Diagnosing and Managing Diabetic Ketoacidosis, Hyperglycemic Hyperosmolar State, and Hypoglycemia

FACULTY SLIDE REVIEW

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Slide 1 – Title Slide
**Guillermo E. Umpierrez, MD, FACP, FACE:** This presentation is just to provide you with some guidance on why we put together the slide set on hyperglycemic emergencies and then hypoglycemia. I will review the first section of hyperglycemic emergencies that will cover both DKA and hyperglycemic hyperosmolar state.

Slide 2 – CME Information

Slide 3 – Disclosures

Slide 4 – Educational Objectives

Slide 5 – Slide 8 – Pre-activity Questions

Slide 9 - Hyperglycemic Emergencies: DKA and Hyperglycemic Hyperosmolar

Slide 10 - Hyperglycemic Crises
Background information on hyperglycemic crises. DKA is the most common hyperglycemic emergency, both as seen in patients with type 1 and type 2 diabetes. It’s relatively frequent. It’s about 4% to 9% of all the patients who are admitted with the diagnosis – the primary diagnosis of diabetes are being reported to have DKA. In the United States, it is estimated that it’s about 135,000 cases of DKA. And mortality rate is being quite low. I will present more data in the next few slides, but, in general, it’s about 2%.

In contrast, hyperglycemic hyperosmolar state is less common. It's approximately 1% or less of all patients admitted with the diagnosis of diabetes, but the mortality rate is 10 to 15 times higher than those patients with DKA.

Slide 11 - DKA Incidence from NHDS
The slide shows the incidence of DKA according to the National Hospital Discharge Survey in 2011, and you see that the prevalence has been going up despite DKA being a preventable disorder and treatable with insulin therapy. It’s 535,000 cases.

Slide 12 - Type 1 Diabetes Accounts for the Majority of Primary DKA Episodes
The next slide shows that that it is seen with both type 1 and type 2 diabetes. About one-third of all the cases with DKA have known to have type 2 diabetes, and two-third has type 1 diabetes. In contrast to general beliefs, DKA in type 1 diabetes is more common in adults than in children. Although, 40 percent of cases of DKA are children, a little less than 20% have type 1 diabetes.. There is much more people with type 1 diabetes as an adult. So it is important to make the point
that this is a disease not only in type 1 diabetes but also in type 2 diabetes, and is seen both in adults and in children.

**Slide 13 - DKA-related Mortality Rates Have Been in Decline Since the 90s**

Next slide is related to mortality, and this is data from the Centers for Disease Controls. the mortality rate of DKA has continuously decreased. Before the discovery of insulin, mortality was close to 95% to 100% of patients. Right now, mortality has decreased to less than 1% of the cases of mortality in this country. It is important to keep in mind that, in other countries, especially those countries or sites that don’t have good protocols or good standard of care, mortality is still above 10% to 15%.

**Slide 14 - Pathogenesis of Hyperglycemic Crises**

Regarding the pathogenesis, it’s a combination of both insulin deficiency and increased counterregulatory hormones. And both lack of insulin and counterregulatory hormones increase lipolysis, generation of ketone bodies, increase free fatty acid circulations, and the accumulation of free fatty acids in metabolic acidosis. We should talk also about the importance of hyperglycemia when using osmotic diuresis, dehydration further increasing counterregulatory hormones, and the role of increased catecholamines suppressing insulin release from the beta cells.

**Slide 15 - Diagnostic Criteria for DKA and HHS**

This is the diagnostic criteria of DKA and hyperosmolar defined at the American Diabetes Association, which defines DKA arbitrarily in mild, moderate, and severe. Diagnosis is “plasma glucose greater than 250”. This has come under criticism by the UK Guidelines which suggest that the diagnosis should be at a lower glucose level in order to diagnose these near-normal glycemia DKA that have been present in about 10% to 15% of patients.

The severity of DKA relates to the severity of acid-based disorders and metabolic acidosis. And we define: “mild” as those who have a pH between 7.25 to 3, bicarbonate – 15 to 18; “moderate” -- pH – 7 to 7.24, bicarbonate – 10 to 15; and “severe” – a pH less than 7, bicarbonate less than 10. The diagnosis of DKA – the hallmark is the presence of ketones, and this could be measured both in plasma or serum or in urine, and they are just positive. The diagnosis of DKA measured by beta hydroxybutyrate or serum ketone is greater than 3 mmol/L. The average beta hydroxybutyrate in a patient with DKA ranges between 5 to 9 in multiple series. It is important to keep in mind that urine ketones is highly sensitive you measure acetoacetate and also beta hydroxybutyrate. It is better to measure beta hydroxybutyrate in plasma called samples or by fingersticks, or by the laboratory because it correlates not only with severity of metabolic acidosis but also with resolution of DKA.

The diagnostic criteria for hyperosmolarity is a glucose greater than 600, a pH greater than 7.3, and bicarbonate that is usually greater than 18, but it can be to 15 to 18.

The criteria for serum osmolality, for a patient with hyperosmolar syndrome is variable but usually elevated in patients with DKA.

The altered sensorium – again, this is arbitrary definition by the American Diabetes Association but, in general, it is seen in those patients who have severe DKA, and those who have hyperosmolar syndrom with stupor or coma.

For many years, metabolic acidosis was not thought to be related to severity of reduction in pH and bicarbonate, but there are a couple of recent reports that not only points to the importance of osmolality but also severity of acidosis with altered sensoria.
About one-third of patients with HHS have a combination of DKA and hyperosmolar, so it’s not a clear-cut differentiation you have DKA or hyperosmolar; patients can combine with ketosis and hyperosmolality. Those patients are going to have higher ketones and higher osmolality, and have poorer outcomes compared to those who have simple or mild DKA.

**Slide 16 - Useful Formulas for the Evaluation of DKA**
The next slide is to review the importance of certain formulas. First the anion gap is sodium minus chloride/bicarbonate. Normal is less than 12. It is important to keep in mind that patients with DKA have metabolic acidosis, so most patients have an anion gap greater than 16. However, there is subset of people -- those who are very dehydrated -- that may present with lower anion gap. In the presence of a normal anion gap, other causes of normal anion gap metabolic acidosis should be established.

The other equation is total osmolality versus effective general osmolality. Traditionally, the osmolality has been calculated with total serum osmolality that is sodium times two plus glucose over 18, plus BUN over 2.8. In recent years, we are using effective serum osmolality, not taking into consideration BUN or urea.

**Slide 17 - Case Study**
The next slide shows just a case, a typical case presented with DKA you can review. This is a recent case that I saw in the hospital.

The cell count shows that he has leukocytosis, he is hyponatremic, hyperkalemic and has increased anion gap, metabolic acidosis and a glucose of 636, and the pH of 7.18, with markedly elevated beta hydroxybutyrate to 8.7 mmol/L. And as the hallmark for DKA is the presence of ketones, this patient has a urinalysis with positive ketones.

**Slide 18 - Precipitating Causes for DKA and HHS**
The precipitating causes of DKA varies. All around the world, infections and lack of adherence with insulin therapy are the most common causes of diabetic ketoacidosis. In our institution, about one-fourth of the patient have an infections, or about 50% to 60% of patients with type 1 diabetes have poor adherence with insulin therapy. Discontinuation of insulin therapy in inner-city hospital is the number-one cause of diabetic ketoacidosis.

It’s reported that 10% to 20% of adults have newly diagnosed diabetes at presentation. In children, up to 40% of newly diagnosed diabetes present with diabetic ketoacidosis.

**Slide 19 – Euglycemic Diabetic Ketoacidosis: A Potential Complication of Treatment with Sodium-Glucose Co-transporter 2 Inhibition**
The next slide shows a very interesting phenomenon, I think first described by Dr. Peters who is a co-chair for this program. She reported an increased prevalence of euglycemia diabetic ketoacidosis in patients with type 1 and type 2 diabetes treated with a new sodium-glucose co-transporting SGLT2 inhibitors.

And of interest is that these patients first present with mild-to-moderate hyperglycemia because the medication works by increasing glucose excretions in the urine. Up to 10% to 11% of patients with type 1, who are treated with SGLT2 or co-treated with insulin plus SGLT2, may develop some ketosis.

The incidence of SGLT2-associated diabetic ketoacidosis in type 2 diabetes is not very common; it’s rare but there are a few cases reported. There are over 20 cases by the FDA, and
there are over 100 cases where the European agencies reported patient with DKAs treated with SGLT2 and insulin combination. Most of these patients have a precipitating cause.

**Slide 20 - SGLT2-I and Risk of Ketoacidosis in T1D Potential Mechanisms**

The next slide is a review paper by Dr. Taylor in *JCE&M* in 2015, about the potential mechanisms involved. This is not a mandatory slide but this is an interesting point, just for your knowledge in case you're being asked and not aware of this.

So the mechanisms are really not clear, but it's likely a combination of reduced doses of insulin, increased concentration of glucagon, and increased ketone body reabsorption from the kidneys in patients with precipitating cause.

First because the patient produced glucosuria, blood glucose is significantly reduced. The insulin dose is usually reduced, which increases the chances to have increased lipolysis. In addition, the SGLT2 has been associated with increased production of glucagon by the alpha cells. The combination of decreased insulin (patients with type 1, and also because you reduce the dose of insulin) and increase glucagon. Increase the activity of the carnitine palmitoyltransferase, or CPT1, increasing ketone bodies.

**Slide 21 – Polling Question**

**Slide 22 - Clinical Presentation of DKA**

This slide just shows the most common symptoms and signs of patients presenting with diabetic ketoacidosis, of course, due to the presence of: hyperglycemia, patients develop polyuria, polydipsia, weight loss, weakness due to dehydration of electrolyte abnormalities, gastrointestinal symptoms, as in the patient that I presented to you, are seen in about 50% to 70% of patients but always present a diagnostic challenge. Usually, these symptoms go away with treatment.

Hypothermia is very common. Tachycardia and tachypnea are also very common, especially with Kussmaul breathing. Kussmaul, in the year 1874, described the sign of deep inspiration and expirations in patient with DKA. It’s a very important clue for the patient with hyperglycemia Kussmaul breathing on deep inspiration/expiration is an alert for diabetic ketoacidosis.

The presence of acetone breath is important, and altered sensorium that is part of the criteria for us diagnosing severity of DKA.

**Slide 23 - Mental Status at Presentation in DKA**

Next slide shows the importance of altered sensorium. Before the year 2001, the DKA was considered a diabetic coma. But, of course, we don’t use “diabetic coma” because only 13% of people with DKA and less than 25% of patients with hyperosmolar syndrome present with coma. Most people are alert or mildly lethargic.

The abnormalities in the level of consciousness correlates with a severity of hyperosmolality. Most people who have osmolarity less than 300 are alert. Those people with osmolarity greater than 320 are stuporous or present in deep coma. The important point of these slides is that, if you see a patient with DKA or a patient with diabetes who has hyperglycemia, and the osmolality is less than 320, and presented with coma, other causes of altered mental status need to be ruled out.

**Slide 24 – Polling Question**
Slide 25 - Initial Laboratory Studies
Everybody admitted to the hospital should get a blood glucose. Those patients who have confirmed hyperglycemia, with or without additional symptoms, who are breathing fast, who have clinical features of DKA should have beta hydroxybutyrate done or ketone bodies determined in the urine, or beta hydroxybutyrate in the plasma or urine.

The best diagnostic criteria is the combination of hyperglycemia and possibly ketones. Usually, CMP takes some time, but you get it in about a couple hours. So the ADA recommends pH, CBC. (Most people have leukocytosis). The CMP, serum or urine ketones. Bacterial and cardiac enzymes should be done as clinically indicated.

Slide 26 - Blood β-OHB Levels in DKA Detection and Treatment
This slide just reminds us about the importance of beta hydroxybutyrate as the hallmark for the diagnosis. A normal beta hydroxybutyrate depends on the duration of fasting, but it’s usually less than 0.5; if increased to a level greater than 3 the diagnosis is definitive. And it is important for the treatment. The group at the Mayo Clinic has reported a couple of years ago that these patients needs to get urgent medical care, with insulin and fluid.

Slide 27 - Managing Hyperglycemic Emergencies
The management of hyperglycemic emergency is the last section that I will cover.

Slide 28 - Management of DKA
The basic criterias are replacement of fluid losses. And Correction of hyperglycemia and metabolic acidosis with the combination of insulin that can be given intravenously, intramuscularly, or subcutaneously.

It is important to keep in mind electrolyte losses, especially potassium in these patients. We need to think about what was the precipitating cause and address any infections and/or comorbidities.

The final point is whether to consider the transition from intensive therapy, usually IV, to subcutaneous maintenance therapy in order to prevent recurrence of admissions or recurrence of diabetic ketoacidosis.

Slide 29 - Fluid Therapy in DKA
Everybody with DKA had a deficit of about 80 to 100 milliliters per kilogram, so it is somewhere about 7 to 10 liters of IV or fluids, and it should be replaced. We usually give the first one or two liters wide open, somewhere about 500 mLs. And you shouldn’t be concerned about too much fluid except for those who have a history of congestive heart failure or chronic kidney disease on hemodialysis or dialysis therapy.

Now, in general, most people got 100 to 1,000 mLs during their first hour or two, and then you continue this with normal saline or half-normal saline. And there has been a debate in the literature if you should continue with normal saline or not.

It is important to keep in mind that, if you give normal saline, patients are going to go from a high anion gap to a normal anion gap metabolic acidosis, which is not associated with poor outcomes, but it may have a role in the resolution of bicarbonate that may be longer in those patients.
In our institution, we give to almost everybody normal saline, one or two liters. We switch them to half-normal saline, and we continue this until the blood glucose is lower than 250. The average time it takes is somewhere around four to six hours.

At that time, you change to dextrose-containing solutions. We usually give D5 normal, D5 half-normal saline, and we continue this until resolution of ketoacidosis.

Giving dextrose is a crucial step because it will allow you to continue to give infused insulin. Resolution of hyperglycemia takes four to six hours where resolution of DKA takes usually more than 10 hours. So dextrose reduces the risk of hypoglycemia.

**Slide 30 - Intravenous Insulin Therapy in DKA**
The next slide is about intravenous insulin therapy. IV insulin has been the hallmark and the mainstay of therapy of patients with DKA. And, since 1971 and 1973, we have been using a low-dosing in an infusion. Before the 1970s, we used to give 4- or 500 units per day for the resolution of DKA. Currently, the total dose of insulin is somewhere around 80 to 90 units for the whole treatment – the acute treatment of ketoacidosis.

You give an IV bolus of 0.1 units per kilo, and continue the drip for 0.1 units per kilo until the blood glucose is 250. At that time, you reduce the dose to 0.05 units per kilo, and you adjust until the resolution of DKA. Again, you need very little insulin once the glucose has been corrected. So doses of 2 to 4 units per hour is more than enough for most people to resolve ketoacidosis once the glucose is less than 250.

There is a chance, though I've very seldom seen this, that some people do not respond to insulin therapy. They may be very insulin-resistant. I believe that the best way to resolve insulin resistance in these patients is good fluid challenge, decreasing the concentration of counter-regulatory hormones in people who do not require high insulin doses. In some patients, you may not need the higher insulin doses at the beginning.

The other thing is the use of IV boluses. You don’t need an IV bolus if you start, with 0.15 or 0.14 units per hour instead of 0.1. A paper published from the University of Tennessee several years ago, suggested that the bolus is not needed in most people.

**Slide 31 - Studies Comparing SC Injections of Lispro vs Continuous Infusion of Regular insulin in DKA**
Another area is the use of subcutaneous insulin with rapid insulin analogs. There are several studies that are shown in this table, that the use of subcutaneous rapid insulin analogs are as effective as continuous IV insulin infusions in patients with mild to moderate uncomplicated DKA.

There are papers published in this area; one of those papers was published in *Diabetes Care* now a few years ago, that shows that subcutaneous aspart -- given one every hour, every two hours is as good as IV insulin infusions. Of interest, these people treated with subcutaneous insulin can be treated in the emergency room, and the duration of hospitalization is shorter.

If you look at the outcome of these patients the resolution of hyperglycemia, bicarbonate, venous pH, beta hydroxybutyrate, and concentration of free fatty acids was not significant difference if given every hour to two hours for IV regular insulin.
Subcu insulin with rapid insulin analog maybe as good in those patients with uncomplicated DKA. In many countries outside the United States and underdeveloped countries, they are using more subcutaneous insulin than IV insulin.

Slide 32 - Potassium Replacement and Bicarbonate Therapy in DKA
Potassium replacement is key. Potassium usually drops because it goes from the outside to inside the cell when insulin infusion is instituted, and acidosis on hyperosmolarity results. The drop in serum potassium is about 0.8 to 1 milliequivalent or mmol/L during treatment; in some people, it’s even more. If a patient present with hypokalemia, potassium can drop to dangerous levels that could dictate an arrhythmias if you’re starting an insulin infusion. So keep in mind we’re trying to keep the potassium between 4 to 5.

Some patients present with hyperkalemia. At the beginning, if it is greater than 5, 5.5, hold the insulin. At 5.5, they don’t need potassium; just give the insulin and fluids. And once the potassium drops below 5, you can start giving 20 to 40 mEq/L of potassium chloride to each fluid, to each liter of fluid, and that usually keeps the potassium between 4 and 5.

Bicarbonate is very seldom used in my institution. Maybe an exception would be those who have severe metabolic acidosis with pH less than 6.9, 7. Multiple studies have shown, that bicarbonate doesn’t change much the outcomes of these patients. Similarly, phosphorus is very seldom given except when the phosphorus is less than 1. You can give these patients skim milk, who has high concentration of phosphorus instead of IV phosphorus. Keep in mind that you may precipitate hypocalcemia with phosphorus.

Slide 33 - Management after Resolution of DKA
Next slide talks about the management after the resolution of DKA. The patient with DKA should be treated with IV insulin, of course, or with IV insulin subcutaneous intensive therapy until the glucose is controlled to less than 250, bicarbonate levels are equal or greater than 18, (and some people say it’s greater than 15); pH more than 7.3.

And the use of beta hydroxybutyrate or anion gap is controversial in people during treatment. In our institution, we follow the acid-base parameters, and beta hydroxybutyrate is measured at the beginning and whenever we get a slow resolution of acid-base disorders. The group at the Mayo Clinic, have shown that beta hydroxybutyrate is a good parameter to follow response to therapy.

Slide 34 - Transition to Subcutaneous Insulin after Resolution of DKA
Next slide is a transition to subcutaneous insulin after resolution of DKA – this is very important. You have to give subcutaneous insulin at least two to four hours before you stop the IV drip. This is the only way to prevent patients to have recurrence of diabetic ketoacidosis.

Slide 35 - Summary
And this slide is the summary statements: one, DKA and hyperosmolar syndromes are both common and serious. There are extensive complications, and they are seen both in patients with type 1 and type 2 diabetes. Even though it’s a preventable complications, good education, strict surveillance of glucose, and aggressive diabetes management may prevent diabetic ketoacidosis and hyperosmolar syndrome, and may decrease the morbidity and mortality.

And finally, setting up good and appropriate protocol has shown to reduce complications and mortality. In this Country, more than 80% or 90% of the institutions have protocols and where mortality is less than 1%. Before the 1970s, mortality was about 15%, so the use of protocols has shown to reduce mortality of these complications.
Slide 36 - Hypoglycemic Emergencies: Hypoglycemia  
Anne Peters, MD, CDE: The second section is on hypoglycemic emergencies.

Slide 37 – Definitions: Hypoglycemia  
And the first two slides go through the definition of “hypoglycemia.” And these are the basic definitions supplied by the International Hypoglycemia Study Group, which just published their findings in *Diabetes Care* last year. It’s important, in part, to review this because definitions of hypoglycemia vary.

First and foremost, is the concept of “severe hypoglycemia,” and this is hypoglycemia that requires assistance. Part of the difficulty of this definition has come from whether it requires that somebody is unconscious or having a seizure and a coma. We certainly don’t need it to mean that somebody is too lazy to get up and get the juice, and asks their family member for a carton of juice to treat a mild low, but I think it’s important to separate this kind of hypoglycemia that requires treatment from another, which is much more dangerous than the other type.

So the other definitions after severe hypoglycemia is the documented symptomatic hypoglycemic where somebody checks their blood sugar when they see a low.

Slide 38 - Definitions: Hypoglycemia (cont)  
On the next slide, asymptomatic hypoglycemia which we find a lot when we do continuous glucose tracings and see that people, and particularly older people, may have episodes of hypoglycemia they’re not aware of. We have probable symptomatic hypoglycemia where people feel low but don’t measure a blood sugar level. And then, finally, relative hypoglycemia, where people feel low even though their blood sugars are not low, and this often happens in people where their blood sugars have been higher, so they’re used to higher numbers and even getting it down a little bit feels abnormal.

Slide 39 – Rates of Hypoglycemia  
The next slide discusses rates of hypoglycemia. And, again, this is composite data from the International Hypoglycemia Study Group. Hypoglycemia is much more common in people with type 1 diabetes. There is an estimated rate of one to three episodes of severe hypoglycemia per year and in about a third of individuals with type 1 diabetes. Rates in insulin-treated people with type 2 diabetes are much lower.

Of course, it’s often hard to distinguish type 1 versus type 2, especially in older-onset patients, but suffice it to say is that being on insulin increases your risk and, if you’re a classic type 1, your risk of severe and mild hypoglycemia is higher than if you have type 2 diabetes.

And, finally, any insulin secretagogue, whether it’s sulfonylurea agent or a glinide, will increase the risk of hypoglycemia, and the longer-duration disease increases the risk for hypoglycemia of any sort.

Slide 40 - Hypoglycemia: Impact on Healthcare Resources  
The next slide and the following slide talk about the impact of hypoglycemia on healthcare resources. These episodes are distressing for the patient, and they are expensive.

Slide 41 - Economic Impact of Severe and Non-severe Hypoglycemia Episodes  
The next slide is a meta-analysis of sorts of the economic impact of severe and non-severe hypoglycemia events, looking at both direct costs and indirect costs.

Slide 42 – Case 1: Hypoglycemia
Slide 43 - Case 1: Hypoglycemia (cont)

Slide 44 - Case 1: Hypoglycemia (cont)
This shows continuous glucose monitoring over two weeks in this individual, each dotted line is one day. It’s a 24-hour period: the far-left being midnight, the middle being noon, and the far-right being midnight again. And what’s apparent in this tracing is this patient is having very frequent episodes of very low blood sugars, you can show how many of these blood sugars are below 70 and how many are below 50. Basically, she’s so low all the time and she’s so physically active that low is begetting low, and she is having episodes of severe lows.

Ideally, you would have her raise her blood sugars so she’s never below 100 for a two-week period of time, so she would begin to get her sensing of lows back. Now, in somebody like this, she’s obviously afraid of being high, so you’d want to work with her gradually. But both her overall dose of long-acting insulin as well as her mealtime doses are too much, because she’s going low both after meals as well as overnight, so she needs to have her total daily dose adjusted to bring up her sugars so she develops her sense of lows back again.

Slide 45 – Polling Question

Slide 46 - Intensive Control Increases the Risk of Severe Hypoglycemia
The next few slides talk about hypoglycemia, in particular severe hypoglycemia in people with type 2 diabetes. And what we’ve found from some of these large trials is that severe hypoglycemia occurs more often in patients in the intensively treated arm of these trials. A meta-analysis looking at 12 randomized-control trials and looks at the intensive arm and the relative risk of a variety of things, and the highest risk there at the bottom is an increased risk for severe hypoglycemia.

Slide 47 - Risk of CV Events and Death in Patients With vs Without Severe Hypoglycemia: (ADVANCE)
Data from the ADVANCE Trial, which looks at the risk of cardiovascular events and death in patients with versus without severe hypoglycemia. And you can see that having severe hypoglycemia increases the risk of: macrovascular events, death from any cause, death from cardiovascular causes, and all-cause mortality, death from non-cardiovascular causes.

Slide 48 - Summary of ACCORD, ADVANCE, VADT: Severe Hypoglycemia and Mortality Risk
The next slide, is a composite slide looking at rates of severe hypoglycemia in ACCORD, ADVANCE, and VADT. And it looks at annual mortality in patients who have had one or more episodes of severe hypoglycemia, and those are the yellow-orange bars, versus those who did not have an episode of severe hypoglycemia, and that’s depicted in the light blue bars. And what you see is that having an episode of severe hypoglycemia -- whether patients were in the intensively treated group or the standard therapy group -- increased the risk for annual mortality.

Now, this doesn’t necessarily say that having an episode of severe hypoglycemia causes an increased risk of death, but we do know that it’s associated with an increased risk for mortality. So it’s important to realize that, in our intensively treated type 2 patients, we’re going to increase their risk of severe hypos, and that’s going to increase the risk of mortality. So we need to be very judicious in how we have patients use insulin who have type 2 diabetes and really try to avoid these episodes of severe hypoglycemia.

Slide 49 – Polling Question
Slide 50 - Hypoglycemia Associated Autonomic Failure (HAAF)
Hypoglycemia associated autonomic failure, and that’s basically what the patient in the case previously has, is a state of being where patients induce a sort of tolerance to hypoglycemia. They no longer have the autonomic warning signals of hypoglycemia and, therefore, they can’t react to hypoglycemia and do something before it’s too late. And this is generally induced by antecedent hypoglycemia. It’s a clinical diagnosis, but the key to this is that it’s reversible, the autonomic nervous system can come back to life if the blood sugar levels are kept at a higher level, and patients could be trained to do this in order to restore their sensing of lows.

Slide 51 - Hypoglycemia Associated Autonomic Failure (HAAF)
The pathogenesis of the hypoglycemia associated autonomic failure, and you can see how this evolves and why patients end up with difficulty, because they develop both hypoglycemia unawareness and defective glucose counter-regulation.

Slide 52 - Management of Hypoglycemic Emergencies

Slide 53 Recommendations of the International Hypoglycemia Study Group
Starts the section on how to manage hypoglycemic emergencies. And, again, I go back to the International Hypoglycemia Study Group and go through what their recommendations are. The first and foremost part of this is that patients need to be educated about hypoglycemia, not only initially but recurrently. Every time I see a patient in clinic, I ask if they’ve had episodes of hypoglycemia. I characterize them as “mild” or “severe.” I try to look at precipitants for their hypoglycemic event, and then I make sure that patients are prepared for a hypoglycemic event, that they know how to treat it and what to do. And, oftentimes, particularly with my type 1 patients in clinic, I’ll have them show me that they have simple carbohydrates with them and then, if they don’t, reinforce the fact that they need to carry simple carbohydrates with them at all times.

Slide 54 - Recommendations of the International Hypoglycemia Study Group (cont)
The next slide talks about what happens if hypoglycemia becomes an issue, how we can: both educate patients, change their regimen, use agents that don’t cause hypoglycemia, use continuous glucose monitoring. I use continuous glucose monitoring as much as I can in my type 1s so that they can understand what their patterns are, and then I will use it episodically in type 2s to see if there are times when they’re going low and are not necessarily aware of it.

There are structured education programs to help patients deal with hypoglycemia. And then you need to reset the targets. So if a patient comes to you and wants to have their A1c below 6, and they’re having recurrent episodes of hypoglycemia, you need to work to educate the patients that their targets should be higher, perhaps 6.5 to 7, and reassure them about the balance between the risks of hypo- and hyperglycemia.

Slide 55 - Rule of 15 for Treating Hypoglycemia Guide for Patients
What I teach patients, which is the Rule of 15 for treating hypoglycemia. And you can read down this list you can teach the providers this but also show them that this is something they can print out and give to patients. I make sure that patients treat their lows with simple sugar and follow it up with some sort of carbohydrates and their protein so they don’t go recurrently low.

In these recommendations for treating lows, it discusses drinking water. And, at first I found that slightly curious, but I think what it does is it helps patients feel fuller and less likely to overeat, because many of my patients, when they’re low or at least having a mild low, use it as an opportunity to eat lots of carbohydrates, and then what happens is their blood sugars go high; then they respond to that high blood sugar by treating it with insulin, and they fall low again.
Slide 56 - Rule of 15 for Treating Hypoglycemia Guide for Patients
So you really want to have a balanced response for patients when they’re treating hypoglycemia. Hypoglycemia doesn’t feel good and it takes a while to resolve, so patients need to have a little bit of restraint in this setting so they don’t become hyperglycemic. Patients should recheck their blood sugars and also, if they eat more than 15 to 30 grams of carbs, they actually may need some insulin because, if they’re eating more carbohydrates than is necessary to treat the lows, you want to avoid that rebound high.

Slide 57 - Conclusions
And the final slide is the conclusion slide, talking about: who’s at risk, that mild is much more common than severe, that severe hypoglycemia is associated with an increased risk of mortality, that it’s important not to have patients develop hypoglycemia unawareness, and that we need to be aware of that so we can help patients reset their set point. And then I think it’s good to train patients as fully as possible as to how to prevent and treat hypoglycemia, as well as the need to be prepared for episodes of hypoglycemia if they happen to be on medications that can cause hypoglycemia.

Slide 58 - CME Credit Instructions