Seattle's Cancer Mystery

This region ranks worst nationwide in breast cancer and near worst in other cancers, and the fault isn't just in our genes.

by Francesca Lyman
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Julie Kofoed is still mystified. Her life had been far too wholesome to deserve any part in this grim plot. A lifelong Washington resident, she'd had a picture-book childhood on an 80-acre farm on Whidbey Island, where she and her family churned their own butter, baked their own bread, and dined on fresh organic meals from their own fruit trees, vegetable garden, and free-range chickens and beef. Then, at age 39, with three children of her own, she found a lump in her left breast. It proved to be an 8-centimeter-wide invasive tumor. The cancer had spread to her lymph nodes.

"When you're diagnosed you start to ask yourself, 'What did I do to get this?'" says Kofoed. She knows she'll probably never learn the precise reasons, but she wonders whether it was a gene or some mysterious environmental factor that marked her for this dread disease.

Kofoed doesn't fit any classic medical profile. Her immediate family had no history of breast cancer. Starting at age 24, she'd given birth to three children, eliminating her from the higher-risk group of women who defer or avoid childbirth. She wasn't a smoker and never worked late nights, two other risk factors. Her early home surroundings raised no red flags. But then she considered Lake Forest Park, where she has lived for the past 20 years, and began to wonder: Eight other women in her immediate neighborhood also had breast cancer. Two of them have since died. Was it jet fuel wafting up from Kenmore Air's small seaplane harbor? she asked herself. The growing traffic around the lake? Something in the milltown of Everett, where she was born, or leaking over from the nearby Whidbey Naval Air Station as she was growing up?

Kofoed moved beyond "Why me?" and started asking, "Why us?" How could this be happening in the shadow of Mount Rainier, in a haven for the health-conscious and nirvana for nature lovers, where kayaking outfits double as office attire and eagles windsurf the thermals over city neighborhoods?

She learned that wholesome stereotypes don't necessarily translate into better health. Washington State has the highest rate of breast cancer of all 50 states, 18 percent higher than the national rate. Among Washington counties, King County has the fifth-highest age-adjusted rate: 195 new cases a year per 100,000 residents, 26 percent above the national average. Kitsap, Pierce, and Snohomish Counties also have high rates. The Puget Sound region ranks highest in breast cancer among all population centers inventoried by the Centers for Disease Control and tops the national average in every other major cancer except colon. Is it something in the water or air, in our diets or habits, our Nalgene bottles or lattes? What demographic, geographic, or environmental factors might explain this epidemic?

NATURE AND NURTURE

Everybody knows someone—a mother, daughter, sister, friend, colleague, perhaps even a brother or father—who's been diagnosed with breast cancer. It is the most common life-threatening cancer among U.S. women; the American Cancer Society projects that some

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214,640 new cases will be diagnosed this year, 4,000 in Washington State, plus 61,980 noninvasive in situ tumors. They also project that 41,430 patients will die of breast cancer, including 770 Washington women. Non-Latina white women have the highest rates of breast cancer. But Latina rates are rising, both nationally and in Washington State. The percentage of African-American women diagnosed with breast cancer has declined in recent years—but the share dying from it is rising, partly because of late diagnoses and lack of access to mammograms.

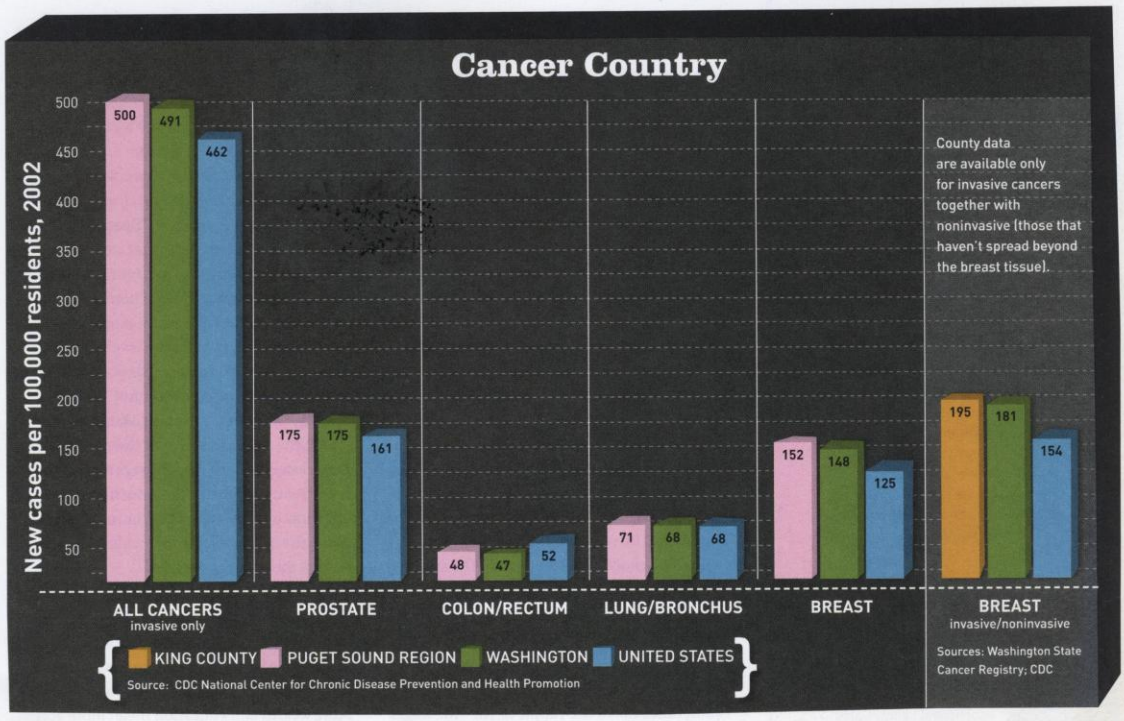
The reasons for these trends are complex and somewhat mysterious. Breast cancer is what scientists call a multifactorial disease; a variety of genetic, environmental, and lifestyle factors may play a role in the DNA damage that causes it. Dr. Michael Hunter, a radiation oncologist at Evergreen Hospital in Kirkland, looks first to the best-confirmed risk factors, starting with family and personal medical history. Having close relatives with any cancer raises the odds; breast cancer in a mother or sister doubles the likelihood. But as Hunter notes, "the vast majority of patients don't have a family history of the disease." The American Cancer Society pins only 5 to 10 percent of the risk on genetic factors.

Basic reproductive history also plays a role. Early menstruation, late menopause, and deferring or delaying child-bearing all boost the amount of estrogen circulating in a woman's body, which according to the American Cancer Society contributes to breast-cancer risk. Early pregnancy reduces that risk somewhat, but Seattle now ranks well below the national average in teen pregnancies (a good thing in many other regards). The birthrate among King County women aged 20 to 24 fell 16 percent between 1997 and 2003. Metropolitan Seattle-Tacoma-Bremerton also has the fifth-highest percentage of single, college-educated young women among major metropolitan areas and the 14th-highest share of 25-to-34-year-olds with college degrees—and such women are more likely to breed late or not at all.

THE "YUPPIE FACTOR"

But Julie Kofoed, with three kids, is living proof that breeding isn't destiny; all these reproductive factors together account for just 25 to 30 percent of breast cancers. That leaves another half or more unexplained. And that's where a wide range of what are broadly called "environmental" factors, from diet and lifestyle to toxic exposures, come into play, even for those with the strongest genetic predisposition.

Pioneering studies by UW genomics professor Mary-Claire King show that women carrying inherited mutations in the genes BRCA1 or BRCA2 have a more than 80-percent lifetime risk of contracting breast cancer. But whether or not even these women at highest risk get the dis-



THE LINEUP

Suspected culprits in this region's breast cancer epidemic

Gender, Age, and Heredity

Men can develop breast cancer, but about 99 percent of cases occur in women. Risk increases greatly with age. Five to 10 percent of cases are due to inherited gene mutations; having close relatives with breast or ovarian cancer is a strong marker.

Childlessness and Hormone Replacement

Bearing no children, or none until after age 30, may increase risk slightly. Likewise early menarche and late menopause. Breast-feeding may confer protection—the longer, the better. Hormone replacement therapy, or at least estrogen and progesterone combined, increases risk; estrogen alone may be safe, though one new study suggests otherwise for women who've had hysterectomies. Oral contraceptives may increase risk.

Vitamin D/Sunshine Deficiency

In sunlight, skin manufactures Vitamin D, which may protect against certain cancers by preventing cell overgrowth. British researchers recently found an enzyme in breast tissue that converts Vitamin D into a cancer-fighting compound.

Radiation

Ionizing radiation—such as X-rays and much more powerful CT scans—is known to cause cumulative chromosomal damage and a very small share of breast cancers. Mammograms, which deliver low doses, are safer for postmenopausal than for young women, but there's a rising clamor for safer detection methods.

Alcohol Consumption

One drink a day confers a 10 percent higher risk, two drinks 25 to 70 percent. Mouth, throat, and esophageal cancers also increase with drinking.

ease depends on additional factors, such as how much they exercise and what they eat. "It was a surprise, but a source of hope, to learn that factors over which we have some control made a difference in the age at which these highest-risk women developed breast cancer," writes King.

King's work also confirms that today's cancer risks dwarf those of the past. Women born before 1940, her study subjects' median birth year, had a 2.4 percent chance of developing breast cancer by age 50; women born after 1940 had a 67 percent chance. Something had changed between the pre- and postwar periods. For King, "This suggests that even when there is a strong genetic risk present, environmental factors play a vital role in determining when cancer occurs."

"The link between environmental exposures and cancer is not getting the attention it deserves from cancer researchers because of all the excitement about the Human Genome Project," says Dr. David Carpenter, a former dean of the State University of New York (SUNY) at Albany's School of Public Health. The successful effort to map the genome "is exciting," he adds, "but that is not telling us enough about the initiating events of cancer—which are not genetic but environmental."

Many of these influences fall under what's sometimes called the yuppie factor—the wages of affluence. In China the slang term for breast cancer is "rich woman's disease"; Jane Plant, chief scientist of the British Geological Survey, notes in her book *Your Life in Your Hands* that when Eastern people adopt Western diets and lifestyles, the disease's incidence rises.

Epidemiologist Kathi Malone, a research professor at Seattle's Fred Hutchinson Cancer Research Center, notes that affluence also leads to greater education, "and that correlates with never having had a child or having a child later in life." It brings greater use of hormone replacement therapy to relieve postmenopausal symptoms, thus raising estrogen levels and breast cancer risk. This correlation has been charted in two renowned breast cancer hot spots, Marin County, California, and Long Island, New York, where the demographics of the disease have been closely studied. Malone says detailed studies of Seattle women's reproductive habits are only now under way, but that hormone replacement therapy is even more widely used here than in those hot spots.

But though she concedes that "it feels like [breast cancer] has been at epidemic proportions for some time now," Malone adds a caveat: "Part of the increasing incidence we are seeing in Western Washington is due to screening." More wealth and education mean more access

to medical services including mammograms, so more cancers get diagnosed. Then again, mammogram radiation is another risk factor: One 1998 report (before the advent of digital mammograms somewhat reduced radiation levels) estimated that a mammogram at age 33 conferred a 1-in-1,112 risk of later breast cancer.

Alcohol consumption, which often increases as women become more affluent, educated, and emancipated, has also gained new recognition as a risk factor. "Alcohol appears to increase estrogen levels," says Malone, "and some studies have shown a relatively high rate of estrogen increase even with a moderate increase in drinking." The state Department of Health reports that both women and men in Washington drink more alcohol than the national average. And Washington has an above-average share of women (though not men) who are classified as "heavy drinkers"—consuming more than five drinks at a sitting.

IS IT IN THE AIR?

But why do several rural Eastern Washington counties where the yuppie factor is not so pronounced have breast cancer rates even higher than Pugetopolis'? (Wheat-growing Garfield's is 71 percent above the national average.) Dr. Juliet Van Eenwyk, an epidemiologist with the state Health Department, notes that these counties' populations are so low that small spikes can have outsized statistical effects; any underlying causes remain unknown.

Facing these uncertainties, many breast cancer advocates look to environmental causes that aren't associated with lifestyle choices. They complain that scientists "continue to dismiss environmental factors and harp on demographics," in the words of Jeanne Rizzo, director of the San Francisco–based Breast Cancer Fund. "This generation is getting sicker rather than healthier, and we need to understand why."

In fact, says Dr. Robert Hiatt, a professor of epidemiology and biostatistics at the University of California at San Francisco, researchers have long hypothesized that chronic exposure to a number of widespread and persistent industrial chemicals may explain the increase in various cancers in industrialized countries. Especially breast cancer, adds Hiatt, "since there's such a vast disparity in breast cancer rates between the U.S. and Europe and Southeast Asia—by a magnitude of as much as fivefold. And women are much the same biologically. It can't be genetic." Studies have found that when women in developing countries, particularly in Asia, migrate to industrialized areas, their cancer rates rise within a generation. They may consume more alcohol, meat, and dairy products, breathe dirtier air, and be exposed to more pollutants—all possible factors in China's "rich woman's disease."

One local environmental factor is noncontroversial: sunshine, or its absence. "My favorite hypothesis is the lack of sunlight here in the Pacific Northwest, which has been linked to lack of Vitamin D," says epidemiologist Van Eenwyk, laughing grimly. "We know that people get less Vitamin D because of less sun, and Oregon is usually right up there in the [cancer] statistics with us."

The baleful effects of automotive air pollution are also undisputed. Benzene is classified as a "probable risk factor" for breast cancer, the second-highest risk category; benzo(*a*)pyrene is a potent confirmed mutagen and carcinogen. And these are just two of many polycyclic aromatic hydrocarbons (PAHs) and other toxic compounds found in gasoline fumes and exhaust.

"Seattle's air pollution is very low compared to the typical Eastern city," says Elena Guilfoil, air toxics coordinator for the state Department of Ecology, "and Los Angeles's car exhaust just dwarfs Seattle's." Nevertheless automobile use, the main local source of air pollution, keeps rising; the Sightline Institute (formerly Northwest Environment Watch) reports that miles driven have more than doubled in the Puget Sound region, from an average 36 million per weekday in 1980 to 80 million in 2004. And the problem isn't just Seattle's: Surprisingly high levels of tailpipe toxics turn up in the suburbs. For example, in 2002 state monitors found mean readings of benzene and other pollutants in leafy Lake Forest Park (where Julie Kofoed lives) that were about 50 percent higher than readings on Beacon Hill and in heavy-industrial Georgetown, and nearly twice as high as those in SeaTac. Lake Sammamish and Maple Leaf also measured higher than SeaTac.

But, sighs Guilfoil, the air-toxic monitoring was discontinued for lack of funding, so what we have is the "best snapshot" we'll get.

PLASTIC HORMONES

Other researchers look to the thousands of new synthetic chemicals developed and widely deployed since World War II. Many are "xenoestrogens," chemicals that behave like estrogen, including ingredients in various cosmetics, lotions, and other body-care products; the ubiquitous plasticizer bisphenol-A, used in water bottles and food containers; PAHs in gasoline exhaust; long-lasting bioaccumulative toxins such as polychlorinated biphenyls (PCBs), once used in electrical transformers; and flame-retardant PBDEs, which accumulate in fish.

Seafood

Most fish and shellfish are rich in omega-3 fatty acids, which can reduce risk of heart disease and stroke, slow mental decline, and promote healthy pregnancies. But many contain mercury and/or bioaccumulative toxins such as PCBs, PDBE flame retardants, and dioxins. Safe seafood guides are available.

Dairy Products

Breast cancer is much rarer in the Far East, where people consume less milk. Fat-soluble pollutants can accumulate in milk; low-fat dairy products may lower risk. Many nonorganic U.S. dairy products contain genetically engineered recombinant bovine growth hormone, which boosts the natural hormone insulin growth factor-1. Several studies link increased IGF-1 to breast cancer.

Household Toxins

Insect and weed killers, cleaners, flame retardants, paints, solvents, wood finishes, plastic containers, nail polishes, and many other common household products contain known or suspected carcinogens, according to studies by the Silent Spring Institute.

Airborne Toxins and Smoke

Factory and tobacco smoke, gasoline fumes, and auto exhaust all contain polycyclic aromatic hydrocarbons (PAHS), linked to breast cancer.

Toxic Waste Sites

Researchers at the Department of Preventive Medicine and Community Health, at the New Jersey Medical School, in Newark, found 650 percent more breast cancer in counties with toxic-waste dumps. This state has 47 of the EPA's top-priority hazardous-waste sites, including Seattle's lower Duwamish River and the 586-square-mile Hanford site, containing both concentrated toxic wastes and low-level nuclear waste with a half-life of 24,000 years.

Night Light/Circadian Disruption

Several recent studies suggest that nurses, flight attendants, and other night workers suffer increased risk of breast cancer because of depressed levels of the hormone melatonin.

A recent review study by Kate Davies, a professor of environment and community at Seattle's Antioch University, suggests that environmental toxins contribute to Seattle's and Washington's above-average rates of breast cancer, melanoma, and other cancers, as well as childhood asthma and ADHD. "It's not that our environment is necessarily more contaminated than any other place," says Davies, "but the environmental factors are clearly playing a role here as elsewhere."

Watchdog groups are trying to determine how contaminated local women themselves are. Sightline tested breast milk from 40 women in Seattle, Oregon, Montana, and British Columbia, and found PBDEs in every sample. The Washington Toxics Coalition also released the results of its "body burden" study measuring a variety of toxins in Washington State residents and found that all had at least 27, some as many as 40, of these chemicals in their bodies, from heavy metals like arsenic, lead, and mercury to Teflon, pesticides, and other synthetics, including the outlawed but persistent PCBs and DDT. "Many of the chemicals do not break down or do so slowly, and therefore build up in human bodies and breast milk," the Toxics Coalition concluded.

Dr. Carpenter of the University at Albany thinks salmon consumption may offer a clue to our high rates of cancer and other diseases. He's found concentrations of dioxins, PCBs, PDBEs, and various pesticides in farmed salmon 10 times higher than those in Alaskan wild salmon. And, he adds, "wild salmon from Puget Sound have been reported with levels comparable" to farmed fish. He urges eating European farmed salmon no more than once every five months, local chinook no more than once a month, and local coho and sockeye no more than twice a month.

> Kofoed still wonders why it hit her, and how "to prevent this from happening in the first place."

The effects of toxic exposures may depend on when those exposures occur. New research is honing in on particularly vulnerable life stages, such as fetal development, infancy, and puberty. Last year researchers at SUNY Buffalo reconstructed a group of women's lifetime exposures to auto exhaust, based on where they lived and historical traffic patterns, and found a correlation between exposure levels at first menstruation and later breast cancer. Others at Tufts University found that newborn rats whose mammary glands were exposed to plastics containing bisphenol-A were more likely to develop breast cancer later. "Our study suggests that if humans are exposed [soon after birth] to BPA, the likelihood is it will make them more sensitive to estrogen and therefore more susceptible to breast cancer," says Tufts University's Dr. Ana Soto.

But as Maryann Donovan, associate director of the University of Pittsburgh's Cancer Institute, notes, "a lot of chemical exposures don't leave a marker," and epidemiologists struggle when they try to link them to cancers that appear 20 or 30 years later. Julie Kofoed wonders if early exposures might have played a role in her breast cancer. "When I was young I used to use nail polish all the time," she remembers. "I was never without polish from 12 to 13 years old until I was 24!" And today? Kofoed runs daily, but unlike other runners, she says, "I don't use water bottles anymore."

AN ATTITUDINAL CHANGE

Donald Malins, a veteran biochemist at Seattle's Pacific Northwest Research Institute, stirred his own share of controversy in the 1980s when he sounded the alarm on toxins and tumors in Puget Sound fish. Today he recommends research on cancer hot spots around Washington, especially if "deficiencies of Vitamin D" or other strong clues appear. And he urges that researchers consider not just one chemical at a time—the way epidemiology usually works—but the combined effects of various chemicals. "We aren't exposed to chemicals one at a time!" he exclaims.

Malins, relaxing in the institute's sunny waiting room across the street from Swedish Hospital, speaks more calmly as he applauds recent advances in cancer treatment. But he wonders, "Why are we putting so little focus on prevention?" Rather than just screening for active disease, he urges "finding early predictors to stop cancers before they progress." Malins was dismayed when cancer surgeons did not embrace DNA tissue tests he's developed, which he believes could help avert cancer just as blood-cholesterol tests do heart disease. "I know these doctors are good people," Malins says, "but at a recent conference one surgeon responded to my talk by saying to the group, 'Well, I guess we'll be doing a lot less lumpectomies!' We need an attitudinal change in the medical profession."

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And so the lines get drawn, with some researchers and many activists urging more prevention, more research into environmental causes, and more of what the Toxics Coalition's Erika Schreder calls "reducing the load of cancer-causing chemicals." Cancer specialists meanwhile remain skeptical. "When the causes of breast cancer begin to be understood better, then I'd be the first to advocate prevention strategies," says state epidemiologist Juliet Van Eenwyk. "But we don't have them yet." The Hutch's Malone urges more study of hormonal and demographic factors: "I'm personally not convinced that there's evidence to show that our exposure to chemicals is a factor here."

Advocates and researchers do agree on one thing: Too little research into environmental factors has been done in the Northwest, in contrast to New York, where advocates persuaded Congress to fund a landmark $25 million study, and California, with the nation's largest state-funded breast cancer research program, which has awarded about $160 million to date. "Seattle has a huge excess of cancer," says University of Pittsburgh professor Donovan, "and it merits better analysis."

But the support for such research may actually shrink. The Bush administration proposes severely cutting the National Cancer Institute's budget, of which only a sliver goes to environmental research. Four research centers on breast cancer and the environment have already been established—but not one is in the Northwest.

On a more hopeful note, although 2005 statistics aren't out yet, Van Eenwyk believes Washington's breast cancer rate may finally have started to drop. Whether that's a trend or an anomaly, screening and treatment keep improving and fewer women are dying from breast cancer, here and nationwide—16 percent fewer in King County in 2003 than in 1994.

Back in Lake Forest Park, Julie Kofoed has been cancer-free for nearly four years. But she still worries that the disease may recur or appear in her daughter or grandchildren. She can't help wondering why it hit her, but she's given up expecting an answer. "I wanted to find out what caused my cancer," she says, "but I finally had to let go of that." Still, she wishes the authorities would keep better track of hormone mimics and other dangerous chemicals, and do more to inform the public about cancer risks: "It's not something we're widely educated about.... It would be great to find out why we're being hit so hard with breast cancer and other cancers in our area. Better yet, what can we do to prevent this from happening in the first place?"