



# The Science of Sex

Historian and philosopher Sarah Richardson interrogates the science of sex and gender.

**T**HE “SINS OF THE MOTHER,” trumpets a headline in the journal *Science*, warning of a “maternal assault” against children. Another headline calls mothers “smoking guns,” the source of incalculable harm. What wrongs have these mothers committed? Not any sort of physical violence: these articles describe a series of subtle, poorly understood chemical changes, passed from mother to child during pregnancy, that cause obesity and other long-term impairments.

But such charges stand on shaky ground, declares Sarah Richardson in her forthcoming book, *The Maternal Imprint* (University of Chicago, 2020). The author, professor of the history of science and of studies of women, gender, and sexuality, has spent her career researching the history of scientific ideas: where they come from,

and what happens once they are unleashed in the public sphere. Historians of science like Richardson are interested not just in the idealized

process of empirical discovery, but in the ways its all-too-human participants are guided and misguided by their scientific tools and the cultures and institutions that support them. *The Maternal Imprint* is a history of the idea that a woman’s actions or environment during pregnancy can affect her children’s and even grandchildren’s health and welfare throughout their lives.

It’s an idea that dates back to Aristotle, who declared that mothers had merely to glance at an object to imprint some quality of that object on her child. But in recent decades, scientists using the tools of epigenetics have examined the molecular basis for such claims as never before. Epigenetics (literally meaning “on top of” genetics) is concerned with chemical modifications to DNA that *don’t*

**by Bennett McIntosh**

change its sequence, but can still be perpetuated as cells divide, affecting genes' function in complex but profound ways. It's a field of compelling possibilities, demonstrating that DNA sequence is not destiny—and putting forward specific chemical explanations for why events during gestation might manifest as health problems later in life.

"I was drawn to it," says Richardson about epigenetics' holistic view of human development, but "I pretty quickly became deeply ambivalent." While *in utero* exposure to specific dangers like the chemical thalidomide or diseases like rubella and syphilis has well-documented effects, those exciting early results seemed to give momentum to far-reaching claims about the dangers (or advantages) of everything from chocolate to the traumas of World War II. These claims routinely reach the public as scientific truth despite their origins in small studies and the even smaller effects they report, and despite study designs that have taken as a given that *in utero* effects—rather than genetic or postnatal effects—were the only effects worth considering.

"Some of these studies don't even include fathers," Richardson says—"and this includes mouse studies, so it's not a question of having access to the fathers." She worried that this bias became self-reinforcing: scientists looking for the epigenetic origins of disease examined primarily maternal effects, because that's where much of the knowledge, funding, and publicity were. As the influence of the father, and of life after birth, are left underexamined, she says, pregnant mothers must bear "fierce, punishingly harsh" blame for their children's ill fortune from scientists, doctors, policymakers, and the media.

"My book doesn't offer pregnancy advice," Richardson is quick to say. What it does offer, she writes, is "insight into how and why claims about the long reach of the womb are at once beguiling, challenging to validate, stubbornly persistent once launched, and beset by scientific controversy."

Her critique gained circulation among fellow scholars years before her ideas became the book. "It's changed my whole outlook, on everything I do," says Gemma Sharp, a lecturer (professor) in molecular epidemiology at the University of Bristol in England, who met Richardson in 2017. The two soon collaborated on a pair of papers examining the "looping effect" caused by assuming the mother's influence is paramount: they urged researchers in Sharp's field not to let previously discovered correlations—or the hype surrounding them—bias what they considered in future studies. "I got a grant last year [2018] that I wrote trying to incorporate a lot of these ideas," in studying the prenatal origins of infant health, Sharp adds. "I built into the grant from the start that I would look at mums and dads." She also specified that the research would be guided by a panel—including Richardson and expecting couples—to help her understand what knowledge gleaned from the study would matter most to parents.

"KNOWLEDGE THAT MATTERS," Richardson says, is her mantra. Throughout her career, such knowledge has come from carefully considering the fraught overlap of sex, gender, and science.

Though "gender," in popular use, is often simply a synonym for "sex," for the scientists and scholars who study them, they are distinct. "Sex" is the biological category: the coalescence of genes, hormones, and anatomy shaped by eons of evolution to differentiate males and females. "Gender" is the cultural category: the "mascu-

line" and "feminine" behavioral expectations and social roles commonly expected of the sexes.

How did the X and Y chromosomes come to be seen as the essence of biological sex? What does that history mean for the researchers who study them—and everyone who carries them in their cells? How can medical research account for the distinct but entangled influences of sex and gender? For Richardson, these questions cannot be answered without interrogating the assumptions embedded in the very words used to ask them.

Much of this questioning now happens during meetings of the GenderSci Lab, a research group that Richardson officially established when she gained tenure in 2017, but which grew from a reading group that began in September 2010, just weeks after Richardson arrived at Harvard as an assistant professor. That group was started by Meredith Reiches, Ph.D. '12, then a doctoral student in the department of human evolutionary biology (HEB), who had just returned from fieldwork in The Gambia. She had all the samples and data she needed to write her dissertation on how adolescent girls' bodies balance the energy demands of growth and puberty. But she had left The Gambia with lingering questions about the unintended impact of work like hers on the women and girls she was studying.

Reiches invited other students and trainees in her field and related areas to a reading group that would discuss the history of their field and of its assumptions about gender and sexuality. She invited Richardson as "a bit of a Hail Mary," she says, expecting a faculty member in a distant department would have other things to do, but "to my astonishment and delight, she showed up." At first, Reiches was more dismayed than delighted at the focused intensity of Richardson's questions throughout the discussion, until "we actually sat down together and talked about our intellectual training, [and] I understood that she was trained as a philosopher and this mode of questioning was a way of conveying interest and respect."

It's a habit Richardson was introduced to as a philosophy major at Columbia, thanks to the happy concurrence of a class taught by philosopher of science Philip Kitcher, which taught her to question the assumptions scientists make, and one taught by the feminist psychologist Lila Braine, which showed her, she says, that when it comes to investigating scientific ideas about sex and gender, "there are so many low-hanging fruit." As a Ph.D. student in Stanford's interdisciplinary Modern Thought and Literature program, she learned as well to study the history of ideas, mining archives, publications, and interviews to try to understand what coincidences of culture, ideology, empirical fact, and pure luck give rise to these assumptions.

The GenderSci Lab now meets in Richardson's basement office in Boylston Hall. Though the only beakers are held by a Marie Curie bobblehead on her desk, the focused and collaborative inquiry on display in lab meetings would be familiar to any scientist. At a July meeting, conversation moved rapidly between a practical task and a high-level theoretical discussion as the lab juggled edits to a soon-to-be-published paper on women in STEM jobs and talk about a nascent project to study how online communities associated with the white nationalist "alt-right" use and abuse ideas from evolutionary theory to prop up their ideology. Lab members discussed their own research projects, ranging from probing large epidemiological data sets to understand whether health outcomes stem from the cultural influences of gender factors (such as high



heels, employment disparities, or discrimination) or sex factors (hormones, genes, and biochemical development)—or both—to a review of *amicus curiae* briefs to understand how scientific ideas about gender become translated—and mistranslated—into policy. And they congratulated Reiches, now an assistant professor of anthropology at the University of Massachusetts, Boston, for winning an international award for feminist scholarship with the publication of a paper on that research in the Gambia all those years ago.

“There isn’t any other space like this operating in the U.S. right now,” says Heather Shattuck-Heidorn, Ph.D. ’17, who also met Richardson at the reading group’s first session. “Where you have a group of scientists and feminists who explicitly are supportive of empirical science, coming together...to ask what’s the science-savvy feminist take on X, Y, or Z?”

THE X AND Y chromosomes were at the center of Richardson’s first big foray into the history of sex and science. The story told in introductory biology textbooks is relatively simple: each set of parents confers 23 chromosomes on each child—22 of which are matched pairs and two of which, the X and the much shorter Y, determine sex. Males have an X and a Y, while females have two Xs, and from this all the other hallmarks of sex—gonads, hormones, genitals—follow. It’s a more complicated story than that, of course: a wide variety of intersex and related conditions exist, for reasons from atypical hormone exposure during development to extra, missing, or atypical X or Y chromosomes. But these exceptions aside, the X and Y chromosomes have for decades been seen as the expression of one’s “true” sex or of “sex itself.” It’s the job of a science historian to uncover where these stories come from, and why.

Richardson’s doctoral dissertation, published in 2013 as *Sex Itself: The Search for Male and Female in the Human Genome*, does just this, tracing the history of the idea that sex is centered on the X and Y chromosomes. Early in the twentieth century, she shows, it was controversial even to refer to them as “sex chromosomes” because they don’t always correspond with anatomical sex. But the fact that sex chromosomes are visible under a microscope (unlike the genetic markers for essentially any other trait) made them useful enough to two groups of scientists—those working to establish the role of chromosomes in heredity and those working to untangle the role of hormones in sex determination—that the association between chromosomes and sex solidified for decades. Since then, scientists have projected not only *sex*-related but *gender*-related expectations on them: some call the X chromosome “she” and the Y “he,” (though men, too, have an X chromosome); others speak of “defend[ing] the honor” of the “vigorous” Y chromosome against competing scientific theories that slander it as “wimpy” and “pathetic.”

Such characterizations, writes Richardson, may be tongue-in-cheek, but equating “sex” with “the sex chromosomes” has serious consequences, such as the “criminal chromosome” theory, the hypothesis popular throughout the 1960s and ’70s that males with one X and two Y chromosomes (a rare disorder whose subjects are taller, and more likely to be arrested, than average) were hyperaggressive “supermales” driven by that “criminal” extra “Y.”

In fact, more “Y” doesn’t mean more male: it’s now widely accepted the tall XYY stature derives from growth-promoting genes found on both X and Y chromosomes, and the arrest rates are driven by intellectual difficulties common to many chromosomal disorders. But the “supermale” theory held sway for two decades against

mounting evidence that males with one Y and two X chromosomes had similar stature and arrest rates to the XYY males. To discount that evidence, some researchers even relied on the widely accepted gendered expectations to explain away the similarities in arrest rates between XXY and XYY males, postulating that problems for XXY males resulted from “hyperfeminine manners...passivity, emotionality, and subpar intelligence.”

The “supermale” theory was finally discredited by the 1980s, but in *Sex Itself*, Richardson argues that it made the Y chromosome the star of sex-difference research in a way that still reverberates. She points to scientists like David Page, M.D. ’84, a geneticist at MIT, whose search for the genes that determine sex meant a laser-like focus, from the late 1980s through the early 2000s, on mapping the Y chromosome and discovering which part of it led to the development of the testes. Such a focus was not inevitable, Richardson writes: from the 1920s to the 1950s, based on evidence in fruit flies, researchers saw the X as the driver of sex-determination. And scientists now understand sex differentiation, in mammals as in other species, as the result of numerous interconnected genetic “switches,” some on the X and Y and others on the other 22 pairs of chromosomes. But from the mid 1980s, Page and his colleagues studying mammals focused on the Y and the testes.

WHEN A HISTORIAN like Richardson turns her critical examination from people long dead and events safely past to those whose participants are still-living experts in their field, they can—and often do—dispute her accounts. Page’s reaction to Richardson’s narrative in *Sex Itself* is illustrative: He agrees there was a focus, even an over-focus, on the Y and the testes in research of that era, he said over the phone. But he does disagree with Richardson’s answer to why the focus on the Y.

In Richardson’s history, the XYY research looms large in later researchers’ decisions to focus on the Y, but Page responds that research on XYY males “did not interest me, it did not impress me, it did not look to be the foundations of a path forward.” Mapping the Y, he says then, was not inspired by the popular image of a masculine Y that XYY research built, but was the most “tractable” research path, and “was very much grounded in the strength of the empirical data.”

Richardson’s intent, she says, was not to disparage the motivations of individual scientists: instead, she shows that, at the start of Page’s career in the 1980s, the structures of sex-determination research were focused on the Y, whatever Page’s personal motivations. XYY research played no small part in this. “What inspires some resistance to these ideas,” says Richardson, “is the assumption that it implies that the work is not scientific. But the tradition that I come from suggests that all science is social, that we use the resources around us to reason about the world.” Science is not motivated solely by *either* empirical reasoning *or* gendered bias. “It can be both!”

As she writes in *Sex Itself*:

XYY studies... represented the primary work on the human Y chromosome for two decades. XYY spurred interest [in the Y]..., prepared the ground for future Y chromosome research, and rallied researchers and resources to the study of the Y. XYY research also helped to cement a working model of the Y chromosome as the chromosome for maleness that... remained extremely influential in the coming decades.

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“That’s the cool thing about the history of science,” she says. “This is where I get very happy, when I’m in that space of trying to hash out the causal story.”

IT COMES EASILY to Richardson to think of science as a human endeavor inextricable from other human forces driving it. Her maternal grandfather, pioneering molecular biologist Martin Rodbell, helped discover G proteins: molecules that help pass signals between and among cells. Richardson recalls his sharing the “genuine joy” he took not only in his research, but also in its wider context: “He constantly talked about the practice of science, the things he valued about it, and about the changes in the field that bothered him. He worked at the [National Institutes of Health] for all his career on basic science, and bemoaned the corporatization of science, bemoaned the need to constantly produce applied findings.”

That commitment to basic science paid off in perhaps the biggest way possible: Rodbell shared the 1994 Nobel Prize in physiology or medicine for his role in discovering the G protein. “I lay claim to picking up the telephone on the day that he received the call, on my little Garfield telephone,” says Richardson. “I was 14, and he happened to be visiting us, so we were together when he won the prize.”

But Richardson’s family had also been touched by one of the most horrific chapters in the history of science. “My grandma, my Oma, was born in Berlin in 1925,” she explains. “At the age of eight, she and her family moved to the Netherlands—they were a Jewish family—and at the age of 15 or so she went underground. Her family was deported, and ultimately murdered at Auschwitz. Her mother, her father, her sister, her grandmother, and many other aunts and uncles.” Barbara Ledermann escaped to the United States, where she met and married Rodbell, but her experience reverberates today: “The unbearable, unspeakable loss, to imagine my mother growing up with no relatives on that side of the family,” says Richardson. “I think it’s foundational.”

She opens *The Maternal Imprint* by contemplating how the consequences of such unfathomable horror can be passed down from one generation to the generations thereafter. She cites research on Holocaust survivors and their descendants from neuroscientist Rachel Yehuda, who argues that mothers who survived the Holocaust may have children more susceptible to trauma, because elevated stress hormones in utero can result in chemical modification of fetal DNA. If these children are female, their own egg cells, developed while they were still in utero, may pass this molecular legacy of tragedy on in turn. “As the matrilineal granddaughter of a Holocaust survivor,” Richardson writes: “I could not help but be curious about these claims.”

*The Maternal Imprint* is written in the context of this eagerness to understand intergenerational connections. Richardson may have come away from her research skeptical of particular claims, includ-

ing Yehuda’s, of the past’s imprint on our genes. But she sees clearly the imprint of her grandmother (now 94 years old and still “bright-eyed” and “formidable”) in her own work. The Nazi state, Richardson points out, guided and justified its murders with the logic of eugenics, an international scientific

movement—supported by Harvard president emeritus Charles W. Eliot, his successor A. Lawrence Lowell, and alumni including Oliver Wendell Holmes Jr. and Henry Cabot Lodge—that resulted in the forcible sterilization of as many as 70,000 people (see “Harvard’s Eugenics Era,” March–April 2016, page 48). “This for me is part of my grounding in a very fierce tradition of social-justice work,” she says. “From a very, very early age, I understood that great wrongs can occur, even by those who purport to be the most educated, the most developed, so to speak, and that what needs to be cultivated is intellectual courage, the ability to speak out, the ability to resist.”

For Richardson and the GenderSci Lab, speaking out means challenging harmful uses and misuses of science, whether by white nationalists or by well-intentioned biologists who might benefit from a fresh look at seemingly fundamental ideas, such as the nature of sex itself.

WITH THE COMPLETION of *The Maternal Imprint*, Richardson has returned to the deep question that animated *Sex Itself*, which she feels remains unanswered: what, actually, is sex?

The “sex essentialist” view interprets sex as a fundamental category that divides humans and other sexually reproducing organisms—whether plant, animal, or fungus—neatly into two types. Evolution may tweak its trappings—hormones, chromosomes, anatomy—between species and over time, but sex itself remains constant.

Yet nature is full of examples that defy this pat view. Plants and some snails are mostly hermaphrodites, many reptiles develop sex based not on genetics but on temperature, female bees have twice as many chromosomes as male drones, and fungi can have dozens, or even thousands of sex-like “mating types.” In the lab, samples of human cells—many of which have been reproducing asexually for years—have been known to spontaneously lose their Y chromosomes or double their X chromosome, raising the question of whether such cells can be rightly said to have a sex at all.

Research into the extent of these differences continues: in July, David Page, the MIT geneticist, published a study of five different mammalian species that compared the sex-related genes that occur on all their chromosomes (not just on X and Y). Even though all these mammals use the same XX/XY sex-determination system, he found that the genes on the other chromosomes that determine *other* sex differences—from brain development to stature disparities—vary greatly from species to species, even between *Homo sapiens* and close cousins such as macaques. In many cases, genes that were amplified in the *males* of one species were amplified in the *females* of other species.

In contrast to “sex essentialism,” then, Richardson proposes a mind-set of “sex contextualism.” Instead of seeing chromosomes (or anatomy, hormones, or some yet-to-be discovered biomarker) as

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“sex itself,” she encourages seeing each of these categories as “sex-linked variables”: they are *related* to sex, but in a changing, contextual way. Biologists generally acknowledge that the biological variables related to sex vary greatly across space, time, and species, but Richardson says this variability must be treated not as a tacked-on caveat, but as central to how the study of sex is conducted.

Thus, she says, scientists need to be extremely careful about applying to humans their results about sex differences—whether in the effect of a drug to a behavior—gleaned from lab animals or even human cell samples (which don’t experience puberty, let alone misogyny). When the NIH promulgated a policy urging scientists to report their findings about male and female test subjects—worm, rat, or human—separately, Richardson and other GenderSci Lab members published opinions everywhere from the *Journal of Neuroscience* to the *Washington Post* urging scientists not to expect those reported differences to generalize to humans. “I’m actually arguing that...a requirement to include both types and to report and compare by sex type [is] inadequate to address the stated goals. You want to address gender inequalities in medical outcomes? It’s inadequate to just study male versus female. You

want to understand how sex is operating in a particular animal or tissue model? It’s inadequate to just compare the two. Sex is working at multiple levels and in different ways.”

Richardson hopes the idea of sex contextualism will be

useful not only to biologists, but also to transgender and intersex people fighting for legal recognition against sex essentialist laws that try to fit them into categories that simply don’t apply. That’s “Knowledge that matters,” from the lab bench to the state house.

Page, the subject of so much of Richardson’s first book, says he’s eager to see how her newest ideas—on sex contextualism—apply to his newest research on sex differences. “The next chapter” of that history, he says, “is currently being written,” in his lab and others around the world, and in Richardson’s own research.

It will take some time, says Richardson, to turn sex contextualism into a fully fledged philosophical theory, thanks in no small part to the countless ways that sex matters for biology, scientific research, and culture. “All of these implications,” she says, “will be fun for me to work out. And then someone can critique it, once it is out there as a fully thought-out, positive system for thinking about what sex is. Then we will really get a debate going.”

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