



IMMIE NG, M.D., a Boston oncologist, started noticing an alarming trend in her work a few years ago. Men in their 20s, 30s, and 40s—runners, CrossFitters, lifelong nonsmokers—were streaming through her door at the Dana-Farber Cancer Institute. They all appeared lively and strong—yet there they were, battling colorectal cancers, a family of diseases that can start in the colon or rectum and are typically associated with older people and those with

risk factors like family history and obesity.

Most troubling of all, many of them were coming in with advanced, metastatic disease. One patient, 46-year-old Dan Luers, an Ironman finisher who worked out close to two hours a day, was given a stage IV diagnosis. Every year, Dr. Ng's concern grew. But the problem didn't totally hit home until 2017, when a healthy-looking marine showed up in her office. Just 29 years old, "he was the youngest person I'd ever treated for this type of cancer who didn't have a family history, and

the model of perfect health—extremely fit and active and a healthy eater." But he had stage IV colorectal cancer. For people whose cancers have spread to distant parts of the body, like his had, the five-year survival rate hovers around 14 percent.

Luers and so many of Dr. Ng's other young patients have asked a haunting question: "How could I have prevented this?" She and dozens of researchers around the country are furiously trying to find the answer. Watching so many young men suddenly get hit, Dr. Ng says, "cemented my resolve to do something about it."

WHY THIS IS SO ALARMING

Colorectal cancers are the third-most-frequent type of new cancer in men (right behind prostate and lung). And while they're declining for older guys, the rates among younger Americans are on the rise. What doctors have been picking up on in their day-to-day work is only now being fully captured in medical research and in the news. In 2017, a large NIH-funded study of invasive colorectal cancers found that people born around 1990 have *double* the risk of developing colon cancer and *quadruple* the risk of developing rectal cancer compared with those born around 1950—a finding worrisome enough to prompt the American Cancer Society to lower its recommended screen-

ing age for people of average risk of colorectal cancers from 50 to 45. If the trend continues, a study in *JAMA Surgery* predicted, by 2030 the rate of colon cancer will rise by 90 percent and that of rectal cancer by a staggering 124 percent in people ages 20 to 34.

It gets worse: New research suggests that early-onset colorectal cancers have distinctly different features from what doctors are used to seeing. These cancers tend to start in other places and mutate differently, "which gives us a hint that even at the earliest steps of these cancers' formation, something may be different about them," says Scott Kopetz, M.D., Ph.D., an oncologist at MD Anderson Cancer

Center. It's "fair to say," he adds, that some of these could be a new version of the disease. For those keeping track, that means there may be new reasons that these cancers are forming; new reasons young men are susceptible; and a new need for alternate therapies. (See? Alarming.)

Along with Dr. Kopetz, teams of researchers at Memorial Sloan Kettering Cancer Center and the new Young-Onset Colorectal Cancer Center at Dana-Farber are racing to figure out what's driving these changes. One of the most intriguing leads is the microbiome, the diverse, teeming community of microorganisms living within us. Among the few things we know is that it's constantly evolving. Some changes could "result in a benefit or insult to surrounding cells," notes Dana-Farber physician and scientist Marios Giannakis, M.D., Ph.D. That means the microbiome may affect cells it touches and possibly play into the development of disease.

Researchers are looking into anything that could be changing the microbiome and affecting these cancers. Right now they know that what you eat and what meds you take are at least part of it. Killing off bacteria with antibiotics can upset the microbiome's balance. So may eating too much added sugar. (Aim for 36 grams a day max for general health.) "With anything that modulates the microbiome," says Dr. Giannakis, "there's an open ques-

tion as to whether it's good or bad. We just don't know yet." A new five-year, \$25 million study led by Dana-Farber researchers aims to tease out some answers.

Until the research results come in, doctors say that the things that make you generally healthy probably help—maintain a healthy weight; eat a diet full of gut-friendly, high-fiber vegetables and whole grains; avoid tobac-

co and processed meats; limit sugar; stay active. But here's the essential thing that guys often don't do: Take notice of symptoms, especially persistent changes in bowel habits, and get them checked out right away.

WHAT SHOULD YOU LOOK FOR?

The great majority of early-onset colorectal cancers start in the rectum, the lowest part of the colon, which can be linked with symptoms like rectal bleeding and constipation, says Robin Mendelsohn, M.D., a gastroenterologist and researcher at MSK's Center for Young Onset Colorectal Cancer. If you're seeing blood in your stool or on the toilet paper; if you notice stools narrowing or changing consistency; or if you have nausea, stomach pain, or bloating—any new or odd symptom that lasts "more than a couple of

weeks," she says—don't write it off. If you get pushback from your doc about testing—and you might, as up to 17 percent of early-onset colorectal-cancer patients are initially misdiagnosed, according to a recent Colorectal Cancer Alliance (CCA) survey—push right back. "When we catch these cancers early, we can treat them more effectively," Dr. Mendelsohn says.

The CCA survey found that 71 percent of early-onset colorectal-cancer patients receive a stage III or stage IV diagnosis. Only about 19 percent of early-onset patients with stage IV cancers survive for five years, according to the most recent available federal data. But some therapies seem to be working. Surgery, chemo, and radiation knocked out Luers's disease, and he was given a clean bill of health earlier this year. Greg Mancini, 42, another of Dr. Ng's patients, learned of his colorectal cancer at 38. The father of two from Scarborough, Maine, was in terrible shape, with cancer spreading toward his spine, when he started an immunotherapy trial

of two checkpoint inhibitors in 2015. Within weeks, Mancini says, the cancer retreated. "I had bulging tumors in my neck that melted like ice cubes. It was unbelievable." But until that's the standard response to treatment at that stage, or until these cancers start giving up some of their secrets to Dr. Ng and her colleagues, paying attention to your body and speaking up about it could help change the trend.



ONE WAY TO GET THROUGH COLON CANCER

SOMETIMES IT helps to have a goal outside of surviving colon cancer. For Tate MacDowell, 38, that was something that would help him reclaim his body, cancer be damned. Inspired by a photo in his treatment center of Grand Teton in Wyoming, MacDowell decided he would climb it. Last summer, a year after his intended climb date, MacDowell (pictured, on the right) made it, despite a slew of setbacks. During chemo, "everything is so sterilized," he says. "To get my hands dirty, to be drinking from a river, scratching my fingers on some granite, I felt alive." See his story in the short film *Mountain in the Hallway* (on Vimeo).