

Epigenetics and Equity¹

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I recently heard someone say, “If you are working on an idea that you can get done in your lifetime, then you’re not thinking big enough.” Aspiration is a powerful force that motivates us. It is a combination of a big idea, a big heart, and a dogged determination to succeed. Obviously, we may have organizations to run, jobs to do, daily tasks to accomplish, and lives to live. But what if we could accomplish something collectively, something that could make a far greater difference than anything we can do individually? The developmental origins of health and disease is an organizing framework for a very big idea, even a social movement. And it is one that can change the world.

Let’s get some definitions out of the way:

First, developmental origins of health and disease is a body of research that has shown that the risk of chronic diseases such as type 2 diabetes, stroke, heart disease and even some cancers is set pre-pregnancy through the first 1000 days, up to about age two. Risk for problems of cognitive function and significant mental health issues is also established.

Second, epigenetics is the process by which our genes respond to environmental cues. These responses can influence how our genes are programmed to regulate biological functions. ‘Epi’ refers to being above or on the genes. The genetic code does not change, but the biological switches that turn those genes on and off do. And here’s the rub: These altered regulatory commands can be passed from parent to child so that altered gene expression patterns that affect one’s health all the way into adulthood can be passed on to the next generation, and the next.

Third, health equity seeks to reduce group differences in health outcomes that are unjust, predictable and preventable. Developmental origins is the ultimate social and health equity lens because it helps us understand how history, sociology and biology combine to create lifelong prospects for health and social success at the earliest stages.

I’ve worked in public health for 40+ years. This profession is grounded in an ethical framework of social justice — the idea that inequality follows from the adverse impact of privilege, power and exclusion, and this social inequality is linked to health inequity. We know that the collective policy decisions we make as a community determine the

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distribution of risks and benefits, obstacles and opportunities, disease and health. The public policies we debate and implement today will predict the public health problems we face tomorrow.

A recent report produced by the Robert Wood Johnson Foundation concluded, “When it comes to your health, *your zip code may be more important than your genetic code*” “... your zip code may be more important than your genetic code.” Epigenetics explains how the environment, our zip code, literally gets under our skin, creates biological changes that increase our vulnerability for disease, and even our kids’ prospects for social success over their life course and into future generations. This science forces us to rethink where disease comes from and the best way to promote health. It identifies the most fundamental social equity issue in our society: that initial social and biological disadvantage, established even prior to birth, in fact even linked to the social experience of prior generations, is made worse by adverse environments throughout the life course. But, at the same time, it provides hope because it tells us that a concerted focus on improving our environments can ultimately change our biology and the trajectory of disease into future generations.

Where does the idea of developmental origins come from? In the 1980s, David Barker, an English physician and epidemiologist, published the hypothesis that the risk for chronic diseases originated in the earliest developmental stages and not later in life. Dr. Barker, who died in 2013, had strong Portland ties in the latter part of his life and was a principal at OHSU’s Moore Institute for Nutrition and Wellness.

In a nutshell, David’s data, and data from around the world, found that chronic diseases such as diabetes, hypertension, stroke and heart disease were *programmed* into our systems as a result of nutritional deficiency during the critical developmental period of pre-pregnancy up to about age two. Poor nutrition, associated with disadvantaged living conditions, slowed fetal growth and forced tradeoffs that harmed longer-term health. Low birth weight alone predicted a three-to-seven-fold increased risk of chronic diseases like type two diabetes and heart disease later in life. This is a huge impact.

So here is where the research inspired by the Barker Hypothesis has led. We now know that:

- The first thousand days from conception to about age two is the most critical and sensitive time for development. *Risk* for chronic and other diseases is programmed into the function of key organs, settings in metabolism and hormonal feedback are altered, and an increased vulnerability to adverse environments later in life is established;
- Our genes, we now know, are not a deterministic blueprint for our health but a collection of infinite possibilities that are switched on-or-off depending on the conditions our mothers experienced prior to and during pregnancy, and on the nutrition and social environment we have as infants. This research suggests that people mostly get chronic diseases *not* because of the genes they inherit but because of how those genes act in response to environmental stresses. This epigenetic process of gene regulation is where nature and nurture come together.
- While the pregnant woman is the environment of the developing fetus, *the community is the environment of the mother*. The two main factors in the

community environment that impact healthy development are availability of appropriate nutrition and the level of social stress. “Toxic” stress and poor nutrition are a developmental recipe for vulnerability at birth, poor school performance and social skills early in life, and poor health over the life course.

Think of it as a double hit. The *first hit* is the vulnerability that is created from the experience of previous generations through the first 1,000 days. The *second hit* comes from hostile environments marked by racial and other discrimination and social disadvantage that will increase the likelihood that the original vulnerability will transform into later disease. Because some of these changes can be transmitted across generations, the “second hit” of one generation can become the “first hit” of the next.

So how does this process work? Remember, the pregnant woman is the environment of the fetus, but the community is the environment of the woman. From the embryonic stage, the developing fetus gets signals from the mother about the environment it will be entering — is there a scarcity or abundance of nutrients; is the environment safe or threatening? These signals are translated into changes in genetic function that provides instructions to the cells — these are epigenetic changes. One scientist explains that the genome is like a computer and the “epigenome is the software that tells the computer when to work, how to work, and how much.” And remember, these epigenetic changes in the womb are made in response to the environment and may be passed on for up to two generations and may, or may not, be reversible.

When the developing fetus gets a signal (some call this a forecast) that the environment has limited nutrients, for example, it begins to program its systems accordingly. This requires making tradeoffs in terms of which organs get the energy for optimal growth. This means that some organs such as the kidney may be built “on the cheap,” with limited capacity. Other metabolic and biological systems are likewise programmed with a strategy for making the most of a nutrient-poor environment. These systems are then set for the life of the person; damage done early is carried forth throughout the lifespan.

The fetus also gets a second forecast regarding how safe or threatening the environment is. If a pregnant woman lives in a highly stressful environment that might be marked by poverty, racial discrimination, lack of opportunity, personal insecurity and other aspects of social disadvantage — a level of toxic stress — then high levels of cortisol are passed to the developing fetus. Cortisol, you probably know, is the stress hormone. High levels of cortisol mobilize our immune system and ensure that all available biological resources are set to maximum to fight whatever threat is before us. Growth and any other non-essential repair functions are suspended so that the immediate threat can be addressed.

In normal circumstances, when the threat is gone our systems go back to normal with all growth and repair functions resurfacing. However, high levels of cortisol in the fetus creates two problems. The first is that, according Harvard’s Center for the Developing Child, when chronic stress is present, the stress response systems in the brain are *permanently wired* to remain on a “short fuse and high alert status.” This takes a heavy toll on the constantly activated immune system. The second problem is that the higher levels of cortisol in the fetus inhibit growth and create the same kind of increased risk for chronic diseases as nutritional stress.

Further, higher levels of cortisol in the womb are associated with cognitive problems including poor self-regulation and impulse control, memory problems, lower language skills, and limited reasoning, planning and judgment. Of course, these are the very skills that children need to be successful in school and beyond.

The exposure to high stress and low nutrition represent the first hit.

Now, think about how this initial vulnerability or risk is amplified by continuing difficult social and economic conditions — the less desirable zip codes. This is the second hit. Multiply these effects by large populations living in conditions that create and sustain high levels of stress, limited access to nutritious food, poor housing, limited educational and employment opportunity, and you can see how chronic disease clusters and social problems are emerging.

Frederick Douglass, the great African American abolitionist, said, “It is easier to build strong children than to repair broken men.” We all want to do this. We have a moment before us where our best science, our most compassionate values, and our desire to act with conviction to make a difference can all converge. I am optimistic because the science of the laboratory and the wisdom of the community point to places where we can make an important difference. We can’t change genes, but we can change the environments that influence how our genes are expressed. We can change the racism, discrimination, and continued disadvantage that get under our individual and collective skin.

Here are some steps we can take:

First, it is difficult to overstate the importance of the social, economic, and nutritional environments of pregnant women and those about to enter child-bearing age. Using an equity lens, we can build more just and supportive environments that increase the chance for both good health and social success.

Second, we need to recognize the good work happening now in our communities on maternal and child health issues, and on broader social determinants, such as housing, racial justice, food systems and economic development. We need to connect these efforts, build and expand that work, and accelerate progress in our communities. Again, the developmental origins science can inform these efforts and increase the impact.

Third, we need to link and leverage efforts in some key areas. For example, Oregon is making substantial investments in early childhood education to address the very problems that the science of developmental origins identifies. Early childhood education programs need to link with pre-pregnancy and pregnancy programs. They need to focus on prevention because there will never be enough funding to provide the kind of early childhood education services that increasing numbers of children will need. We can build on the excellent 2006 City Club report on this topic by taking a new look with the science of developmental origins. We can build on the Oregon Business Council’s Poverty Reduction Initiative and help build the pathway to prosperity with what we have learned from developmental origins.

These are starting points. But, at the same time, we will require bigger ideas and greater efforts to make necessary progress. Social services are necessary but not sufficient. It will take real social change focused on the underlying, interconnected social conditions that are at the root of health inequity. This magnitude of change will require the kind of political will driven by a social movement.

There is a wonderful quote from Thomas Pynchon's book *Gravity's Rainbow*: "If they can get you asking the wrong questions, the answers don't matter." Here are some right questions that we need to be asking:

- If the Portland Metropolitan region were the healthiest place in the world to be pregnant and have a child, what would it look like?
- How would it be different than it is now? What would need to change?
- What kinds of policies would be required to move toward that vision?
- How can we create a social movement built on this collective vision to force the necessary political will to demand change? How can existing partnerships be expanded? How can we develop new partnerships with new allies to move ahead?

Can we "get there from here?" We have to. We need to find points of leverage that can move us from the level of change on which we are now engaged to a much more expansive level. Crisis is a good motivator for change, and obesity and diabetes may be the prompt we need. What will our health care and social systems do in 2050 when roughly one in three adults is projected to have diabetes? What will economic opportunity look like with increasing income inequality and large pockets of educational failure that lock populations out of social mobility? We can use the science of developmental origins and focus on prevention to make a difference.

A while back, a colleague in San Francisco gave me a beautiful framed calligraphy of a Chinese symbol that his mother had created. The symbol represents the Carp Dragon and is the story of a carp fish that swims upstream until it reaches a waterfall that blocks its journey. Despite great struggle, the carp cannot get over this waterfall. At the point of maximum urgency but also almost fatal fatigue, the carp transforms into a dragon and flies over the waterfall.

What will it take for us to transcend our waterfall? I believe that we are aware enough to appreciate the urgency of this; I know that we are smart enough to figure this out, but I hope that we are wise enough to understand we can't succeed simply by doing more of what we have been doing. We all have to work on this as if our future depends on it, because it does.