Exploring Links between Arsenic and Diabetes, with Ana Navas-Acien

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Arsenic is a problem in communities around the world, from Bangladesh to New Hampshire. It’s one of the environmental chemicals the National Toxicology Program explored at a recent workshop as possibly contributing to the worldwide rise in diabetes. In this podcast, Ana Navas–Acien talks about a new review by investigators at that workshop, who summarize the evidence for a link between arsenic exposure and diabetes.

AHEARN: It’s The Researcher’s Perspective, I’m Ashley Ahearn.

Arsenic exposure is a problem in communities around the world, from Bangladesh to New Hampshire. It’s been linked to cancer and cardiovascular problems.

But diabetes?

The National Toxicology Program organized a workshop to explore how environmental chemicals, like arsenic, might be contributing to the rise in diabetes.\(^1\) Dr. Ana Navas-Acien took part in that workshop and was a coauthor on a review\(^2\) that summarized the findings on a possible link between arsenic exposure and diabetes.

Navas-Acien is an associate professor of environmental health sciences at the Johns Hopkins Bloomberg School of Public Health.

Hello.

NAVAS-ACIEN: Hello, Ashley.

AHEARN: What made the National Toxicology Program curious about this link? Why was this panel convened?

NAVAS-ACIEN: This panel was looking overall at all environmental chemicals that could potentially be related to diabetes, and one of those chemicals was arsenic. And the evidence for arsenic to be potentially related to diabetes came from Taiwan, especially in areas of Taiwan where arsenic is found in drinking water at relatively high concentrations, and they found this increased risk of diabetes. And then the evidence was found in areas of Bangladesh that were also exposed at very high levels in drinking water. And when I say high levels of exposure, we mean levels that are 100, 150 micrograms per liter and higher. And to give us a reference, the current standard for arsenic in drinking water in the United States, and most countries around the world, is 10 micrograms per liter. So that means in places where the
arsenic levels were at least 10 times higher than the current standard, the evidence has been quite consistent.

One limitation that we have, even at those high levels of exposure, is that most of the studies were cross-sectional, and that means that the evaluation of exposure (in this case, arsenic) and outcome (in this case, diabetes) was done at the same time. And because of that we are not exactly sure if the exposure really precedes the outcome.

There is, however, one prospective study, also done in Taiwan, and in that prospective study, with long followup, they also found the connection. So I would say overall, we concluded that the evidence was “sufficient,” but because of not enough prospective evidence—only having only one single study—our final conclusion was “limited to sufficient” evidence for an association between arsenic and diabetes at high levels of exposure in drinking water.

AHEARN: And now in the U.S., where our levels of exposure may be lower, much lower than, than the levels you cited in Taiwan—what does that mean at the low-level exposures for us, and could it be linked to diabetes; how strong is that connection?

NAVAS-ACIEN: At these low/moderate levels, such as found in the United States, in most parts of Europe, in most parts around the world, the level of evidence is much weaker, and this is because we have a number of studies that have been done, but the findings in those studies are inconsistent. So in some studies we find an association, in others we don’t. However, this is a very important question, because diabetes is a very important health problem in the United States and in many countries around the world; it’s an emerging epidemic, and many risk factors contribute to it, including obesity, diet, lack of physical activity, but in addition to that, there is concern that these environmental chemicals, among them arsenic, could be facilitating and contributing to this diabetes epidemic.

AHEARN: We should be clear here, though—when we talk about arsenic, there are two kinds, right? And which one did you focus on in your research? Which one are we more concerned about as a public health risk?

NAVAS-ACIEN: As a public health risk, when we talk and think about arsenic we are referring to inorganic arsenic, and there is another kind of arsenic that is called organic arsenic, or organic arsenicals, and those forms of arsenic are mostly found in seafood. So people who eat seafood are going to be exposed to very high levels of arsenic, but in this case it’s this type of organic arsenic that is actually nontoxic, so when we do research we need to always be very careful about exposure assessment, and we need to distinguish between inorganic and organic arsenic. The good thing is that we have good laboratory methods that allow us to distinguish between the two.

AHEARN: So when we consider inorganic arsenic, what’s the mechanism here? How might it be interacting with our bodies to potentially cause diabetes?
NAVAS-ACIEN: There is a large body of mechanistic research that was conducted following those epidemiological findings that I’ve mentioned earlier. And among the mechanisms I would classify them in three large groups. The first one is related to insulin resistance, and this is related to the fact that in the body we need insulin; insulin has a very important role to facilitate the uptake of glucose by the peripheral tissues. And so if arsenic could affect that insulin-resistance mechanism, then that could explain that arsenic could be diabetogenic. But I would say, putting all the evidence together, it seems to be that the human data that we have is less supportive of insulin resistance to play a big role, so that I would say it's kind of an open question still.

So, the other mechanism that has also been evaluated is at the pancreatic level. So, the pancreas is the organ that produces insulin, and so of course the pancreas needs to work well so that insulin is produced adequately as, as we need it. And the cells in the pancreas that produce insulin are called beta cells, and so if they don't work well we call this beta cell dysfunction, and there is a number of studies, and I would say they are quite consistent, supporting this potential mechanism for beta cell dysfunction, including some inflammatory and oxidative stress mechanism going on, especially at low/moderate levels of exposure. So I would say the mechanism at the pancreatic level seemed quite important.

And then the third one would be liver function, and there is more and more recent evidence suggesting that this could also be important. I would say that for liver function we have very little human data with respect to mechanisms for diabetes, although we know that arsenic is a well-known toxicant for the liver, so that definitely could be possible also.

AHEARN: Dr. Navas-Acien, what are the major research questions that remain for you in understanding this association between inorganic arsenic and diabetes?

NAVAS-ACIEN: The main research question is at these low/moderate levels of exposure. And in order to get that evidence, in order to know if really arsenic is contributing to diabetes at low/moderate levels of exposure, we need to have prospective studies in human populations exposed to from low to moderate, maybe also to high—to have the overall exposure range so that we can evaluate the dose-response relationship. And I think that dose-response relationship is going to be quite important, and it’s an, it’s an open question: Is the risk the same through the range of exposure levels? Is the risk even maybe higher at low/moderate levels of exposure, and then it kind of plateaus or gets stabilized? So that’s a critical exposure question.

The other type of research that is needed, I think we need to continue to do this mechanistic research at low relevant levels of exposure for humans, and that remains critical to see which could be the really relevant mechanism at low levels. Then, I would say another question that is very interesting right now and that
people are looking at is which are the susceptible populations, which are the groups that are at the higher risk? And that could be related to additional risk factors, maybe obese people might be more susceptible if they are, in addition, exposed to arsenic, so we need to look at this effect-modification type of studies between obesity and diet and arsenic exposure.

Other conditions could be socioeconomic status and also this idea of genetics and epigenetic mechanism. These are the open questions that I think remain, and these are all very exciting and intriguing questions, so it’s very interesting research for me to be involved [in] right now, and with the studies that we have going on we hope to be able to provide some answers to these questions in the next two to five years. I don’t know—in science it’s hard to predict when are you going to get those conclusive findings, no? But I think we are not so far away, so that’s a good thing.

AHEARN: Dr. Navas-Acien, thank you so much for joining me.

NAVAS-ACIEN: Thank you very much for your questions.

AHEARN: Dr. Ana Navas-Acien is an associate professor of environmental health science at the Johns Hopkins Bloomberg School of Public Health.

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.

References and Notes


4 The reviewers classified the evidence from each study they evaluated as “sufficient,” “limited,” or “insufficient.” “Sufficient” indicates evidence of a causal relationship. “Limited” indicates evidence of a potential causal relationship, although other explanations cannot be ruled out. “Insufficient” indicates evidence for which no conclusions can be reached.