Podcast Transcript: The Exposome and Health (Part I)

[Theme music]

Ashley Ahearn (AA): You're listening to Environmental Health Chat – a show from the National Institute of Environmental Health Sciences that explores the connections between our health and our world.

I'm Ashley Ahearn.

[Music fades out]

Understanding and protecting public health means understanding our exposures. What are the things in our lives that can lead to us becoming sick or developing diseases down the line?

Doug Walker (DW): So, we know as humans that we experience thousands, potentially millions, of exposures across our lifetime.

AA: Doug Walker is an associate professor in the Gangarosa Department of Environmental Health at Emory University.

Traditionally, environmental health researchers have studied one exposure at a time. So, for example: If you drink water with lead in it, you are more likely to develop neurological problems. If you live in a place with high levels of air pollution, you are more likely to develop cardiovascular and pulmonary disease.

But life is not so simple. We are exposed to countless threats throughout our lives – from our time in the womb to a walk down the street this morning.

DW: …pesticides, flame retardants, drugs, commercial products, you know, many, many different classes of compounds that we are routinely exposed to in our day-to-day life.

AA: And those exposures can interact in different ways for different people, leading to different health outcomes. In fact, each one of us has a different suite of exposures that changes day to day, minute to minute.

This concept is called the exposome. It refers to all the environmental exposures – and the body's response to them – that an individual experiences throughout their life.

DW: So, I can leave my office and walk outside and get in my car and drive to a different part of Atlanta and my exposome there may be very different from the exposome I'm experiencing here in my office at Emory. And so, there's this temporal aspect that changes throughout our life, that's very important. But another really key consideration of that is that exposures at different time points in your life may have different effects.

AA: Our bodies are more vulnerable to certain chemical insults in utero or during key developmental phases, like childhood, puberty, or pregnancy. Exposures that take place during those key periods could lead to worse health outcomes than exposures that happen later in life.

But it doesn’t stop there. There are more layers to the exposome – just as there are many layers to one individual’s life.

DW: When we are discussing the exposome, we're not just referring to the chemical exposome, but also many other factors that can affect your health, for example, stress or socioeconomic factors, dietary factors, many, many others.

AA: For example, if you grow up in a stressful environment your body may be less equipped to withstand certain exposures. And that can lead to different health outcomes compared to someone who grew up experiencing less psychosocial stress.

Walker says that our exposome is a complex web of exposures, lived experiences, and chemical interactions – and scientists need to take a more holistic approach to understanding the connections between all these factors and their combined effects on health.

DW: Many of these traditional exposures that have been studied aren't acting in isolation. They're interacting, there's mixtures of exposure. And so, your exposome is continuously changing over your lifespan, it can include many different exposures from many different sources. And this is really the complexity that we hope to better embrace when we develop and apply these exposomic strategies to understand how environment impacts our health.

AA: So, how to do that? Studying the exposome is about using cutting edge computer modeling and technology like high resolution mass spectrometry to analyze thousands upon thousands of biological samples in greater detail than every before.

But it’s also about widening the lens – changing the research approach from one that starts with a hypothesis and then seeks to prove or disprove it, to one that looks across massive data sets and explores connections or patterns that may emerge. Walker compares it to changes in how we conduct genetic research.

DW: And so, in our traditional measurement methods, typically we are selecting an analyte or a gene or protein that we want to measure in a population. So, for example, I could have the hypothesis that protein A is linked to increased risk for a disease. And so, I would find a way to measure protein A, I would identify samples from individuals who have the disease I'm interested in and match for controls. I would then measure protein A in all of those samples and perform my statistics to see if it is different in the diseased individuals relative to the control individuals.

AA: Walker says it’s time to switch that paradigm around. Rather than developing assays to measure specific proteins or biomarkers, scientists are developing analytical approaches that allow them to measure as many factors, or exposures, as possible in order to attempt to interpret and understand the broadest possible swathe of our potential exposures – and how they may interact. It’s called untargeted analysis.

DW: And so, in an untargeted study, rather than focusing on protein A, we would develop a method that allows us to measure as many different proteins as possible. Measure all the proteins in our samples from healthy individuals and diseased individuals, and then apply data science methods to see which of the proteins we've measured are actually different between the controls and disease group. We’re moving away from a focused analysis to really trying for

comprehensive characterization so we can use different data approaches to prioritize the most important changes in those measurement profiles.

AA (on tape): That must be a boatload of data. I can't even imagine, I mean, I would think a lot of your job is figuring out how to best sift through all of those datasets.

DW: Absolutely, and that's one of the real exciting things to me about the exposome field. So, in my lab, we're developing the analytical approaches that are using untargeted methods, just like I described. But rather than focusing on things like genes or proteins, our methods are actually focused on measuring different chemicals that arise from outside of our body that have, you know, essentially been internalized through our exposures. And so, with our measurements of blood or tissue, we're routinely detecting up to 100,000 different signals. That can be everything from pollutants to commercial chemicals to drugs and dietary chemicals, as well as metabolites that our bodies produce endogenously, or naturally. And so, when we're analyzing our studies – and often we're analyzing hundreds, if not thousands of samples – so you're absolutely right, we end up with a boatload of data. And it's our responsibility to take that very complex data and generate usable knowledge from it.

AA: As you might imagine, there are many areas Walker could apply this research approach.

He and his colleagues are particularly drawn to understanding how the widespread presence of plastics in our environment and in our bodies may be combining with other factors to affect people's health.

DW: Our latest research and some of the methodology that I'm very, very excited about is leveraging our exposomic instrumentation to develop some of the first strategies for characterizing what we like to think of as the plastic exposome. So, with these methods, we're not only characterizing additives and plastic-related chemicals, but we're also developing approaches that allow us to very accurately and with a high degree of sensitivity measure microplastic and nanoplastic particles in different biological samples and tissues. And so, the methods that we've developed in my lab are really focused on that and looking at a number of different outcomes, particularly how early life microplastic exposures, whether in utero or within the first year of life, may have impacts on development in children.

AA: Now, combine the ability to study an individual's exposome with the ability to analyze their genes. Say you have the gene that could predispose you to breast cancer… what if exposomic research could help scientists understand how exposure to plastics, for example, could trigger that gene and make you more likely to develop breast cancer? Or even help you make changes to your diet or environment that could help reduce your risk of facing that outcome?

Walker says the potential to use predictive precision medicine to protect people is immense and the analytical and data crunching technology is only getting faster and more effective.

DW: I hope that we reach a point in the future where we have the exposome assays prepared to a point where this is actually something that you could bring into the clinic. And you could get your annual or biannual exposome scan that will provide you an accounting of your exposures, how your exposure levels are relative to the population, what are the diseases have been linked to these exposures, and what are the steps you can take to reduce these exposures – whether it's changing your commercial product you use or making dietary changes. But essentially providing interventions that can reduce exposures that could be increasing risk for a disease.

AA: Exposomics is a booming area of research that Walker says will only continue to thrive as more scientists with different backgrounds bring their expertise to the table. Walker himself has been exploring this concept since graduate school and he's now approaching 40.

DW: In a sense, I have kind of grown up with this concept. But it's also been very, very exciting over the years to see just how powerful the methods we've been working on have become, and just how widespread interest in the exposome and environmental exposures and recognition of the complexity of the environment has become over the years.

AA: As he looks ahead, Walker sees a bright future with so many more avenues to explore. Collaboration across different areas of expertise is the name of the game, he says, and there's room for researchers from all different backgrounds. Whether you're in data science, epigenetics, cancer research, or beyond, Walker says, "jump in!".

DW: I think the key to our success is going to be embracing a multidisciplinary approach to studying the exposome. So, to researchers and early-stage investigators and students who are interested in this I would suggest just reaching out and reading more and really thinking about how their skills and their knowledge can really contribute to advancing this field. I think personally, right now is an incredible time to be in science, the amount of data we can generate, and our ability to very, very comprehensively characterize so many different aspects of biology is really providing insight that has been impossible until now.

[Music comes up]

AA: How are exposomic researchers broadening the lens of their field and engaging with diverse communities?

We'll find out in our next episode.

I'm Ashley Ahearn. Thanks for listening to Environmental Health Chat.