EPISODE 5:
DNA IS NOT DESTINY:
How the Outside Gets Under the Skin

TRANSCRIPT

TRT 36:23 MIN

00:00 DVD Chapter 1: Prologue

A girl enjoys a spinning carnival ride.

A father helps his daughter on to the school bus.

NARRATOR: We've long known that what happens to us in childhood can leave a lasting imprint on the adults we become.

A girl is served a birthday cake. A boy runs and flies a toy plane.

NARRATOR: The places we live.

Two girls jumping rope.

NARRATOR: The people we know.

Grandfather walking with grandson and fishing poles. Mom tickling son.

NARRATOR: The best of times, and the worst.

Homeless mother on the street, holding child. Child swinging on swing.

NARRATOR: They all somehow become part of us.

Scientists work in a lab.

NARRATOR: Now, a new science is telling us that our experiences go even deeper than we thought.

Graphic: DNA sequence

NARRATOR: It happens on the genetic level. Experiences, scientists have learned, can leave chemical marks on our DNA. Those marks can switch genes on or off, changing the way our bodies and our brains function. The changes can prime us to thrive, or they can impede development affecting health and well-being for life.

Students take tests.

MARILYN ESSEX: We're talking about processes here that are at a biological level. It just gets under the skin in a variety of ways.

Graphic: DNA sequence

A woman is having an ultrasound.

NARRATOR: These chemical tags are set in place during critical periods of biological change.

MARIE LYNN MIRANDA: There's these special vulnerabilities in utero, during pregnancy, in infancy, in early childhood.

A baby plays with a mobile. A toddler walks to a caregiver.

NARRATOR: Everything in an infant's experience can help or hinder: diet, environmental toxins, housing, safety, even the parents' stress levels.

A toddler is fed yogurt. A multi-lane highway with a lot of traffic.

Tracking shot of rundown housing. A father and son at a lunch buffet.

Tracking shot of babies in a nursery.

NARRATOR: These new discoveries have profound social and political implications. Because if social influences can alter the way our genes work then early environments can result in biological obstacles to success that are beyond personal choices.

Graphic: DNA sequence

DARLENE FRANCIS: The poorest kids in our society, not surprisingly, are the most vulnerable to just about every health outcome we can measure.

A boy with a dirty face in front of a trailer.

DARLENE FRANCIS: These are fairly healthy young children who, with time, are going to suffer the consequences of their social class.

A baby plays with a mobile.

02:51 **NARRATOR:** New evidence shows that social and economic stressors can affect children in infancy, causing changes in gene expression, changes that may last a lifetime.

Teen girl standing on the subway.

MARILYN ESSEX: It affects their way of thinking, it affects their views of themselves, it affects their social relationships.

A school bus picks up children in a rural area.

NARRATOR: But along with a new understanding of how early experience influences development, this science brings hope.

Tracking shot past a house with children playing in the yard. Two young boys running down sidewalk.

Gene sequencing chart.

Young girl on swing with teddy bear.

NARRATOR: Improved social conditions, the evidence shows, can actually provide the biological foundation for lives that are healthier, and more likely to thrive.

MARIE LYNN MIRANDA: The science is clear about this. What we need is for the policy to follow the science and get us to more protective environments for children.

RAISING OF AMERICA TITLE SEQUENCE

04:26 DVD Chapter 2: Identical Mice, Which Aren't Identical

Dana Dolinoy walks into office with container of lab mice.

NARRATOR: Some of the first clues that our lived experience could alter the way our genes work came from a set of experiments involving some genetically identical mice, that somehow weren't identical.

Dana Dolinoy weighing mice.

DANA DOLINOY, Environmental Epigenetics and Nutrition Lab, University of Michigan School of Public Health: The brown pseudo Agouti mouse weighs around 27 grams. Here is the yellow mouse that weighs around 52 grams.

A photo of the brown and yellow mice together.

NARRATOR: How could it be that some mice are brown and thin, others yellow and obese, when they all share the exact same DNA?

Graphic: Floating molecules

NARRATOR: It's what their mothers were fed while they were pregnant. Some were fed pellets rich in methyl groups, a molecule commonly found in fruits and vegetables.

Dana Dolinoy weighing mice.

NARRATOR: Those mice were more likely to give birth to brown skinny pups.

NARRATOR: But mothers fed a diet with fewer methyl groups were more likely to give birth to pups that were yellow and obese.

Dana Dolinoy continues to weigh the mice.

DANA DOLINOY (in scene): Whoops! Tipped the scale.

05:25 **NARRATOR:** These studies were first conducted at Duke University under biologist Randy Jirtle. Jirtle's team, including Dana Dolinoy, zeroed in on one particular gene in search of an explanation.

Graphic: DNA sequence to fetus

NARRATOR: The Agouti gene codes for yellow fur. Curiously, it's also related to obesity. Jirtle's team found that the methyl groups fed to the pregnant mothers passed through to the developing pups and attached to their Agouti genes. It's a process called methylation.

DOLINOY: DNA methylation is the addition of a single carbon in the form of a methyl group. So this is a carbon and three hydrogens that sits down on DNA and shuts genes off.

Graphic: DNA sequence with animated yellow and brown mice

NARRATOR: With the gene on, or active, more mice were born yellow and grew obese. With the genes silenced, more mouse were born brown and remained thin. Same genes, very different results.

CU of mice in cage.

NARRATOR: The difference is whether particular genes are switched on or off, expressed or silenced.

06:55 DVD Chapter 3: The Epigenome

Graphic: DNA sequence

NARRATOR: The genes we inherit are fixed for life. But there's an entire network of molecules that influences which genes are expressed by making them active, or shutting them down, like a volume control or a dimmer switch. It's called the epigenome.

DOLINOY: Well, literally it just means "in addition to," or "above" the genome.

Graphic: Molecules attaching themselves to DNA

NARRATOR: The epigenome – it's a system of molecular switches that interacts with our genes. Scientists are only just beginning to understand how it functions. Some epigenome molecules sit literally on top of genes, fixed like barnacles on the hull of a ship, working to switch genes on or off.

MICHAEL MEANEY, Sackler Program for Epigenetics & Psychobiology, McGill University: When we talk about epigenetics we're talking a collection of biochemical signals that control the way in which the genome operates.

Archival: Scientist looking at DNA strips hanging in front of him.

MEANEY: We each have our own genetic make-up. That's fixed from the time we're conceived forever. What changes though is the activity of genes.

Gene-sequencing chart

NARRATOR: The pattern of gene activity can be absolutely critical, even producing differences in the form and function of cells.

Different slides of cells.

08:24 **MEANEY:** If you think about it, your body is made up of over 200 different cell types. But they all have exactly the same DNA. The same genes are in your liver cell, brain cell, your muscle cells. So something has to happen to allow these cells to become specialized to do what they're supposed to do in your body. And that's where epigenetics comes in.

Graphic: Molecules attaching themselves to DNA

NARRATOR: Epigenetic signals also turn on and off some of the genes that are constantly active throughout our lives, like those involved in appetite, disease-fighting, fear, focus, elation, even love.

Series of clips, including baby being fed, girls watching a movie, and guys watching football.

Archival: Still of yellow obese mouse next to skinny brown mouse

NARRATOR: In the mice, the Agouti gene influences not only fur color, but also body size and shape. Different epigenetic settings result in different appetites, metabolic rates, and fat storage. That accounts for the radically different weights.

Graphic: DNA with molecules

NARRATOR: It's a revolution in thinking about how genes work. DNA, it turns out, is not the master blueprint.

MEANEY: So now you start thinking of DNA not just as an inevitable bank of information, but you start thinking of it as a molecule like any other molecule, that can be more or less active.

Graphic: Molecules attaching themselves to DNA

NARRATOR: If gene activity is so sensitive to a naturally occurring molecule, like a methyl group, could the synthetic substances of our modern world be affecting the genome as well?

Tracking shot past processing plant, with overlay of molecules.

CU of mice in cage with overlay of molecules.

NARRATOR: In a follow-up experiment, Dolinoy fed her pregnant mice Bisphenol A, or BPA. It's a chemical commonly found in plastics, and associated with adverse health effects in humans. This time, she found less methylation, more active Agouti genes and more yellow obese pups born to mice fed BPA. And these pups had a host of health problems.

Lab mice playing in their cage.

DOLINOY: These epigenetic changes were also correlated with an increased risk of things like heart disease and metabolic syndrome and obesity later in life.

Overhead view of mice in cage.

NARRATOR: Then Dolinoy wanted to see if she could protect the mice from the effects of BPA. So she exposed pregnant mice to both BPA and a diet rich in methyl groups. Again, the genome responded. The mice were born brown and skinny.

DOLINOY: So this showed, at least in a mouse model, that nutritional interventions could counteract the effects of toxicants.

A woman having an ultrasound.

DOLINOY: This also shows, at least in this experiment, that the epigenome is quite plastic and adaptable during development.

11:33 DVD Chapter 4: The Social Environment - Under the Skin

Overhead shot of backyard zooming out to reveal town.

NARRATOR: The idea that the epigenome, and therefore gene expression, could be modified by environment was a radical finding. But the Agouti mice were studied under controlled laboratory conditions. Human environments are far more complex.

Fast-motion shot of mom carrying baby and pushing shopping cart.

NARRATOR: A child's environment is everything in his or her world.

Girl running down street in suburban neighborhood.

MARIE LYNN MIRANDA, Provost, Environmental Health Researcher, Rice University: Neighborhoods are defining for them. It's where they live.

Aerial view of neighborhood.

MIRANDA: It's where they go outside and play. It's where they see their friends. The amenities, the good things, the local park, the sidewalks that you can ride your bike on are really wonderful things for children.

A sad looking girl is holding a teddy bear on swing.

MIRANDA: The disamenities, things like litter and abandoned vehicles and overgrown lots and crime, those have an equally important effect on children.

Brooklyn and parents walk past "Make Way for Ducklings" statue in a Boston park.

NARRATOR: It's not just the physical environment. For a young child the social and economic environment is also key.

Young children drawing together at a table.

NARRATOR: Personal relationships, exposure to stressors, feelings of safety or insecurity, all of these can get under the skin.

Father carrying son into classroom. Tracking shot past rundown rural area.

NARRATOR: An adverse social environment, the science indicates, can change a baby's epigenome just as toxic chemicals can.

13:24 DVD Chapter 5: Social Toxins and Gene Expression

Archival: image of Michael Meaney

NARRATOR: In the early 1990s at McGill University in Montreal, neurobiologist Michael Meaney set out to understand how stressful conditions in early life could have effects that last a lifetime.

MEANEY: The first thing we wanted to do is to look at an environmental influence that we know has a profound effect. So we looked at maternal care.

A single rat in the tub experiment next to gloves and some rope.

NARRATOR: Meaney and his team, including then-doctoral student Darlene Francis, observed that some adult rats seemed to be more skittish and fearful, more stressed, than others. They went looking for factors in the rats' early social environment that might be a clue to the difference.

DARLENE FRANCIS, Behavioral Neuroscientist, University of California, Berkeley: We observed hundreds of litters, hundreds of different types of behaviors. And then when you put all of the data together, the most powerful predictor of stress profiles in those babies growing up was the amount of licking and grooming they had received from their mothers.

CU of a rat mother standing over her litter of newborns.

NARRATOR: Rat mothers typically lick and groom their pups. But some do it more than others. And the difference between high-licking mothers and low-licking mothers was reflected in their pups' behavior as adults.

Darlene Francis and colleague observing rat.

14:47 **NARRATOR:** The team found that rat pups that were licked and groomed more grew up to approach the world with greater confidence.

FRANCIS: So these animals we put them in a little bit scary, big empty open tub. They explore the outer perimeter, they explore the inner perimeter, they're doing what rats do, which is explore.

CU of rat cage and the mother is not near the newborn rats.

NARRATOR: Not so for the low-licked rats.

CU of rat in large plastic tub.

FRANCIS: Animals that were raised in low licking and grooming environments hug the walls, they don't explore so much. They have significantly impaired exploration profiles or behaviors.

The tub experiment is conducted with a low-licked rat.

Off-camera colleague: We don't want to stress them out.

NARRATOR: The low-licked pups grew up to be vigilant and hypersensitive to noise or movement, on constant alert for threats, even when there were none.

Graphic: Brain animation

NARRATOR: In both rats and humans, the stress response evolved to help us survive danger. It begins with stress hormones like cortisol, flooding the brain in response to threats and challenges.

Graphic: Stress response in child's system

NARRATOR: A cascade of changes puts the body on red-alert, and we're prepared to fight or flee on a moment's notice. When the threat has passed, specialized proteins called glucocorticoid receptors bind with the cortisol, neutralizing it and shutting down the stress response.

CU of mother rat in cage.

NARRATOR: But the low-licked rats seemed unable to calm down. Meaney's team wanted to know why. So they looked at the regions of the rats' brains that process stress.

A machine is slicing a rat's brain into sections.

Off-camera colleague: So we're looking at rat brain sections, and we're slicing hippocampus sections.

Brain scans from the rats.

NARRATOR: When the team compared glucocorticoid receptors in the brains of high and low-licking rats, they had an answer.

FRANCIS: The red represents expression of the glucocorticoid receptor message. You can see with the naked eye, significantly less expression of the glucocorticoid receptor in offspring raised in low-licking and grooming environments. And that's crucial for dampening down further activation of the stress response.

Slide comparing high licked and low licked rat brains.

17:20 **NARRATOR:** Despite being genetically identical, the pups that had been licked less had fewer glucocorticoid receptors. With fewer glucocorticoid receptors, their stress response remained high. These rats stay on a fight or flight hair trigger.

Scientists working in a lab.

NARRATOR: Meaney turned to a second research group to study the genes responsible for producing these receptors.

Graphic: Methyl groups covering DNA model

NARRATOR: In the low-licked rats they found that methyl groups had attached to many genes, covering them up and preventing them from doing their work. The genes themselves hadn't changed. But with methyl groups in place, the genes can't produce as many glucocorticoid receptors and the result is ongoing stress.

Slide comparing high licked and low licked rat brains.

NARRATOR: This enduring physical change in the brain structure of the rats was brought about by purely social factors in early life: less licking and grooming.

CU of mother rat.

NARRATOR: Meaney and his colleagues found that the changes typically last for the lifetime of the rats. And they went far beyond the hypervigilance he initially observed.

MEANEY: You can see changes in the actual metabolic function of the animals. For example, animals that are licked more are less likely to become obese. And we know that in part that's because of the way the brain is then guiding the endocrine systems that determine metabolic health. So mother's licking is actually shaping an enormous array of traits that are then established in the pup and carried into adulthood.

19:03 DVD Chapter 6: Scarcity and Toxic Stress

A mother rat licks pups.

NARRATOR: Another group of researchers wanted to know why some rat mothers might provide less care than others.

Darlene Francis and colleague working in lab.

NARRATOR: And it turned out that that a social condition could influence that difference as well.

A mother rat frantically pushes around material in a cage.

FRANCIS: We're watching this mother do the best that she can. Her stress hormone levels are through the roof.

COLLEAGUE: It's like trying to build a nest in the middle of the desert. Not the most hospitable place.

Split screen of rat mothers trying to build nests.

NARRATOR: Rat mothers like to build nests for their pups with soft materials. But these moms have only been given hard, scratchy, inferior building supplies. It's a replication of an experiment first conducted by David Swett.

FRANCIS: They really devote a lot of resources to trying to build nests, because we took their nesting materials away, horrible researchers that we are.

A mother rat with bad materials neglects her pups as she pushes around materials.

FRANCIS: I think it's obvious that she's trying really hard, and she's tried really hard to provide as much of a nest as she can to her litter.

20:13 **NARRATOR:** The stressed mothers spend as much time with their pups as unstressed moms. But they lick and groom far less. The strain of providing shelter with few resources impeded the rats' efforts to care for their young.

FRANCIS: It wasn't a time issue, but the quality of what they were doing and how they were interacting with their pups was different, and we were able to identify that that directly related to measures of the stress response.

CU rat mother in cage with poor materials.

NARRATOR: A stressful environment led to a low-licking mother. That low-licking mother produced offspring that had trouble turning their stress response off. And this triggered a cascade of health and behavioral effects.

A fast motion shot of a crowded street.

NARRATOR: But laboratory rats are one thing. Would the same pattern hold true for humans?

21:45 DVD Chapter 7: The Wisconsin Study - Can Early Life Last a Lifetime?

A girl feeds her baby outside a rundown house.

NARRATOR: Many American families face an increasing load of stressors. More demands from their employers.

Archival: stills of struggling families.

NARRATOR: Less job security. Less time. Living paycheck to paycheck. Anxiety about the future. Could these growing stressors affect not only the parents, but their children as well?

Overhead view of University of Wisconsin.

NARRATOR: In 1990 a team of researchers at the University of Wisconsin began to measure the stress levels in working families that were about to have children.

Pregnant woman giving presentation.

NARRATOR: Some were well paid and relatively comfortable, others less so.

Pregnant woman watering garden with kids in background.

NARRATOR: But the strain of coping with an increasingly precarious middle class life was taking a toll on many.

MARILYN ESSEX, Sociologist, University of Wisconsin: They were stressed you know economically, they were stressed by having to work two jobs, you know just on and on and on with the stresses those families were experiencing. So we turned to them to looking at the long-term development on the children.

CU of infant being bottle-fed.

NARRATOR: Might parental stress alter the developmental paths of their young children? Essex and her team followed the families for more than two decades, charting stress levels, behaviors, school performance, and other indicators in the children.

Mom cooing at baby, followed by dad with kids at school.

22:54 **NARRATOR:** Stress was measured both by what the families reported and by the level of stress hormones in their blood and saliva. The results were clear: the higher a parent's stress early in a child's life, the more stressed the children became and the more that showed up in their behavior later in life.

Three young children look at the camera from a bed.

ESSEX: If you imagine a child that you're looking at in a kindergarten class, it's that child that, you know, is, is kind of anxious, isn't interacting with kids very well, but is aggressive and is impulsive.

Girl in classroom with her head down on her desk.

NARRATOR: As the kids grew, their stress levels remained high, even if their parents' stress level had fallen. In adolescence their lives still reflected their early life experience.

ESSEX: They have worse peer relationships. They have more problems with their teachers. So that is all kind of part of the package. I mean it has very long-term consequences that can go into adulthood. I mean the development of substance use, you know, teen pregnancies.

A blond girl looks at a train as it goes past.

NARRATOR: How was it that the early experience of their parents' stress had such a lasting impact on the children? The answer was hiding in their epigenome.

Graphic: DNA model epigenome

NARRATOR: Essex had been collecting cheek swabs and saliva samples from her subjects for many years so she could test for stress hormones. A leading molecular biologist heard about her work and realized that those samples also contained a treasure trove of genetic and epigenetic evidence.

Study subjects giving saliva samples, followed scientists working in a lab.

24:52 **MICHAEL S. KOBOR, Canada Research Chair in Social Epigenetics, University of British Columbia:** She had done absolutely fascinating and groundbreaking work. And so we teamed up and we got enough money to epigenetically profile a hundred children in her cohort. What we found is that in these sixteen-year-old kids or adolescents, their dimmer switch pattern could be correlated to the level of maternal stress during infancy.

Adolescents mill around in school hallway.

NARRATOR: Kobor had discovered epigenetic patterns in the teenagers that corresponded to the amount of stress their parents had experienced fifteen years earlier.

Gene-sequencing chart.

NARRATOR: This was a first: hard evidence that simply living in a home full of stress could modify the epigenome of infants. The second-hand stress they experienced as infants had increased their risk for long-term behavioral problems.

Pedestrians at busy Boston intersection.

NARRATOR: The struggles of working families in America, the study showed, had exacted a price on the lives of their children through changed epigenetic settings.

Split screen shows both rats with poor materials and adolescents in school.

NARRATOR: It was an eerie replay of the earlier study of rats. In both cases severe and consistent maternal stress in infancy had resulted in persistent epigenetic changes in offspring. And the children suffered the same host of knock-on effects as the rats.

ESSEX: Over a lifetime it wears and tears on your system. You end up with association with cardiovascular problems, with all kinds of psychiatric problems, with obesity, and you know a wide range of kind of health and mental health kinds of problems.

Young girl walks down street with her backpack.

A paper on the Wisconsin study.

NARRATOR: If the development of the mostly middle class children of the Wisconsin study can be altered, what about the millions of American children further down the socioeconomic pyramid?

Rundown neighborhood.

27:11 DVD Chapter 8: The Wealth-Health Gradient

Tracking shot of newborn babies in the hospital.

NARRATOR: In societies around the globe, researchers have found a correlation between family wealth and well-being. The more affluent and high status the families, on average, the fewer adversities their children are exposed to, and the better their outcomes. While many factors contribute to this wealth-health gradient, the Wisconsin study raises the question of whether epigenetic changes might occur throughout the population on the same sliding scale that connects wealth, power and status to well-being.

Father walks with son out of gate and across street.

NARRATOR: The idea is unproven but provocative. Because if social and economic adversities can alter the epigenome along a continuum corresponding to social status, then addressing social conditions becomes not just a moral question, but a necessity for the success of our society.

A young girl stand outside a door in a red coat, with her family on the steps.

NARRATOR: Twenty-five percent of U.S. children, one out of every four, are born into poverty. They live with food and housing insecurity and with safety concerns. They are exposed not only to more environmental hazards, but more noise, more hardship, more violence, and more social stressors than their wealthier peers.

Working mom in her office with her son.

NARRATOR: And in the middle class, so many families are increasingly pressed for time, for money, and for resources. Could the epigenomes of these children be modified by their social and economic conditions just as those of the Wisconsin children were? Are they too being biologically primed for more difficulties in life?

Kids playing on monkey bars.

NARRATOR: And if they are, what can be done?

29:33 DVD Chapter 9: Reversability

Children and their mothers/caretakers playing in a park.

NARRATOR: Humans are resilient organisms and studies show that negative epigenetic effects need not be permanent.

DOLINOY: Unlike a genetic mutation, which we can do nothing about, an epigenetic change we may be able to do something about.

CU of brown and yellow mice.

NARRATOR: When Dana Dolinoy fed her pregnant yellow obese mice an enriched diet, they gave birth to healthy, brown slender pups. The right environment was able to reverse the effects of a chemically induced epigenetic change. And Michael Meaney was able to reverse the epigenetic effects of his nervous, low-licked rat pups.

MEANEY: At the time of weaning we put them into enriched circumstances similar to a daycare environment. And we then studied these animals in adulthood and when we looked we found that in fact there was a huge effect of enrichment.

Archival: stills of rats in play environment.

A shot of a rat in the tub experiment.

NARRATOR: The low-licked rats in this study behaved more like high-licked rats, exploring their surroundings with more assurance and less fear. The enriched environment induced new changes to the epigenome, which overcame the effects of their early epigenetic programming.

Graphic: DNA Epigenome Sequence

NARRATOR: The research led to a key new understanding of how the genome works. While genes never change, the epigenome can, at key points in life, be remarkably plastic, adapting to individual experiences and changing social conditions.

31:28 DVD Chapter 9: Biology and Public Policy

Shots of children in rundown areas.

NARRATOR: Epigenetic changes have been linked to adverse environments associated with a host of ill effects: anxiety, depression, poor learning, obesity and even cancers. They can change the course of a child's life. For a growing number of scientists, the implications of these findings are clear.

MIRANDA: At some point or another we need to decide as a country that we will not tolerate one out of five children growing up in poverty. That we have to invest in our children.

DOLINOY: We do have the responsibility to try to mitigate against these effects.

MIRANDA: I think it means strengthening our schools. I think it means universal pre-K. We have got to do something to create more protective environments for our children.

Shots of toddlers learning to walk.

NARRATOR: The evidence from Wisconsin and other studies suggests that children do better when their families and communities do better.

Children running with caregiver.

NARRATOR: Assuring all children safe, stable and nurturing conditions could leave a profound biological imprint, increasing their chances for better mental and physical health and for more resilient and successful lives.

MEANEY: We know, for example, that when populations move into more favorable circumstances, when populations are freed somewhat from oppression, politically and socially, that they become healthier.

Children running on playground. Young children in classroom.

NARRATOR: The question for the United States is: How can we create environments that enrich the lives of all young children, and their families, allowing them the opportunity to realize their full human potential?

MIRANDA: Our obligation in this situation is to be optimistic, to say the science is helping us to understand this better. The science is giving us more opportunities for creative interventions that can lead to better outcomes for children, and you just have to keep working at it, and working at it, and working at it and trying to be optimistic that we can change outcomes for children.

Two children are playing on a roundabout. Toddler taking steps.

MEANEY: There are going to be constraints. But in large measure we can engineer environments that make individuals healthier, happier, more prosperous and more productive. And there's a very real biology to that.

CU of young child on roundabout.

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