

**SPEAKER:** So let's talk about those. So we think that this is a lot of why PCOS ultimately has become a multi-system disorder. So basically, when you have insulin resistance in the skeletal muscle, you end up with elevated levels of insulin circulating in the blood. The resistance that's seen in the skeletal muscle, though, is not really replicated in the ovary. The ovary, for a variety of reasons, is still sensitive to that insulin.

So the excessive insulin now affects the ovary, probably through this IGF receptor. And now, all of a sudden, the ovary is reacting in ways that are not necessarily what we want.

We have excessive androgen production, which means excessive testosterone production or androstenedione. This then leads to clinical hyperandrogenism-- so classic skin findings of acne, hirsutism, and androgenetic alopecia-- so hair loss. It also leads to irregular cycles. So that, then, can lead to infertility or trouble conceiving.

We also know that the elevated hyperinsulinemia has effects on the liver. We're finding increased levels of fatty non-alcoholic fatty liver disease. And it also has effects on the sex hormone binding globulin that basically accentuates the hyperandrogenism.

And then of course, just like any other sort of health issue, we know that hyperinsulinemia can downstream, lead to hyperglycemia-- like a diabetes type of picture. So we know diabetes is really common in this population and has a host of other issues that can result.

And then another factor that we're looking at a lot now in our PCOS population-- we'll talk about this-- is the increased rates of depression. And it's not really clear why that increased rate of depression exists in PCOS. There's some people who think maybe it's the increased androgens. Some of our work that we're doing on a research basis suggests it could be the insulin that's a factor.

So we know that PCOS affects people across the lifespan, but what we're really learning is that the way it affects you changes as you age. So we think that in the younger adult population, one of the most important things first is to establish the diagnosis. And many of our patients who are younger are just struggling with what the symptoms are. They don't know that they have PCOS yet.

In the reproductive age, and once the diagnosis is made, it really is primarily focused on managing symptoms-- so helping women have control over their menstrual cycle, preventing overgrowth of the lining, hirsutism, and things of this nature. Of course, during the reproductive age, at some point, fertility becomes a factor. That's desired by the patient, at least in some cases. And that's obviously something that we also help with.

In the post reproductive age, though, as well as continuing to manage some of the symptoms, there often becomes metabolic alterations that should be screened for and potentially treated.