INTERVIEW

WE BUILT THIS CITY ON POLLUTION AND MOLD

How urbanization inadvertently promotes the development of asthma and allergic disease

An interview with **DR. STUART TURVEY**

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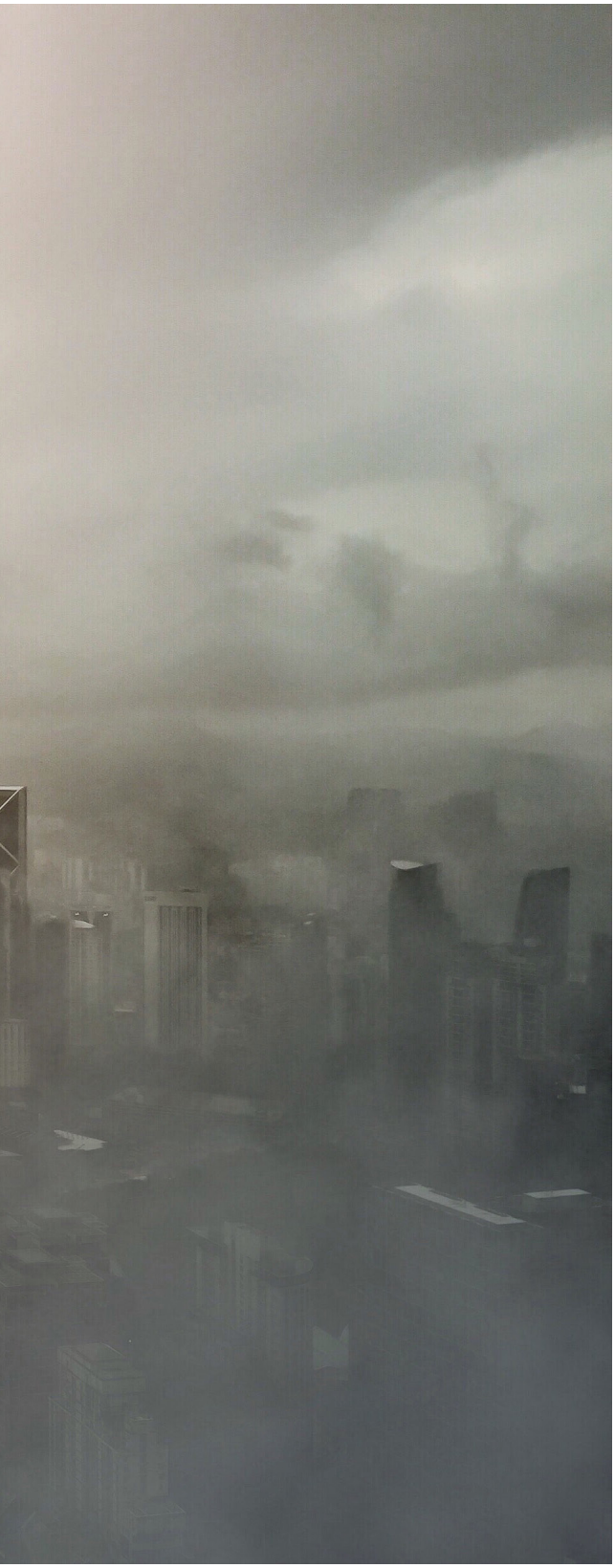

Malaysia - photo HASSAN ISHAN

Asthma is often allergic in nature, primarily triggered by exposure to airborne allergens such as pollen or cat dander. Although we have long known that asthma and other allergic diseases are caused by interactions between environmental triggers and our own genetic predisposition, the complexity of these interactions has made it difficult to develop concrete disease prevention strategies. Furthermore, researchers have been faced with a great challenge in identifying and cataloging the cumulative impacts of the many environmental exposures identified to this point.

Our 'exposome' is our entire history of environmental exposures – beginning in the womb and extending to our time as adults. In recent years, it has become clear that the exposome has vast effects on overall human health [1], in large part because of the way it impacts our microbiome – the bacteria, viruses, and other microbes that live on and in our bodies producing substances that are required for our optimal health.

Research has shown that the presence or absence of specific microbes in an infant's microbiome can increase or decrease the risk of asthma and allergic disease development [2-5]. The infant microbiome is thought to be primarily affected by exposures in the first days and weeks of life, like mode of delivery (vaginal or caesarian section), infant antibiotic use, and method of feeding (breastfed or bottle-fed). While these factors have the greatest impact [6-9], the microbial colonization process is also shaped over time by other internal and external environmental exposures before eventually settling into a more stable community by the age of three [10-12].

As the global prevalence of asthma and allergic disease continues to climb at an alarming rate, some researchers argue that it's worth looking at our collective exposome, the exposures that are common to everyone living in an urbanized environment. Doing so might help us understand the detrimental effects that urbanization has on developing microbiomes [13].

With urbanization, the prenatal and infant exposome has shifted drastically from what it has been for most of human history; in general, babies have less microbial exposure than ever before. This is in part due to the over-use of cleaning products and other toxic substances that kill microbes, but it's also due to reduced exposure to naturally occurring sources of microbes, like pets and farm animals, natural greenspace, and soil. Not only does this make it difficult to establish a healthy microbiome, but it also doesn't allow our immune system to develop the tools it needs to function effectively. Furthermore, the exposome of an urban society is wrought with toxic exposures: vehicle-related pollution, smoke from solid fuel burning and tobacco, mold, household pests, and toxic components of plastics, like phthalates and bisphenol A (BPA). These toxic but common urban exposures are detrimental to our microbiome health and immune function. It also affects those with a lower socioeconomic status disproportionately; low income individuals often live in aging or poorly maintained structures with increased levels of unfavorable microbes and toxin-producing pests [14,15]. By viewing the exposome as a byproduct of our built society, we can better understand why asthma and allergic disease are on the rise in urban centers, and what we can do about it.

Dr. Stuart Turvey is the Director of Clinical Research at the British Columbia Children's Hospital and the Canada Research Chair in Pediatric Precision Health. As a clinician and immunologist, Turvey's lab is working to identify underlying microbial, cellular, molecular, and genetic differences between disease-affected and healthy children to elucidate mechanisms of disease pathogenesis and identify new targets for disease prevention and management. As co-director of the Canadian Healthy Infant Longitudinal Development (CHILD) Cohort Study, Turvey also collaborates with researchers across the nation to carry out Canada's largest population-based birth cohort study, which is quickly becoming one of the world's most informative studies of its kind.

Since 2008, CHILD study researchers have been following over 3,500 pregnant women and their children to examine how mode of delivery, infant antibiotic use, maternal diet, breastfeeding, household chemicals, stress, and other factors influence the development of chronic diseases like asthma and allergies. This work will help identify novel approaches to disease management, inform policymakers of the required preventative updates to our society's medical and urban planning standards, and inform the general public on the implications of cleaning behaviors, diet habits, and parenting strategies. We sat down with Turvey to discuss his involvement with the CHILD cohort study, and to reflect on the implications of his research on our society's status quo.

Your research on infant exposure to phthalates really struck a chord with me as a mother because it's such a difficult exposure to control. We live in a plastic society, where exposure to phthalates is inevitable. I think my phthalate-exposure concern echoes across many of the exposure risks that have been identified so far; how do you manage those inevitable, but less-than-desirable exposures within your own family?

Parents, I think, appropriately worry about their children and try to optimize their health in general. My job as a researcher is to sort of help identify risky exposures, problematic exposures, but also kind of put that in context so that people can still live their lives and not be anxious. So, I think your approach is sensible, which is to recognize that there can be exposures that are problematic.

I think you've got to live your life and encourage kids to be outside, sleep well, to eat a broad and healthy diet, to get exercise, and not to chase them around with hand sanitizer. That being said, I think these things we've researched are real exposures that do have potential health outcomes, so we try to educate families about them and also change policy. Most of us are doing a pretty good job. Things will inevitably happen, but we shouldn't, nor can we control everything.

Research from your lab also digs into prevention measures that would likely require municipal involvement, such as increasing biodiverse greenspace in cities and updating building codes. Do you expect that it will be difficult to convince policymakers to take heed and come up with the funding required for these preventative measures?

This preventative research was championed by Hind Sbihi, a post-doctoral fellow who worked with us.

Sbihi had an engineering background and I wanted her to think

Turvey Lab (left to right) – Bhavi Modi, Stuart Turvey, Kate Del Bel, Mehul Sharma, Alicia Jia, Meriam Waqas, Susan Lin.
Not pictured – Henry Lu, Darlene Dai

about the microbiome as an interactive system. When we think about the gut microbiome, we often think about it in terms of this micro level – how we might be influenced by the dog, or the antibiotics, or breastfeeding. Sbihi's push was this macro-idea, that society has, over time, become more and more industrialized, and as a consequence of that, we've lost biodiversity. We see that we've lost big charismatic fauna, like pandas and gorillas, but we've also lost lots of microbes that we as a human species evolved with. So, the idea that maybe you can be less sanitized and 'rewild' the environment, is intriguing and people have done experiments like this that seem to suggest it works.

I think city planners are really interested in making healthy environments. It may be as simple as encouraging less manicured green space with a diversity of trees and plants. I think our job is to challenge city planners to think about these things. I do think these messages are universal so that families and individuals can participate as well.

What are some manageable ways we can integrate research findings from the CHILD study into our own lives to reduce the risk of chronic disease in our own families?

What we know is that a diverse microbiome is important for health. When babies are born, they are relatively sterile and are suddenly exposed to a huge community of microbes. There are things we can do to facilitate exposure to these diverse microbes. If a baby can be born via vaginal delivery, and that's safe for the mother and the baby, that should be encouraged by the health system. Breastfeeding is also very important for modifying and establishing that microbiome, so anything that the health system can do to support mothers and successful breastfeeding is great. Another big factor is around the use of antibiotics; I think we should cherish antibiotics, but we should use them very thoughtfully because they kill off microbes that are important to maintaining our health, as well as those causing problems. Antibiotic stewardship efforts have been powerful in reducing exposure to antibiotics in young kids, but there's still more to be done.

Indianapolis - photo DAVID LEE

In the CHILD study, about 20 per cent of children were reported to have received a course of antibiotics in the first-year, which is much better than the reported statistics from 15 years ago, but it's still a lot, and it's likely too many. I think that's a message for pediatricians and family doctors, but also for parents. They shouldn't go to the doctor demanding antibiotics and feeling it's the only way that the child is going to get better, when with a bit of time, they'll get better without intervention.

If we were able to catalog the list of microbes required in a microbiome to support healthy immune development, could we wipe out asthma and allergic disease using tailored probiotic supplements?

Part of the research that we're doing considers that question: if we can identify the health promoting bacteria, are we able to start to replace them? If a child really needs antibiotics, maybe there's a way to then supplement them with a therapeutic cocktail of microbes that would help restore the lost microbial diversity that is inevitable with antibiotic use. I think we don't know that answer yet, but some of the research that we do with the CHILD study is looking to understand the microbiome

structure that's linked to health and disease. Kids at highest risk for asthma and allergies seem to be missing some specific microbes, and in a couple of mouse studies, we were able to show that supplementing with those microbes protected the mice from asthma.

That's sort of my long-term hope, but there's lots of work to be done to define the missing microbes, as well as looking at how they can be grown and then proving that they can be safe in young babies. In the market there are aisles and aisles of probiotics, so there's a market for it and a sort of acceptance in the general public, but the problem is that the organisms that are being offered commercially now aren't the right ones, at least for the diseases that we are talking about. We need specific organisms that make specific metabolites that will do the job.

I think it does have the possibility of working, but in the meantime, we should just work towards the population-based interventions like minimizing the use of antibiotics.

In one way or another, many of the disease-promoting factors you identify in your work are in some way tied to socioeconomic class. Do you see any way to minimize the influence socioeconomic class has on the development of asthma and allergic disease in our society?

If, as a society, we can improve the quality of life and the support for our community, particularly the most vulnerable members of the community, I think that's where we can have the greatest impact on health. I think the message is that we should be looking to the most vulnerable, the ones experiencing these adverse exposures and really committing to support them. I don't think there's any one exposure or any one magic bullet, but poverty, low socioeconomic status, educational challenges, high stress, and poor housing all go together. So, if we can identify and support that group as a society, I think that will have huge impact on the lifelong trajectory of the kids growing up in those tough environments. It's really a package of exposures that we put under the banner of socioeconomic status, and it boils down to be our society's responsibility.

I think it'll be interesting to see how all of this plays out. BPA was a huge concern in the early 2000s and now it's quite easy to find BPA-free containers, canned food, and toys. As people become more aware of other exposure risks, it'll be interesting to see how things change.

I think that's right. I think it's our job to identify the problems, to call them out, and then to try to mitigate the exposure to these things through regulation. However, with technological advancements we'll always be exposed to new things that aren't always great, and we'll have to identify them as well. It's really a cycle of scientists identifying the problems and then regulators regulating, and the families being aware. It's a cycle of trying to do better.

EDITOR'S NOTE: This interview has been edited for length and clarity.

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