

FUELING GENDER

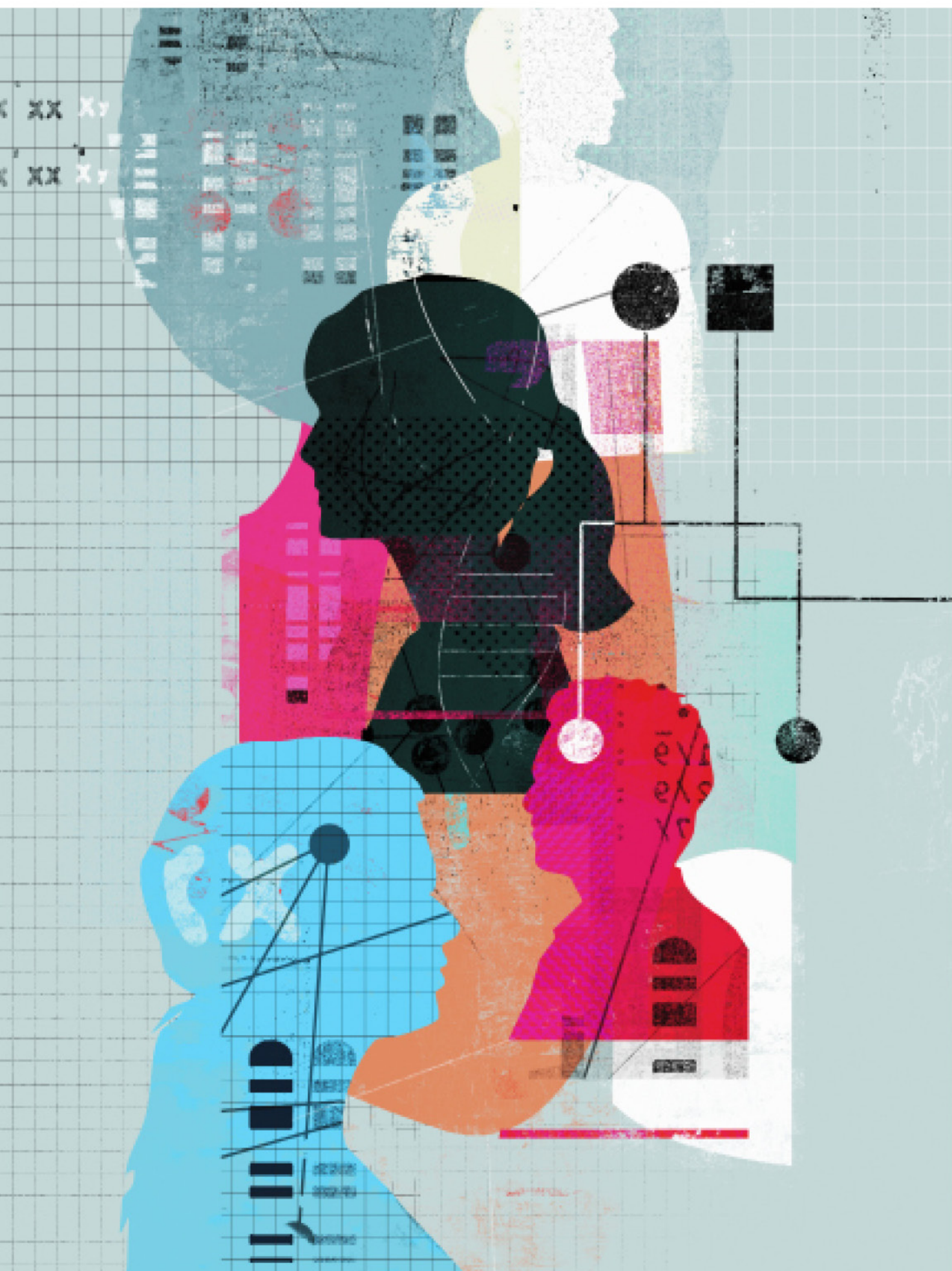
From in the womb to well past puberty, genes and hormones shape and drive gendered behavior—whatever that means—and gender identity too

BY JEANETTE BEEBE

T“THESE ARE MY FAVORITE SHOES,” 12-YEAR-OLD LC, WHO LIVES IN Cincinnati, says, pulling a size-6 pair of heels from her closet, “because they’re like a rose gold, and they’re really pretty.” She’s proud that she can walk in them easily, but she concedes that the experience is not without pain. “My feet get blisters, because it’s tight around the toe area,” she says. Maybe she’s OK with that because she already knows that being uncomfortable sometimes is part of being a girl—wearing too-small shoes and shrugging it off, as long as they’re cute.

LC is the oldest of three, and as with all firstborns, her childhood milestones are a new experience for her parents. “I’m a little nervous for the day when she can wear my shoes,” her mother, Jessica Cicchinelli, says with a quick laugh.

That day is coming, as LC approaches puberty—and as a transgender girl who was assigned male at birth, she’s likely to face a few more struggles than her classmates. “Chromosome-wise, she was born a boy, as far as her anatomy and things like that,” her father, Chris Cicchinelli, explains. Though Chris admits he struggled at first and even





For most of early childhood, despite heavily gendered clothing and social norms, there is little that biologically distinguishes boys from girls. That begins to change at the onset of puberty.

blamed himself when LC began her social transition with new pronouns, new clothing and a new name around the third grade, he eventually adjusted.

“This is our child. This is her process. It’s her life,” he says. “I don’t want my child to look in the mirror and hate themselves or not like the way they look because they were born a certain way. I want to do everything I can possibly do to help this child look and feel like who they are inside and on the outside.”

To ensure that this happens, LC will undergo hormone therapy to put puberty on pause. “It’s not even a question. She wants to do this,” Chris says. “She does not want to develop the Adam’s apple, the dark hair on her legs and facial hair. She’s scared of that,” Jessica adds. “She’s made it very clear that she does not want to be a boy.”

“She wants to be a girl. I mean, that’s who she is,” Chris says. “As a parent, what we have to do is give her the best odds.”

LC’s parents aren’t alone in discovering that gender is not as simple as it once seemed. From the time the human species emerged, it was clear to us that we were binary beings, designed in two varieties,

male and female (within Western industrial society, that is—hundreds of cultures throughout time have recognized more than two genders). The more we learned about biology, the more we thought we understood that there were two basic drivers of the gender divide: our genome—especially the X and Y chromosomes that determine a male and the two X’s that determine a female—and our hormones, the fuel for the genetic engine. These hormones, which are with us for life, operate most dramatically at two developmental moments: in the womb and, later, during puberty, when they trigger explosive physical and emotional changes, turning the child into a sexually mature young adult.

But we knew less than we thought we did. If our growing understanding of LC and other transgender people proves anything, it is that although genes and hormones are surely key players in determining our gender and our sexuality, they are only part of the equation. There are other factors—still only partly understood—that play a role in how gender works. The more closely we look, the more we are teasing them apart.



Hormones could play a role in different types of behavior. For example, testosterone has been linked to more aggressive behavior and increased risk-taking, as well as attempted dominance.

THE HORMONE THAT gets to work especially early is testosterone, which is produced by fetal testes at around eight weeks of gestation. It triggers many of the anatomical changes that distinguish baby boys from baby girls. Before that, we are all unsexed, with genitals that haven't turned into penises or vaginas and gonads that haven't turned into testes or ovaries. And if you've ever wondered why males have nipples, it's because everybody starts out with them, but it's only in females that they're eventually put to work.

Distinctive as those differences are anatomically, at birth and through much of babyhood and childhood, they're not always evident. Dress a young boy and a young girl in gender-neutral clothes and give them gender-neutral haircuts, and it can be awfully hard to guess which is which.

But dramatic changes occur again at the outset of puberty, when androgens (sex hormones responsible for male-type sexual development) and estrogens (sex hormones responsible for female-type sexual development) surge. Working in an axis with the hypothalamus and the pituitary gland, they

make the human body sexually dimorphic—with boys more physically male-typical and girls more physically female-typical. The hormones are manufactured in the gonads—the testes and ovaries—and they're synthesized elsewhere in the body.

One of those places is the brain, where they shape behavioral development during puberty and well into adulthood. This is especially true for the amygdala, the portion of the brain that processes and gives rise to some of our most powerful and primal emotions. Hormones affect how we think and feel, which affects mental and physical health in our day-to-day life. They can also play a role in complex issues such as substance use, sexual activity, and impulsive or even violent behavior.

"Hormonal mechanisms seem to have an impact on things we're probably not aware that they have an impact on," says Lisa Welling, a behavioral endocrinologist at Oakland University in Rochester, Mich. "They affect our relationships with others, various aspects of our psychology, our mood and things like jealousy, mate guarding and who we are attracted to."

Testosterone, for example, has been linked to

aggressive and risk-taking behavior, as well as attempted dominance. It works in response to the environment—how the boy or man lives, including how much pressure he’s under and whether he lives in a stable or unstable home, goes to a good or bad school and holds a satisfying or unsatisfying job.

Cortisol, a marker for stress, is also part of the hormonal soup, released in what the body sees as fight-or-flight situations—even if all that’s being fought or fled are everyday stressors like work deadlines or heavy traffic. Some studies have indicated that females tend to have higher cortisol levels than males, though that can change depending on age and circumstances.

Of course, courtship and flirtation can get hormones spiking. In one study, researchers found that when heterosexual males merely talk to a woman they find attractive, testosterone levels jump by 14%. In both men and women, flirting leads to a surge in the brain chemical nor-epinephrine, which acts as both a neurotransmitter and a hormone.

HORMONES DON’T OPERATE independently. Much of what they do happens in collaboration with genes. In the womb, the sex-determining region Y (SRY) gene and the hormone dihydrotestosterone (DHT) are the joint spark plugs that get sexual differentiation going. With high levels of DHT and the SRY gene on the Y chromosome, the journey toward being male begins. Lower DHT and no SRY gene leads to a female.

Not everything, however, always works out according to the blueprint. Sheri Berenbaum, a professor of psychology and pediatrics at Penn State University, has worked with children and teens with classical congenital adrenal hyperplasia (CAH), a rare genetic disorder in girls with the normal pair of XX chromosomes (in some rare cases there may be three X’s) caused by exposure to a high level of androgens in the womb. This overexposure can cause a fetus with two X chromosomes to develop ambiguous genitalia.

That part of CAH was always obvious, but Berenbaum posits that the condition is associated with other changes as well, seemingly nudging girls toward activities that are typically thought of as boy-like. “We basically find that prenatal androgens

influence what children play with and the activities they engage in, but not very much their gender identity,” she says. The girls, in other words, identify as girls, even if they sometimes act in ways that are traditionally identified as boyish.

Cognition and learning too may be affected by gender hormones, especially testosterone. That’s an idea fraught with potential bias, because it’s a slippery slope to the idea that males or females are inherently better at some disciplines and worse at others. A recent paper reported that girls with CAH tend to express more interest in STEM careers than other girls. A meta-analysis of studies looked at whether girls with CAH do better on spatial-

reasoning tasks in the lab—such as the ability to mentally rotate an object—and it did find an association. That’s in keeping with consistent findings that men tend to outperform women on spatial tasks.

Still, what is broadly true for a gender is not always true for an individual. Although men and women “do exhibit differences in brain formation and behavior,” Welling says, “the variance within each sex is far greater than the variance between each sex.” In other words, the sexes are more similar than different.”

WHAT THIS MEANS for LC and other transgender children and adults is a larger and more complex question. As with sex, the gender with which a person identifies surely has its origin in the womb. “This is almost the opposite of gender as a social construct,” says Karissa Sanbonmatsu, a structural biologist at Los Alamos National Laboratory, who is transgender. “Even though all of society—parents, school, TV, social media—is telling someone that she’s a boy, somehow, inside her, she knows she’s female. And we think this is due to the brain differences,” she says. “The working model is that generally speaking, the genitals tend to differentiate to male or female much earlier than the brain differentiates during pregnancy.”

The theory, says Sanbonmatsu, is that in that interval, “there’s some change in the hormone mix inside the womb that somehow causes the genitals to transform one way but the brains to transform the other way.”

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Research suggests that being transgender may depend on genetics and environmental factors in the womb. Additionally, researchers believe that it may run in families, but more research is still needed.

Sanbonmatsu is now exploring another part of the gender puzzle: brain structure. She and Rupert Lanzenberger, an associate professor in the department of psychiatry and psychotherapy at the Medical University of Vienna, are conducting neuroimaging to look for any telltale anatomy that acts as a marker of gender identity. It is, in many respects, terra incognita research. “There have been no extensive studies done to date,” says Sanbonmatsu. “So we’re trying to do the first one.”

Even if Sanbonmatsu and Lanzenberger do find something in the architecture of the brain, it still won’t fully explain the ineffable nature of gender identity—the deep sense of simply knowing who we are, whether our anatomy agrees with that or not. “Gender is an internal sense, a conviction,” says Lee Ann Conard, who manages LC’s gender treatment and directs the Living with Change Center at Cincinnati Children’s Hospital.

The center is open to any transgender, gender-expansive or gender-questioning child, adolescent or young adult who walks in the door. Launched in 2013, in the past six years it has supported 1,500

patients ages 4 to 24, with about 75 patient visits a week. A physician or nurse practitioner performs an assessment, and patients may be seen by a social worker and therapist as well.

“With younger children who are just starting through puberty, what we do is [hormonally] suspend puberty to give them time to figure out who they are,” Conard says. “These treatments are totally reversible, so there’s no harm, no foul.” If a child’s family chooses to, the child can “continue through the puberty of the gender that you were assigned at birth or through the gender that you are.”

There are obstacles along that path, but there is surely a sense of adventure too—one that demolishes the binary male-female divide and opens instead a new gender frontier. Anne Fausto-Sterling, a leading expert in biology and gender development and professor emerita at Brown University, has long argued that gender—biological, behavioral, social—should exist on a continuum. For all of the challenges children like LC might face, they may be paid back in a journey of discovery that the cisgendered never experience. □