the average of other livestock categories such as pork and poultry. Beef production also creates five times the amount of greenhouse gases and six times as much water-polluting reactive nitrogen.

"Farmers do a bunch of things" to the earth's surface to affect the rate at which hydrobiogeochemical processes occur, Eshel told his audience. Most importantly, they add nitrogen as fertilizer and they modify drainage so irrigation water leaves the soil almost as quickly as it arrives, to speed plant growth and keep roots from rotting. But these chemical and physical modifications have an unintended consequence: they degrade the ability of soil biota to neutralize reactive compounds. Such microorganisms require soil that retains water to do their work, which takes place slowly and steadily, he explains. By speeding up surface and soil hydrology, "You basically degrade an ecosystem's ability to render those otherwise dangerous compounds harmless." Ultimately, the reactive-nitrogen-laden runoff reaches the coastal ocean, where it severely depletes levels of dissolved oxygen, leading to massive fish kills in places like the northern part of the Gulf of Mexico "near the Mississippi River mouth."

Beyond its contribution to water pollution, agriculture is a significant source of greenhouse-gas emissions: nearly 10 percent of the total in the United States for agricultural production, rising to roughly a quarter when the entire food chain, from farm to plate, is considered. But the vast majority of those emissions are attributable to livestock. Almost half of the total land area in the lower 48 states (1.9 billion acres) is devoted to agriculture: various pasturelands represent about a third of that, while corn, hay, and other feed crops account for almost all the rest. By comparison, all the lettuce, tomatoes, fruits, and nuts people eat (including apples, citrus, and almonds) are grown in less than *one-half of 1 percent* of the agricultural lands: "a minuscule fraction of the total," Eshel pointed out. Switching to a plant-based diet, his research has shown, would eliminate about 80 percent of greenhouse-gas emissions attributable to agriculture in the United States, because most of that comes from ruminant livestock emissions, and growing their feed grains.

Beef production also threatens biodiversity in Western rangelands. By the time grasslands have been moderately or intensively used for grazing cattle, research shows, more than half the species once native to the landscape have been lost.

Although Eshel has for the past decade emphasized the benefits of switching to a purely plant-based diet (in which foods such as peanuts, soy, and lentils play a prominent role), he recognizes that veganism is not for everyone, despite the clear health benefits. Now he's calculated what would happen if all the national resources required to produce the beef Americans consume annually (about 65 grams per person per day) were devoted to poultry production instead. The number of useful calories produced would increase fivefold. Such a diet would also deliver four times the amount of protein, enough to meet the dietary needs of an additional 140 million people. Given the resources required to produce it, the idea that beef is indispensable, Eshel said, "just doesn't make sense."

But if people demand beef, how much can be grown sustainably? Eshel calculates that by combining feed that originates as an industrial byproduct (orange peels from juice production, for example) with the best half of all the *pastureland* in the country, 33 percent of the current beef supply could be maintained. Using *all* the pastureland, including arid, minimally productive Western rangelands, would affect more than 370 million acres and produce only 5 additional percent of the current supply, at the great environmental costs enumerated above. The high-quality *cropland* used to grow cattle-feed—if repurposed for crops that people eat—would deliver nine times the supply of protein if planted with wheat or spelt.

When making their dietary choices, Eshel said in summing up his research, individuals "get to tip the scale of environmental, social, and political contests," as well as improve their personal health. Eating healthy foods that use less land, therefore, "is one of the callings of our time...." —JONATHAN SHAW

GIDON ESHEL E-MAIL:
geshel@gmail.com
GIDON ESHEL WEBSITE:
www.radcliffe.harvard.edu/people/gidon-eshel

HM Explore More

For more online-only articles on research in progress, see:

A Breakthrough in High-Pressure Physics?

Metallic hydrogen could revolutionize energy use, space exploration, and more.
harvardmag.com/hydrogen-17

A Robotic Fix for Heart Failure

An experimental device could someday restore the ability to pump blood in patients with heart failure.
harvardmag.com/heartsleeve-17

THE X FACTOR

Why Is Cancer More Common in Men?

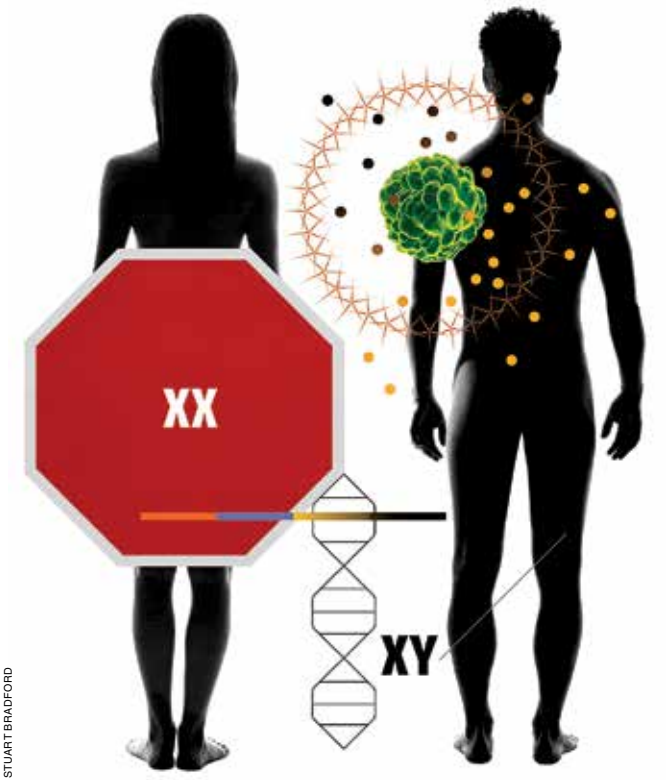
ONCOLOGISTS KNOW that men are more prone to cancer than women; one in two men will develop some form of the disease in a lifetime, compared with one in three women.

But until recently, scientists have been unable to pinpoint why. In the past, they theorized that men were more likely than women to encounter carcinogens through factors such as cigarette smoking and factory work. Yet the ratio of men with cancer to women with cancer remained largely unchanged across time, even as women began to smoke and enter the workforce in greater numbers. Pediatric cancer specialists also noted a similar "male bias to cancer" among babies and very young children with leukemia. "It's not simply exposures over a lifetime," explains Andrew Lane, assistant pro-

fessor of medicine and a researcher at the Dana-Farber Cancer Institute. "It's something intrinsic in the male and female system."

Now, discoveries by Lane and the Broad Institute of Harvard and MIT reveal that genetic differences between males and females may account for some of the imbalance.

A physician-researcher who studies the genetics of leukemia and potential treatments, Lane says that he and others noted that men with certain types of leukemia often possess mutations on genes located on the X chromosome. These mutations damage tumor-suppressor genes, which normally halt the rampant cell division that triggers cancer.



STUART BRADFORD

Lane initially reasoned that females, who have two X chromosomes, would be less prone to these cancers because they have two copies of each tumor suppressor gene. In contrast, men have an X and a Y chromosome—or just one copy of the protective genes, which could be "taken out" by mutation. But the problem with that hypothesis, Lane says, was a "fascinating phenomenon from basic undergraduate biology called X-inactivation." In a female embryo, he explains, cells randomly inactivate one of the two X chromosomes. "When a female cell divides, it remembers which X chromosome is shut down, and it keeps it shut down for all of its progeny."

If female cells have only one X chromosome working at a time, then they should be just as likely as male cells to experience cancer-causing gene mutations. So Lane and his team dug deeper into existing studies and encountered a little-known and surprising finding: "There are about 800 genes on the X chromosome," he says, "and for reasons that are still unclear, about 50 genes on that inactive X chromosome stay on."

In a "big Aha! moment," Lane's group realized that those gene mutations common in men with leukemia were located on genes that continue to function on women's inactive chromosome. The research-

ers dubbed those genes EXITS for "Escape from X-Inactivation Tumor Suppressors." Women, Lane explains, thus have some relative protection against cancer cells becoming cancer because they, unlike men, *do* have two copies of these tumor-suppressor genes functioning at all times.

To determine whether this model applied to multiple cancers, Lane partnered with Gad Getz, director of the cancer genome computational analysis group at the Broad Institute, to comb through gene-sequencing data for more than 4,000 tumors that included 21 different cancers (but omitted cancers such as prostate and ovarian, which occur only in males or females). Their results were startlingly clear: of the approximately 800 genes located on the X chromosome, the scientists identified six genes more frequently mutated in men than in women—and five fell into the subset of genes that escape X-inactivation in women.

Lane says this points to the need for medical research to pay closer attention to the differences between men and women. Since these findings were published in *Nature Genetics* last fall, he has heard from researchers who have run clinical trials in which male and female subjects responded differently to treatments, and now wonder if factors like the EXITS genes in women might have played a role. "It's possible," Lane says. "This tells us that at the fundamental level of the cell itself, there may be differences simply based on the genetics." It also suggests that cancers thought to be the same in women and men actually develop differently. "This could have implications for the behavior of the disease or treatment," he adds. "To me, the coolest thing about this work is that it opens people's eyes to the possibilities."

—ERIN O'DONNELL

ANDREW LANE WEBSITE:
www.dfhcc.harvard.edu/insider/member-detail/member/andrew-a-lane-md-phd

PREDICTION AND PREVENTION

Foreseeing Self-Harm

PSYCHOLOGY PROFESSOR Matthew Nock has spent his career studying self-harm, but he remains humbled by how little is yet understood about why people kill themselves. Suicide is the tenth highest cause of death in the United States, and the rate remained roughly steady across the population for the last century, before rising somewhat during the last few decades.

Academic theories of suicide emerged in the nineteenth century. Émile Durkheim wrote about social determinants of suicide in his foundational (though now controversial) text on the differences in suicide rates among Protestants and Catholics in Europe. Freud thought depression and suicide reflected inwardly directed anger. As psychology became the domain of empirical research, clinicians came to rely on factors correlated with suicide—like depression, poor impulse control, or substance abuse—to determine whether a patient was at risk. But a recent review of several hundred studies of suicidal thoughts and behaviors during the last 50 years, co-authored by Nock and a team of fellow scholars in the *Psychological Bulletin*, finds that risk factors have been virtually no better than random guesses at predicting suicide.

One shortcoming of traditional risk factors is that they require clinicians to rely on self-reported information from patients. What if patients aren't forthcoming because they don't want to be hospitalized, or are unable to report their emotional states? The bigger problem, Nock explains, is that each factor individually contributes so little to suicide risk. Depression, for example, may be *correlated* with suicide, but the proportion of patients with depression who attempt suicide is still vanishingly small. The clinical human brain, Nock continues, "isn't well prepared to assess dozens of risk factors at a time, weigh them all, and then combine those weights into one probability that a person is going to attempt suicide. So clinicians will focus on one or two risk factors, or they'll ask a patient, 'Are you thinking about hurting yourself?' and just rely on

Illustration by Davide Bonazzi