Module 3, Vignette 1, Pharmacokinetics and Pharmacodynamics of Ultra-rapid Insulins

Dhiren Patel, PharmD, CDE, BC-ADM, BCACP

What I'll do here is summarize a little bit regarding the PK/PD benefit as well as go into some of the safety and efficacy data of rapid-acting insulins (Note: see Vignette 2 for safety and efficacy data). In order to appreciate the features, I think it's important to understand where and how human insulin works. Human insulin, as you've seen throughout the modules, has a tendency to form hexamers in the pancreas during storage, which results in slow absorption into the circulation. And so when we talk about the second-generation insulins, you'll notice that there are different excipients that are used within the different preparations to help overcome this.

The modifications to affect the time-action profile of these insulins include a variety of different excipients or buffers, and what that does is change the absorption of the insulin, in these cases to be much quicker. I'll review some of those examples in a second, but I think it's important to also understand that the commercial rapid-acting insulin formulations contain a mixture of insulin hexamers, dimers, and monomers.

Only the monomeric form of insulin is active, and thus the dissociation from the hexamer to the monomer is rate limiting for the therapeutic action. The ultrafast insulin formulations primarily contain insulin monomers and no insulin hexamers for rapid insulin absorption.

On the market we now have various different formulations. Many of you may recall some of our first-generation rapid-acting insulins were insulin glulisine, insulin lispro, and insulin aspart. Now when we think about what our second-generation insulins are, we've been able to improve upon the profile as well as the onset of the insulin. And the need for faster insulins is because they better reflect the physiologic insulin response that we need, response to food intake, as well as to minimize postprandial glucose excursions.

And so in that category, we have insulin aspart, and it's called faster aspart depending on where you might be located, ultra-rapid lispro, and BioChaperone lispro. And as alluded to earlier, they all have different added excipients that vary from niacinamide to citrate that help the mechanism of action be much faster. And so when we think about when this insulin is injected, the onset is much, much quicker. To give you an example, the onset is 5 to 6 minutes quicker than what you normally have with a first-generation rapid insulin.