



FA Connect: Question & Answer Transcript

Session Title: Nutrition & Metabolism in FA: Tracing nutrients from consumption to energy production

Invited Speaker: Dr. Lindsey Romick-Rosendale, Cincinnati Children's Hospital Medical Center

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Access a recording of Dr. Romick-Rosendale's presentation by visiting www.fanconi.org. The recording has been uploaded with Spanish subtitles.

Have additional questions for the speaker? Email Dr. Romick-Rosendale directly at Lindsey.Romick-Rosendale@cchmc.org

Q: Are different subtypes being taken into consideration or looked at in the study?

A: We have access to FA subtypes through other studies. The plan would be if we can get enough participants and other data from urine and blood samples, we would see baseline differences in metabolism between FANCA and FANCC. We will account for subtypes if we can meet the statistical needs.

Q: Do you have any early theories on why with your first patient in the clinical trial you saw their body basically shut down after being given glucose?

A: I've talked about this before. I think that clearly the body immediately recognizes the glucose but within 30 minutes the body is shutting down. That alone is so unexpected. Typically, in a person without FA, you see no response or upward change. Glucose is being recognized and for some unknown reason either due to a receptor or a hormone response (insulin, etc.) the body isn't metabolizing it the way you would typically see. This could be indicating that when a person with FA receives glucose it may be triggering a hormone response for some unknown reason. The body is sensing glucose and then shutting down. The downside is then the body wants to utilize stored skeletal fat which is the last thing we want it to do in this population since many people with FA have low body fat percentages. The idea being that we may be able to pin down where this is happening and block the reaction and hopefully force the body to use the glucose properly. We are trying to figure out where in the pathway it is getting hung up through the clinical trial.

Q: There are many in FA community that are underweight and many that are overweight, would you expect to see the same mechanism at play for those that are overweight?

A: Yes, and the thought process now and the plan for the trial is to enroll the three different BMI subtypes, overweight, underweight and the 'normal' within the FA community. I at least at this point think it may be the same mechanism where it is turned all the way on, or it is turned all the way off.

Q: What could it mean as a consequence if we aren't expending enough carbon dioxide when breathing after consuming the glucose? * This question was asked after Dr. Romick-Rosendale explained that her patient in the trial had very low levels of CO₂ produced after receiving the glucose.

A: If you look back at the little metabolism diagram, when someone takes in food, you use oxygen to create a chemical reaction which largely produces heat and then the body should generate carbon dioxide and water. So, this patient's body for

whatever reason isn't using the energy it is given. Often people with FA don't have much fat stored to begin with. Without fat left, it will breakdown skeletal muscle into protein. That's probably the process that is happening and the body isn't using the fuel (glucose) it was given. I believe that is part of the issue. There may be a sensor that is turned off that blocks their body from using the glucose and then we need to figure out if the body is struggling to turn the sensor back on. Clearly, we know that it is coming back on at some point. The patient eventually started to generate more carbon dioxide, so we know it comes back on eventually. I believe a lot of people with FA are in this state of metabolic starvation and their bodies can't get out of it. Eating more won't necessarily help if the mechanism can't turn back on quick enough.

Q: How does the lack of appetite feed into all this?

A: This specific patient (the patient from her clinical trial) noted almost no appetite and I'm sure many of you are forcing yourself to get even 1200 calories in daily. It makes perfect sense because if your body thinks it doesn't need calories, it's not going to trigger a hunger response. That is the downside of what is occurring when the body receives glucose. I'm already thinking of additional studies looking at what happens if instead of carbs under fasting conditions, I give individuals in the trial protein. Maybe that is the key for someone with FA. Step one is to get more participants in the current trial so we can confirm these results. We know so much about metabolism that it should be 'easy' to fix once we know where in the mechanism it is getting hung up.

Q: Regarding the future diets for people with FA, do you have any assumptions about what can be done?

A: What we saw with the individual from the trial are results you would expect to see from a body builder. The difference is that a body builder wants to lose fat mass and has extra protein to give. So, we would want to see their bodies respond to glucose in the same way we saw with the patient in the trial. In terms of the results from the patient, I've been looking through all the literature to find any other case where the body shuts down like that in response to glucose. I personally wonder if focusing on a higher protein diet may be the key. What if we give the body something higher in protein and lower in carbs and I wonder if the body wouldn't shut down in the same way, plus now it would have extra proteins to give up. Same way with consuming more healthy fats like coconut oil and avocados. If you are going to cook, think about using healthy fats so your body doesn't break down your skeletal fats. Even if you need to get blood work and you need to fast for around 12 hours, choosing wisely of which snack to consume before you start fasting like cheese, yogurt, or things that have proteins and fats with less carbohydrates

Q: What are some ways to increase or induce an appetite when you don't feel hungry?

A: That is a tough question. Metabolic rate is difficult. I don't know if there is a natural way to help with this though. Choosing when you eat can be a big deal, particularly when you have a high protein meal. Premier Protein has a lot of flavors and is easy to find. This protein tastes good with about 30 g of protein and is more like a milkshake, not as chalky. Protein shakes should have less than 5g of carbs. A lot of people with FA struggle with textures or swallowing and getting enough protein can be difficult if you aren't able to eat things like meats, beef sticks, cheeses, etc. A lot of softer foods like pastas don't have a lot of protein in them or a lot of fats.

Q: Can you give a recommendation about macro percentages or grams of protein that someone should be consuming?

A: You can use calculators online that will tell you what macros you should consume to maintain your weight or lose weight. I use an app called MyFitnessPal. The app is super easy and will loosely track each of your macros. You can tell the system what specific macros you are trying to reach, or you can tell it you want to gain two pounds a week and will estimate how many grams of protein, fats, and carbs you should eat.