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Editor's Summary:

When you think about the health effects of air pollution, what comes to mind? Lung disease? Cancer? One health effect you might not immediately think of is low birth weight, a risk factor for a variety of other health problems later in life. Yet a growing body of evidence indicates that birth weight and other gestational outcomes can be influenced by a mother's exposure to fine particulate matter air pollution. In this podcast Tracey Woodruff discusses new findings on this link from a global consortium of investigators who, between them, have analyzed more than 3 million births.

AHEARN: It's *The Researcher's Perspective*. I'm Ashley Ahearn.

People who live near freeways or other sources of air pollution have been shown to have higher rates of asthma and certain types of lung disease and cancer. But in recent years our understanding of the range of potential health effects related to exposure to air pollution has broadened.

A collaboration of researchers from around the world has focused their attention on the potential connection between exposure to certain types of air pollution and low birth weight—with some interesting findings.[1]

Joining me to talk about it via Skype is Tracey Woodruff. She's the director of the Program on Reproductive Health and the Environment in the Department of Obstetrics and Gynecology at the University of California, San Francisco.

Hi Tracey, welcome back to *The Researcher's Perspective*.

WOODRUFF: Hello. Thank you, Ashley.

AHEARN: Let's start with air pollution itself. How do scientists break down the different types of air pollution?

WOODRUFF: Well, there's many different types of air pollution, and the focus that we have in our studies where we're looking at prenatal exposures to air pollution and adverse pregnancy outcomes, particularly focusing on the effects on fetal growth, is particulate matter [PM] air pollution. And particulate matter air pollution is essentially little particles in the air, almost like dust, but they're measured on a very, very small scale—smaller, essentially, than the width of a human hair.

AHEARN: So it's broken down between $PM_{2.5}$ and PM_{10}, are the most common categories. Tell me about those different sizes.

WOODRUFF: Originally when U.S. EPA [Environmental Protection Agency] started to regulate particulate matter in the air they were looking at those kinds of particles that could get into your body, basically things we call respirable particles—things that you could breathe in, get into your mouth, into your nose, and then go down into your lungs. And so originally EPA was very focused on particles that measured 10 microns or less [i.e., PM_{10}], and those are kind of in the convention of the air pollution world considered larger particles.

But as research started to evolve there became to be more of an understanding about the particles that were smaller than 10 microns, so particles that were 2.5 microns or less [i.e., $PM_{2.5}$]. And those, people think, go farther, potentially have more toxic particles on them, and have the ability to be more toxic than the larger particles. And so EPA slowly over time has focused their regulatory activities on these smaller particles because people have identified them to be more toxic than the larger ones.

AHEARN: So tell me what you found.

WOODRUFF: We started this with a meeting just among researchers in 2007 where people became very interested in this idea.[2] We worked with the researchers from many different countries around the world—in fact, we have collaborators

from every continent except for Africa.[3] We were able to have everyone go back to their individual studies, provide the same method. We then standardized the estimates, and then we did a meta-analysis to look at what was the overall synthesis of the maternal exposure to air pollution and pregnancy outcomes.

We focused on effects on gestational growth: Would higher levels of air pollution be associated with effects on decreased gestational growth? And what we find was when we aggregated all the studies there was an increased risk of low birth weight for increasing levels of particulate matter air pollution.

AHEARN: And when you say particulate matter air pollution, are you talking specifically about $PM_{2.5}$ or PM_{10} or both?

WOODRUFF: So, we started by focusing on PM_{10} because that was the air pollutant that most of the centers—or almost all the centers—had an exposure measure for. But we also asked the centers to look at the relationship between exposure to $PM_{2.5}$ and low birth weight or effects on gestational growth because we knew that that's potentially more toxic than PM_{10}.

And so what we found was that 13 of the participating centers looked at PM_{10} and low birth weight and also effects on gestational growth, and 7 of the centers were able to look at $PM_{2.5}$. And we saw a slightly stronger relationship for maternal exposure to $PM_{2.5}$ and effects on gestational growth than we did for PM_{10}.

AHEARN: And what might be the mechanism there? What's happening?

WOODRUFF: Well, this is a very interesting question and an area of ongoing research, and so some of the things that people have hypothesized or have looked at in terms of air pollution during, exposure during pregnancy and adverse pregnancy outcomes is perhaps does the air pollution interfere with the ability of the embryo to adhere to the uterus, develop the placenta—so both that you have poor placental development and function because if you have poor placental development and function, that will lead to effects on gestational growth. So some people have hypothesized and have looked at that as one potential mechanism.

Some people have hypothesized that inflammatory responses may be responsible for some of the observed adverse pregnancy outcomes, and there have been some studies that are looking at more what I would say "upstream" markers of adverse health effects during pregnancy and how that might be influenced by particulate matter air pollution. So, for example, PM is associated with increasing blood pressure generally in adults, and of course if you create increased blood pressure during pregnancy, that may adversely also affect pregnancy outcomes. So I think there's a range of mechanisms that people are looking at, but I think it's still an area where we need more information.

AHEARN: Tracey, once the baby is born, what potential problems can low birth weight cause for that baby, either in infancy or later on in life?

WOODRUFF: Low birth weight is a very important risk factor that is of general concern among clinical and public health audiences. Babies who are born too small for their gestational age are at increased risk of a variety of morbidity outcomes either during infancy or during childhood—things like increased risk of infection, they could be at risk of neurodevelopmental problems later in childhood, and now we know from very interesting research that even the effects that occur early in gestation, which may be manifested through observing this low birth weight, can also be a marker for increased risk of adult disease—so, increased risk of cardiovascular disease, increased risk of diabetes and other types of metabolic disorders.

So, effects on gestational growth or increased risk of low birth weight can have implications during your entire lifetime. And the other thing that's very interesting about low birth weight is it's kind of an indicator variable for some type of effects on development that is occurring during pregnancy.

AHEARN: I'm curious about how you control for certain things. You know, living in more heavily polluted areas can often go hand in hand with having a lower income, being less nourished, more stressed. I'm wondering, how do you sort out the impacts of these factors on a pregnancy outcome as opposed to the outcomes that might come from exposure to PM?

WOODRUFF: In this study there's a couple of advantages that we have to what we're doing. First of all, we asked the centers to look at the relationship between particulate matter air pollution and low birth weight or effects on gestational growth without adjusting for these factors. We then asked them all to adjust for what they used as a marker for socioeconomic status—essentially, maternal education and those factors that they think are important to their local study. So for example, in the United States, adjusting for race and ethnicity is an important factor to evaluate when you're looking at exposures to environmental chemicals and pregnancy outcomes, but it might not be so important in some of the other countries where the population may be more homogenous. So we were able to look at the relationship in this meta-analysis across all the centers looking at these various factors that were adjusted.

AHEARN: So you controlled for all these factors, and you still saw that relationship.

WOODRUFF: Yes, we did, through the meta-analysis. I would say the other thing that makes this more compelling is that we have over 3 million births in this study, so that gives us a lot more strength in order to evaluate the relationship between air pollution and pregnancy outcomes, and to have a better ability to see that signal if it exists.

AHEARN: So Tracey, what happens next, and what do you with all this data? How do you hope it's used or applied?

WOODRUFF: There are many applications for this that could be useful. For example, the U.S. Environmental Protection Agency, when they're looking at cost and benefits of the Clean Air Act, one of the things that they need are estimates about the relationship between exposure to $PM_{2.5}$ and the health effect that they're interested in so that they can estimate benefits. So now this meta-analysis could be very useful for those kinds of efforts for looking at another benefit of implementing their regulations for air pollution. And then we hope that other countries might find this also useful when they're looking at trying to determine how they're going to address air pollution, particulate matter air pollution, and evaluate the benefits from that.

AHEARN: I can't help it, my brain is going to Beijing right now with the horrible air pollution they're suffering from.[4] From your perspective, what does that look like to you? What kind of questions would you be asking as babies are born in subsequent years?

WOODRUFF: When I think about Beijing and the high levels of air pollution, I think back to the other air pollution episodes like in London,[5] like in Donora,[6] and that after these events you saw measurable health outcomes in the population—more people going to the hospital and even more deaths. And it's very interesting because the original London air pollution episode in the 1950s, which was the basis eventually of EPA's particulate matter air pollution standards, where they saw a high increase in elderly mortality, we actually went back and looked because they also saw an increase in infant mortality. That was actually how I first got into this research, was I was interested in this idea of whether air pollution could be an explanatory variable in the disparities we see in birth outcomes and infant mortality.

When I think about Beijing, I would anticipate that they would see an increase in both either very extreme events such as mortality or an increase in chronic events such as respiratory-related events, admissions to the hospital room, asthma attacks . . .

AHEARN: And smaller babies.

WOODRUFF: And smaller babies, yes.

AHEARN: Tracey, thanks so much for joining me.

WOODRUFF: Thank you, Ashley.

AHEARN: Tracey Woodruff is the director of the Program on Reproductive Health and the Environment in the Department of Obstetrics and Gynecology at the University of California, San Francisco.

And that's *The Researcher's Perspective*. I'm Ashley Ahearn. Thanks for downloading.

Ashley Ahearn, host of *The Researcher's Perspective*, has been a producer and reporter for National Public Radio and an Annenberg Fellow at the University of Southern California specializing in science journalism.

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