. B is a 51-year-old man who was diagnosed with diabetes when he presented to the emergency room six months ago with acute cholecystitis. He had never known that he had diabetes. His sugar was almost 400 and his A1C was 9.4%, indicating that it didn't just happen right when he started having the pain and inflammation of the gallbladder. His sugars had to be high for several months. He has not been receiving any kind of regular healthcare.

While he was in the hospital, his sugars were well-controlled with IV insulin. And when he was discharged, he was prescribed Detemir 20 units twice a day, and Aspart 10 units TID with meals. During his hospitalization, he was found to have no evidence of microvascular disease. So they had done a 24-hour urine collection, that was fine. They had the eye doctor see him, his eyes looked good, no neurologic deficits and then they told him them to find a provider quickly and so here he is in your office.

Six months after surgery when he sees you, his A1C is 6.8, his blood-pressure and lipids are well-controlled, he's lost 23 pounds and now has a BMI of 28. He walks 2 miles a day, five days a week, bicycles with his grandchildren on weekends. He and his wife have gone to cooking classes and they are beginning to eat a vegetarian or vegan diet at least a couple of days a week, very typical patient response.

And your options are to:

- A. Clone him.
- B. Ask him to talk with your patient Mr. A.
- C. Hire him as a diabetes educator.
- D. Congratulate him on the wonderful efforts he has made to improve his health status and advise that he just continue his diabetes medications. After all if it's not broken you don't need to try to fix it. Ask him to start checking his sugars at random times, and have him come back in three months with repeat A1C.
- E. Discuss other options for diabetes management.

So you can probably get rid of options A and B and I would maybe consider C, at least in some capacity. But I would choose option E because he is on a really complicated schedule of medication. He's taking five injections a day when we discussed. Just as an aside, when we use Detemir for our patients we always start trying to use it as a once a day medication and actually I probably have only seen maybe once or twice a time when we had to go to Detemir BID. So, on his fairly low dose, twice a day Detemir, even if we were to continue that, might be changed to once a day.

Okay, so you could consider a trial of oral agents. When he was diagnosed, he needed surgery. They went straight to insulin. If we give him insulin sensitizers, like Pioglitazone, Metformin or Sitagliptin, those would not make his sugar go low and it's always a good idea to save someone from the chance of low sugars if it's possible.

Also on those medications there are no data showing that we need to have him actually checking his glucose. And I know all of us, no matter what the studies show, just kind of want to know what our patients are doing during the day and to adjust their meds. But there actually aren't data that if you're using something that is not going to make your sugar go too low that it's necessary to test. Or you could inquire as to his eating schedule and see if a simpler regimen might be effective. So now I want to talk about some of those.

Some people eat continually during the day; they graze, and if that's the case, taking three shots a day for three meals, when all the meals are of the same size and that means you're leaving them uncovered three times a day. That might not be a good regimen for him to follow. Oral agents would be a reasonable option or even a simpler insulin regimen. If you felt that you just didn't want to play around with orals and you wanted to see if you could just simplify his regime, possibly a basal insulin and then one or two shots of a prandial insulin or even twice a day 70/30, which I use quite a bit. Those could all be simpler options that should give you the same degree of control.

### **Case Study C**

Okay, Ms. C is a 28-year-old Casino Floor Manager. She had gestational diabetes during her fourth pregnancy which she delivered about a year ago and during that time she was treated with NPH BID and NovoLog QID with meals. After delivery she started Metformin and then after that Pioglitazone and Sitagliptin and Glimepiride were added. She eats three meals a day, she prepares them at home. She doesn't eat fast food or junk food and she's pretty consistent with what she eats day-to-day. She's very active, exercises regularly and when she sees you in the office her A1C is despite all that she is doing to control the sugars, her A1C is 8.9.

- A. You suggest adding Acarbose, the only oral agent, actually there is another med for sitagliptin now and I didn't change that, so I'm sorry about that. Adding Acarbose.
- B. Starting Detemir BID with TID Lispro.
- C. Getting her an appointment with a nutritionist and exercise counselor to see if she could do some lifestyle changes.
- D. Starting 70/30 at a dose of six units twice a day with breakfast and supper and helping her adjust according to an algorithm.
- E. Or you could start Byetta.

So, you want to think about those. Acarbose would probably not get her A1C down to targets. So that would be another oral medication and she would probably still have A1Cs that are high. She's young, it's early in the course of her illness and you want to keep her blood sugars well controlled, definitely not 7 or above. She is a patient in whom tighter control would be most advantageous. So Acarbose alone wouldn't do it. And just as an aside, when patients are on Acarbose if they're taking something else that would make their sugar too low like a sulfonylurea, if they do go too low, they have to take glucose, pure glucose tablets because remember Acarbose stops the cleavage of disaccharides. So

that even if the glucose is part of the molecule like in sucrose they wouldn't be able to get at it because that disaccharide wouldn't be cleaved. So you know that treating with a lot of the other things we commonly use, crackers, things like that, would not work and I looked to find a list of what kinds of food you can use and I just really could not find it anywhere. So I'm not a huge fan of that type of medication.

She is already active. I cannot imagine her eating better or exercising more. So I don't see how we get her A1C down much. I didn't put in the initial statement but she is not overweight. Exenatide can decrease the A1C by about 1%, so it would get you close, but she's not overweight. And in general, the only time we use that type of therapy is when the unique benefit of decreased appetite and weight loss would be worth the expense of the Exenatide and she doesn't fit that category.

This is just a reminder that we really want to use the simplest thing that works. So I've just mentioned this trial here, the 2009 trial, where they did get good glucose control, starting with 70/30 insulin, six units, 15 minutes before breakfast and supper. You can start them on a different dose if you have reason to believe they'll be very insulin resistant which many of our patients are. In the study, the patients ate three meals a day, which is exactly what she is doing and they check their sugars before breakfast and supper, and made their adjustments. Now also this would be the scale you would give the patients. And I usually have them change a dose every two to three days, not day-to-day, just so they can get a pattern. So I would ask my patient to titrate the breakfast dose of 70/30 based on what her pre-supper sugars are, every two to three days and then either at the same time or later ask her to titrate the supper dose based on the fasting sugars every two to three days.

I'm sure you know how confusing this concept is. When somebody wakes up and their sugar is 253, they're going to want to increase their morning dose of insulin. They are not going to want to wait until evening to increase their supertime dose of insulin, so that it will impact on their fasting sugars.

I finally came up with a way that I think works to explain this to patients. What if you had someone -- you worked in the kitchen or a restaurant or something and you had somebody come in to wash the dishes at midnight, from midnight to 12 noon and then you had someone else come in from 12 noon to 12 midnight?

Well, if at 12 noon, there was a whole pile of dishes that hadn't been washed, you wouldn't tell the person just coming in that they needed to work faster or that they weren't doing their job. You would have to tell the person who is coming off schedule that when they got there again for their midnight shift, they have to work faster and get all those things washed. So you wouldn't punish or change a work activity of somebody whose work wasn't being assessed during the time you were checking. So actually as I say that, I think that that might be just as confusing, but you've got to come up with something.

Now another question, we put her on 70/30, she is titrating. What would we do about her oral agents?

- A. Do you want to stop all the orals?
- B. Do you want to continue all the orals?
- C. Do you want to stop half of them? Just do it at random or throw the bottles up in the air or whatever.
- D. Or stop Sitagliptin because it's non-formulary and expensive. Continue Metformin and Pioglitazone and stop Glimepirid, because it could increase the risk of hypoglycemia.

Okay, we'll go through what decision we made. So D would be my suggestion. Now there is actually, as an aside with Glimepiride, you can use that as a prandial or mealtime treatment along with the long-lasting insulin such as Glargine or Detemir. So if you gave Detemir or Glargine to control the basal sugars and gave Glimepiride with breakfast and supper, you might be able to get their postprandial glucoses into a good range.

So actually that could be an option. But in general when I start someone on insulin, even though the data have shown there is really no one, no particular regimen that's any better than any other, I usually start them on a mixed prandial basal insulin. But you could consider using Glimepiride as your prandial medication. If the person had insurance, you could use one of the drugs like Prandin, which is just very focused and will give you a little squirt of insulin right when you're eating. So using that with the basal insulin might actually be a good choice and decrease the number of injections they can take, but for some reason it has just not gone generic and it costs a lot.

Okay, so she comes back to your office. She started the 70/30. She's made the adjustments. She's taking 32 units with breakfast and 22 units with supper. Her fasting sugars and her before supper sugars are great. They are right exactly where you want them. And she's not having any low sugars during the day. It just so happens that she came in for a mid-morning visit and when she was being put in the room, her sugar was checked and her post-breakfast glucose is 278. When she sees that, she reports to you that she sometimes checks her sugar after breakfast and supper and it's always up in the 200s or sometimes a little higher depending upon what she has eaten, but she doesn't worry about it because it comes back down at the time that she's been directed to check her sugars, so she's thought maybe that was okay.

So your best strategy would be to:

- A. Accuse her eating too much carbohydrate and send her to the nutritionist;
- B. Tell her that she was not asked to check her sugars after meals and that's what happens when you don't follow directions. Refer her to behavioral health, to help with her adherence to the directions her provider gives her;
- C. Ask your nurse to show her how to mix a little bit of rapid insulin such as Aspart with the 70/30 and have her add eight units of the Aspart to her current dose of 70/30. So you'd be giving her a little more prandial insulin; or
- D. Submit non-formulary request.

So what do you think? I think options A and B are probably not a good idea. She's already eating and exercising well. So I would not choose those. Remember that there are data suggesting the postprandial glucoses are as important, possibly more important, and may correlate more closely with vascular disease, than pre-prandial readings. In the article about using the 70/30 titration, he suggested that it was unnecessary to focus on the postprandial glucoses, that they did not check them and they still were able to get normal A1Cs.

70/30 insulin is manufactured as a combination because most people need about 70% NPH and about 30% mealtime coverage or 75/25, that's in general the most common ratio. But there is no way to adjust her 70/30 to decrease her postprandial sugars without making her go low in the morning and before supper. If you increase her morning dose, so she's not so high after breakfast; she is going to be really low before supper.

Remember, going back to the time when we were actually diagnosing the person with diabetes, some patients will have impaired fasting glucose, some patients will have impaired glucose tolerance, so that there are some people who can handle their fasting, handle sugar, and so they're fasting, and non-eating glucoses are normal, but every time they eat, it goes up.

There are other people who can handle food, you don't see much of an excursion, but they wake up in the morning with a high sugar. So you are going to have to deal with this type of problem periodically where you get one normalized, and the other one gives you trouble.

So I would submit non-formulary request here for 50/50 insulin which shockingly enough is a mixture of 50% NPH and 50% of a prandial insulin, short acting insulin. And I would predict that in a patient like Ms. C that proportion, that mixture of insulin, would take care of her problem. She'd get more prandial

coverage than she's getting with the 70/30 and that probably would straighten out her sugars and then she can just -- actually, she's not using the algorithm anymore since her 70/30 is perfect. So unless this has done earlier in the game. If it were done earlier she could use the titration algorithm.

Now some patients may need something at lunch. In the morning the 70/30 might -- the NPH peak might - just not be enough to take care of her lunch time. So if that's the case they may need either a shot of regular or NovoLog or Humalog at lunchtime or they may need another shot of 70/30 or 50/50 at lunchtime. The only way to know is to have her check of sugars and see what's she is doing, okay.

A long acting basal insulin and rapid mealtime insulin is definitely the most physiological approach, other than an insulin pump. But it's cumbersome, it takes strong patient commitments to learn just to make carbohydrate content in the meals and inject multiple times during the day and check glucoses multiple times during the day. So you definitely have to weigh the benefits against the risks or the inconvenience or the impossibility of monitoring and injecting more frequently. Always remember, if it works, if the A1C is at goal, if her sugars are at goal then that's the regimen you should use. In studies, the basal and then mealtime injections always tends to give better control, but in real life having patients be able to do that oftentimes it just can't happen.

### **Case Study D**

Okay, last patient. DD is an active, 14-year-old honor student who has BMI of 54, she is 5'1" and she weighs 285 pounds. She has had diabetes for two years, although before that people had mentioned that she was borderline for several years. Her liver tests have been abnormal and she was recently sent for biopsy that showed extensive fatty infiltration and one area with early cirrhosis. She also has hypertension and hyperlipidemia.

She does not wake during the night to eat. She has missed meals without becoming sick or shaky or feeling like she has to eat. She did not appear to be Cushingoid and at some point in her life her mom had been told she did not have Prader Willi. Just to go over that a little bit. Waking up during the night to eat and having a low sugar, if she goes for a long time without eating. Those could clue you in to a patient having problem with their insulin production, with -- even perhaps an insulinoma, in someone who is not already on insulin and may be the kids just eating to feed the insulin they are making, although now that I say that, that's not, certainly not as common in someone who has diabetes.

But I wanted to make the point that in a patient who is gaining weight, it's always a good idea to find out if they have -- if they are driven to eat and eat to feed their insulin, not to ever forget to think of insulinoma. But that doesn't really apply in this patient. Always, always, always think Cushing's disease and Acromegaly or in a child Cushing's syndrome and Gigantism. Both growth hormone and cortisol will antagonize insulin effects. So in any person with diabetes who walks into the office, you don't need to do a bunch of tests but you need to at least look at the patient and rule out Cushing's or growth hormone excess as contributing.

Okay, she was a large child when she was born and she continue to be large. Her A1C is 9.2, she has got a little albumin in her urine already. Her feet and her eyes are good. She Metformin and a lot of insulin, 50 units twice a day of Detemir and 25 units Lispro three times a day with meals. She is a very adherent to the schedule as much as a 12-year-old can be. When she comes in to see you and sees what her A1C is, she said that even though she wants a normal sugar, she's not going to take any more insulin because she gains weight every time she does.

The best option would be:

- A. To tell her yes she is going to take more insulin, 60 units twice a day and 30 of Lispro with meals. Register her for a kickboxing classes because even though she and her mom says she is active, you think she could be more active and tell her that insulin does not make her gain weight, which is what we usually tell patients. That it's not the insulin, it's the loss of the

glycosuria that causes weight gain, as her sugars improve. But there really that is still an open question as to whether it does and how it does, okay.

- B. You could refer her for Bariatric surgery.
- C. You could refer her to a nutritionist and put her on a zero carbohydrate diet. Cut her insulin down and have her monitor carefully. And in most patients adhering to a zero carb diet, you will get them off of their insulin, when they're not eating carbs. When you get them back on carbs, they will not need as much insulin as they did before they had that carb-free week and so you can titrate up more slowly.

It's hard to believe I had a patient last week who is on close to 200 units a day of insulin. We took away carbs; by the second day she was getting hypoglycemic even though she had cut her dose down to a quarter of what she had been taking before. So she stopped her insulin altogether, when she saw us a week later, her sugars were almost always below a hundred. We put her on a -- we then put her back on carbohydrates emphasizing that carbohydrates should not be eliminated from the diet. It's a nifty way to try and get her to be more sensitive to insulin but it's not good in the long run. So we are able to take her off the u-500 that she had been taking and just have her on a little bit of 70/30, and hope that she'll adhere to the 45 grams carbohydrate per meal regimen that we gave her. Okay.

- D. Or you could start U-500, a concentrated insulin twice a day.
- E. Or you could refer her for deep brain stimulation.

Now in the past we probably would've just given her more insulin and told her that we don't believe her and then she is really, probably not exercising and eating well. But this kid at age 12 has major serious health problems and you need to address them now, rather than just piling on more medication.

Option B, would that be a good option? Probably in a few years we'll just be saying, can you believe they used to send patients for Bariatric surgery to get them to lose weight, can you believe that people would ever had to our resort to that. Research is going on now looking at the neurochemistry, the relationship between fat hormones, gut hormones, brain neurotransmitters, and once we figure out what causes people to be hungry and what causes people to feel full we should be able to turn that into some kind of medication that we would be able to use to help patients to eat in a different way.

I am a really, really strong believer that weight -- once weight, how one eats, when one eats is to a very large degree related to what is going on in their body chemistry, and that is a genetically determined issue. So I really believe that thinner people have different signals to eat and stop eating than heavier people do. That's why I think we have such abysmal success with diet and exercise.

Anyway, we are using Bariatric surgery a lot more often now because we can cure diabetes. We can -- better than any combination of medication, diet and exercise, the cure rate associated with Bariatric surgery is unquestionably higher. Now when I first gave this talk in April, I put this line in: "Bariatric surgery" and I wrote, has a greater chance of curing diabetes if it's performed early in the disease process. There are now some data coming out suggesting that perhaps we should not be doing surgery on people with the lower end of the approved BMI.

Perhaps we should be waiting later on -- waiting until they have a higher BMI. So I just really don't know what's the best time to send someone for a surgery and I don't think anybody does. I was really surprised to find out that the American Academy of Peds has listed Bariatric surgery as an option for morbidly obese adolescents since 2003. I had no idea that people were even considering Bariatric surgery in children or adolescents. So these are their criteria, BMI of greater than 40 with comorbidities greater than 50 without. So DD would fit that criterion. Status post six months of organized weight loss program and she has done that, she really has. Completion of the majority of skeletal maturity - greater than 13 years in most girls and greater than 15 in most boys. I did not look into that, I'm assuming that

you would look at their growth curve or do films of their hands, to see if the bones are fused, I'm not really sure how you determine that.

There are some major centers in the country that do this surgery. I subsequently found that they do it also at Duke in North Carolina and there may be others. I would not ask our adult Bariatric surgeons to do it in a child. I don't think they would want to perform the surgery in a child. I think this is -- if you're considering Bariatric surgery for our 51 BMI patient with lots of comorbidities. If you consider Bariatric surgery, I would get her into a pediatric Bariatric centre if at all possible.

Anyway, recent studies in JAMA looked at adolescents who had had gastric banding, after two years there was greater than 50% weight loss in 84% of the surgical patients and 12% of the lifestyle patients. So I actually think that's a really good result for the lifestyle patients. A lot of times we don't achieve that much weight loss. So I'm impressed with that statistic, although clearly the Bariatric surgery was better. The mean weight loss with 76 pounds in the surgery group compared with 6.6 pounds in the control group.

Another article looked at adolescents who had had either gastric bypass or routine management and again most of the patients had remission of their diabetes. They lost 34% of their average body weight and none in the routine management group. Well, I guess in this article none lost weight and none had a cure of their diabetes.

In 2007, Archives of Peds, they found that adolescents undergoing any type of Bariatric surgery have fewer complications than adults. There are no good statistics of morbidity or mortality in children or adolescents. We just don't know what they are, but we do know that they do better in terms of their postoperative complications. So that's good to know.

Another, there is nothing in life is simple, that's another lesson that I learn everyday. Now there is -- we are seeing a plateauing of the effect in kids, sooner than we do in adults. In anywhere from a year to two years, in that range we see a plateau. Even though the weight loss is excellent and they do not regain the weight, they may not lose as high percentage of body weight as people do, as adults do, although in this study they did lose a good amount.

Okay, so you can just look at these in the slides that you have. There definitely are adverse events. There were no deaths but there are definitely more side effects. Revisional surgery was necessary in the patients who had had the gastric bypass and actually looking back that was 2007. So I would suspect that in 2010 those numbers would be lower. Okay.

In Diabetes Care Supplement this is data for adults just to show you what the 30-day mortality is, with restrictive or bypass procedures, and those numbers are comparable to what you see in procedures like, cholecystectomy, appendectomy, hip replacement, knee replacement. That's the kind of numbers that we are seeing, and you can look at all that stuff. The last part about decrease in all cause mortality, those numbers are very strong and reproducible. Now of course if they are not dying of kidney disease, diabetes, cardiac disease or cancer disease, they have to die of something. So they will die of other causes more often. Accidents, collagen vascular disease, whatever; their suicide rate is lower. I didn't include that.

This is just what I talked about very briefly. I would never ever, ever do this without reading about it, speaking to people who have done it, working closely with your nutritionist and diabetes educators so that everyone understands what you're doing, what the diet consists of, what the goals are and why it works. Make sure that she understands, and this is just a review. Make sure they understand that carbs are important, but get them when you do reintroduce them to carbs, get them on good carbs, not the low fiber processed carbs.

U500 insulin, I'll just briefly talk about that. We use this a fair amount. It's five times as concentrated as any other insulin. Every other insulin you use is U-100, a hundred units per mL. This is 500 units per mL. We use standard insulin syringe and when we talk about doses how much are they taking. We talk about the volume that's in the syringe. So when we say they are taking 50 units that means they're pulling in the U-500 to the 50 mark on standard syringe. Even though we all know that when they're taking -- when you pull that U-500 to the 50 unit mark it's really 250 units of actual insulin medication.

When high volumes are injected, absorption can be uneven; the insulin can become degraded, sequestered. Studies have shown that injecting insulin in a smaller volume helps to solve this problem. So when you're giving people 100 units a couple of times a day or 150 units, they are probably not getting that amount of insulin and you really have no idea how much they're getting. It acts kind of like 70/30, not exactly. You take it about a half-hour before you eat. It is often able to cover the post meal rise in glucose as well as the pre-meal glucose at the other end, lasts for about eight to ten hours. We generally start out twice a day, if you're getting to higher doses and again your worried about volumes if someone is taking 40 units twice a day, I probably split it into three or even four times a day. And there is literature on this. If you Google U-500 or better yet go to *PubMed* U-500, you can find lots of stuff about this.

I have recently started -- and this is how you calculate the dose. It's not magic, you divide the number of units that the patient is currently taking by 5, that tells you how much to pull into the syringe, divide that by two, because you're going to give it as two doses. And you may want to give her a lower starting dose than what she is now taking, because you'll guarantee that all that insulin will be absorbed. Whereas, the patient may not have been absorbing what they were currently taking. I used to do this a lot. Now, I generally do not. I give them the equivalent of what they are taking and move on from there.

And then you would have her inject it, give her a schedule for titrating, and again I have started doing this more-and-more, putting them on a zero carb diet to see if they actually use, need U-500. And I have done that partially in deference to the economics of the pharmacy U-500. Although unit per unit, it's not more expensive. A vial of U-500 is expensive. So that maybe something to think of.

As they are gathering their coats, the mom mentioned that DD's grades have been slipping, and at the recent conference found out that DD falls asleep in class a lot. So you should tell your mom that

- A. Adolescence do this all the time and don't worry;
- B. You should start Prozac;
- C. Order sleep study;
- D. Order bunch of labs; or
- E. Ask a few questions.

And the hint is, whenever it says, ask a few questions or check a few labs, those are the right answers. There are a zillion reasons why that child may be sleeping in class or and have grades that are sleeping. But you need to ask her about anything that could cause those symptoms and the differential diagnosis as you see here is huge - anemia, hypothyroidism. Maybe she is up all night because she is peeing so much because of glycosuria. Maybe she is sleeping with three other people, one of whom watches TV all night. I had a child who had bedbugs, that I found out about. It was probably the third time she told me about having trouble sleeping at night, that I asked the right question that she did in fact have bedbugs. I know that because she brought one in and showed it to me. And I would get the lab test to rule out other metabolic conditions that could be causing her to be tired and sleeping poorly. I definitely would ask about sleep apnea. It is so much more common than we realize.

When I looked in her mouth, which I had not done for quite a while, I noticed that her tonsils are huge and so I did refer this patient for a sleep study, and ENT consultation. She did have actually her tonsils taken out, and her sleep apnea after that was extremely mild, and we actually are not using CPAP for her.

Anyway, okay, so you talk about all this with the mom, you ask all the questions and as you're turning the knobs to get out of the room, you're running late, her mom mentions that a younger child GG is getting chubby and she wonders if there is any way to prevent her from ending up like DD. So you:

- A. Throw your stethoscope across the room and say, I don't have time to deal with this now, you need to ask all your questions at the beginning of the visit, and stomp out of room.
- B. Tell her don't worry. You will deal with GG when she shows up in your office with diabetes.
- C. Suggest she start a little bit of medication.
- D. Refer her for a nutrition visit and suggest buying a jungle gym.
- E. Burst into tears and say, I don't know what to tell you, then throw your stethoscope across the room and stomp out, or
- F. Say that's an excellent question. Several studies have looked at diabetes prevention. We're in the process of talking with anyone involved in care and what we could do to help improve diet and exercise, options to make healthier food more available, less expensive.

And just in closing, diabetes care is unbelievably complicated. If you have heard me say some things that you have not done or thought of or heard of, then it's only because diabetes is really complicated and I've done that for a good long time. And so I have seen a lot of things and have tried things, read about things, but it is [complicated] and you'll never know exactly what people are doing because it keeps changing all the time. There's no algorithm, meds are expensive, sticking fingers is not fun, food is expensive, prescriptions are expensive. Plus new studies keep coming out and tell us that what we used to do, we don't have to do anymore.

But it's what we do. We're stimulated by the challenges, we are motivated by our patients who are strong, and resilient, and share their lives with us in some of the most amazingly beautiful places in the world. I'm now in the Smoky Mountains in Cherokee. I left New Mexico and beautiful Sandia Mountains and the mesas and the desert landscape and it's an honor and a privilege for which I am thankful every day.