

Mixed Metals Exposures in Children, with Robert O. Wright

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In our daily lives we're rarely exposed to just one chemical at a time. Metals, for example, are ubiquitous in the environment, and most of us are exposed to different combinations of metals each day through air, water, and food. Simultaneous exposures to different metals may have synergistic effects in children, whose developing brains are particularly vulnerable to adverse effects from these potentially neurotoxic agents. In this podcast host Ashley Ahearn discusses the neurodevelopmental effects of metals mixtures with researcher Robert O. Wright.

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

When it comes to environmental exposures, they say the dose makes the poison. The next logical question is: What's my level of exposure, and is it poisonous?

The answer can be complicated. In our daily lives we're rarely exposed to just one chemical at a time. Take metals: They're ubiquitous in the environment, and most of us are exposed to different combinations of metals each day through air, water, and food.

The key word here is *combinations*. Joining me to parse this out is Dr. Robert Wright. He's a pediatrician and an associate professor in the Department of Environmental Health at the Harvard School of Public Health. Wright coauthored a paper in *EHP* titled "Associations of Early Childhood Manganese and Lead Coexposure with Neurodevelopment."¹

Dr. Wright, thanks for being here.

WRIGHT: Thank you.

AHEARN: So, you were looking at the combination of lead and manganese and what those health effects might be. Could you tell me a little bit about what you found?

WRIGHT: Well, we found that if we measured a group of children for exposure to both of these metals, and we looked at subgroups of the children with respect to how much manganese they were exposed to, and we looked at how toxic lead was within each of these subgroups, we found that lead was a little bit toxic in the lowest subgroups of manganese exposure, but in that subgroup of children who had very high exposure to manganese, lead was much more toxic than it was in the other subsets. So, in other words, the combination of both having a high exposure to manganese and a high exposure to lead was more toxic than only having exposure to one of those two metals. And if you don't measure both metals there's really no way to sort of parse out or figure out that particular combination is actually driving some of your results.

AHEARN: Why is this happening?

WRIGHT: Well, both metals are known to be toxic to the brain. There are experimental studies that have been done on animals for manganese toxicity. There are many experimental studies that have been done on animals for lead toxicity. But the kinds of studies that actually look at both of these metals combined actually are very, very few. So we know that both them are toxic, and at some level it may make sense that the combination of the two would be more than just additively toxic—in other words, it may be synergistically toxic. And so I think that was really something that underlies this hypothesis is that if you look through the literature you can find evidence of toxicity and where this toxicity may be more important actually is when you're exposed to relatively low doses of both. If you're exposed to really high levels of lead it may not matter whether or not you're exposed to manganese, but when you're exposed to relatively low doses of lead, having a joint exposure with manganese actually may be what sort of tips you over the edge, so to speak, with respect to toxicity.

AHEARN: We're all exposed to different combinations of chemicals and metals every day, and I'm wondering, do joint exposures always exacerbate health impacts, or do they ever mitigate them? Is this ever a good thing?

WRIGHT: I think it's likely that there are combinations of chemicals that may actually mitigate toxicity. Certainly there are chemicals, or even minerals, that are actually nutrients in relatively low to moderate doses, and actually manganese would fit that description—it's actually a nutrient, but others such as copper and iron also fit that description. It may be that having sufficient amounts of particular minerals that are nutrients actually would tend to mitigate some of the toxicity of other chemicals such as lead, which don't actually—some chemicals don't have any biological value. Lead would actually fit in that, and mercury would fit in that, PCBs [polychlorinated biphenyls] would all fit in that. But having good nutrition—that is, having a sufficient amount of iron, a sufficient amount of copper, a sufficient amount of manganese—actually might mitigate that toxicity. However, you can also overdo it. If you have too much manganese, too much iron, too much copper in your diet you may actually start to exacerbate toxicity. So you actually may see both combinations that at some doses are protective and at other doses are actually synergistically more toxic.

AHEARN: What kind of metals or combined exposures do you hope to study next?

WRIGHT: Well, there are certain populations in which you can predict the combinations of chemicals that they're exposed to. For example, there are hundreds of Superfund toxic waste sites around the country, and we know what's in these toxic waste sites, so presumably people that live near these sites are more likely to be exposed to the chemicals in those sites. So I think a logical place to start would be to actually look at what's in these sites and at least for the people that live around those sites, you know, conduct studies that actually look at those combinations of chemicals, because we know that there are people being exposed to those particular combinations. That's a good place to start. Otherwise it really sort of becomes overwhelming when you think of all the thousands of potential chemicals any individual person can be exposed to. I think it makes sense to sort of start with these populations in which we know about the combinations that they're exposed to.

AHEARN: Are there any particular metals that you feel are understudied or need to be further examined?

WRIGHT: Well, when you talk about combinations I think you almost have to include lead because we know it's a very common exposure. We know that it is toxic, and so even though we may feel that we understand lead poisoning very, very well, I don't think we understand the combinations of lead with other chemicals. So I think understanding the combination of lead with mercury or PCBs, which are other chemicals, which are actually very, very common, would be sort of a starting point. I think combinations of chemicals that are sort of newly arising as being potentially toxic such as bisphenol A or phthalates is also very, very important, and certainly as we learn more about what is in the environment and the potential toxicity of those chemicals I think those should be sort of added to the list of what we should look at in combination.

AHEARN: Dr. Wright, human beings don't exist in a vacuum. Do you think scientists will ever be able to give us a 360-degree view of our exposures—you know, all those combinations in our daily lives—and what they might be doing to us in terms of health impacts?

WRIGHT: That's a great question. It's very difficult to imagine a study that can measure every chemical that people are exposed to. It would be extremely difficult to do that, but having said that, these combinations of exposures actually represent what's going on in real life, and I think we have to start thinking about at least the more common dual exposures and maybe even triple exposures and try to look at whether or not we can get a better handle at what doses they become toxic, because that is really a closer approximation to real life than what we're currently doing.

AHEARN: Dr. Wright, thanks so much for joining me.

WRIGHT: Thank you.

AHEARN: Dr. Robert Wright is a pediatrician and an associate professor in the Department of Environmental Health at the Harvard 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.

Reference

¹ Claus Henn B, et al. Associations of early childhood manganese and lead coexposure with neurodevelopment. *Environ Health Perspect* 120(1):126–131 (2012); [http:// dx.doi.org/10.1289/ehp.1003300](http://dx.doi.org/10.1289/ehp.1003300)