

Cancers Can Vanish Without Treatment, but How?

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Call it the arrow of cancer. Like the arrow of time, it was supposed to point in one direction. Cancers grew and worsened.

But as a paper in The Journal of the American Medical Association noted last week, data from more than two decades of screening for breast and prostate cancer call that view into question. Besides finding tumors that would be lethal if left untreated, screening appears to be finding many small tumors that would not be a problem if they were left alone, undiscovered by screening. They were destined to stop growing on their own or shrink, or even, at least in the case of some breast cancers, disappear.

“The old view is that cancer is a linear process,” said Dr. Barnett Kramer, associate director for disease prevention at the National Institutes of Health. “A cell acquired a mutation, and little by little it acquired more and more mutations. Mutations are not supposed to revert spontaneously.”

So, Dr. Kramer said, the image was “an arrow that moved in one direction.” But now, he added, it is becoming increasingly clear that cancers require more than mutations to progress. They need the cooperation of surrounding cells and even, he said, “the whole organism, the person,” whose immune system or hormone levels, for example, can squelch or fuel a tumor.

Cancer, Dr. Kramer said, is a dynamic process.

It was a view that was hard for some cancer doctors and researchers to accept. But some of the skeptics have changed their minds and decided that, contrary as it seems to everything they had thought, cancers can disappear on their own.

“At the end of the day, I’m not sure how certain I am about this, but I do believe it,” said Dr. Robert M. Kaplan, the chairman of the department of health services at the School of Public Health at the University of California, Los Angeles, adding, “The weight of the evidence suggests that there is reason to believe.”

Disappearing tumors are well known in testicular cancer. Dr. Jonathan Epstein at Johns Hopkins says it does not happen often, but it happens.

A young man may have a lump in his testicle, but when doctors remove the organ all they find is a big scar. The tumor that was there is gone. Or, they see a large scar and a tiny tumor because

more than 95 percent of the tumor had disappeared on its own by the time the testicle was removed.

Or a young man will show up with a big tumor near his kidney. Doctors realize that it started somewhere else, so they look for its origin. Then they discover a scar in the man's testicle, the only remnant of the original cancer because no tumor is left.

Testicular cancer is unusual; most others do not disappear. But there is growing evidence that cancers can go backward or stop, and researchers are being forced to reassess their notions of what cancer is and how it develops.

Of course, cancers do not routinely go away, and no one is suggesting that patients avoid treatment because of such occasional occurrences.

"Biologically, it is a rare phenomenon to have an advanced cancer go into remission," said Dr. Martin Gleave, a professor of urology at the University of British Columbia.

But knowing more about how tumors develop and sometimes reverse course might help doctors decide which tumors can be left alone and which need to be treated, something that is now not known in most cases.

Cancer cells and precancerous cells are so common that nearly everyone by middle age or old age is riddled with them, said Thea Tlsty, a professor of pathology at the University of California, San Francisco. That was discovered in autopsy studies of people who died of other causes, with no idea that they had cancer cells or precancerous cells. They did not have large tumors or symptoms of cancer. "The really interesting question," Dr. Tlsty said, "is not so much why do we get cancer as why don't we get cancer?"

The earlier a cell is in its path toward an aggressive cancer, researchers say, the more likely it is to reverse course. So, for example, cells that are early precursors of cervical cancer are likely to revert. One study found that 60 percent of precancerous cervical cells, found with Pap tests, revert to normal within a year; 90 percent revert within three years.

And the dynamic process of cancer development appears to be the reason that screening for breast cancer or prostate cancer finds huge numbers of early cancers without a corresponding decline in late stage cancers.

If every one of those early cancers were destined to turn into an advanced cancer, then the total number of cancers should be the same after screening is introduced, but the increase in early cancers should be balanced by a decrease in advanced cancers.

That has not happened with screening for breast and prostate cancer. So the hypothesis is that many early cancers go nowhere. And, with breast cancer, there is indirect evidence that some actually disappear.

It is harder to document disappearing prostate cancers; researchers say they doubt it happens. Instead, they say, it seems as if many cancers start to grow then stop or grow very slowly, as has been shown in studies like one now being done at Johns Hopkins. When men have small tumors with cells that do not look terribly deranged, doctors at Johns Hopkins offer them an option of “active surveillance.” They can forgo having their prostates removed or destroyed and be followed with biopsies. If their cancer progresses, they can then have their prostates removed.

Almost no one agrees to such a plan. “Most men want it out,” Dr. Epstein said. But, still, the researchers have found about 450 men in the past four or five years that chose active surveillance. By contrast, 1,000 a year have their prostates removed at Johns Hopkins. From following those men who chose not to be treated, the investigators discovered that only about 20 percent to 30 percent of those small tumors progressed. And many that did progress still did not look particularly dangerous; although once the cancers started to grow the men had their prostates removed.

In Canada, researchers are doing a similar study with small kidney cancers, among the few cancers that are reported to regress occasionally, even when far advanced.

That was documented in a study, led by Dr. Gleave that compared an experimental treatment with a placebo in people with kidney cancer that had spread throughout their bodies.

As many as 6 percent who received a placebo had tumors that shrank or remained stable. The same thing happened in those who received the therapy, leading the researchers to conclude that the treatment did not improve outcomes.

The big unknown is the natural history of many small kidney tumors, many of which are early kidney cancers. How often do small tumors progress? Do they ever disappear? Do they all need surgical excision? At what stage do most kidney cancers reach a point of no return?

These days, Dr. Gleave said, more patients are having ultrasound or CT scans for other reasons and learning that there is a small lump on one of their kidneys. In the United States, the accepted practice is to take those tumors out. But, he asks, “Is that always necessary?”

His university is participating in a countrywide study of people with small kidney tumors, asking what happens when those tumors are routinely examined, with scans, to see if they grow. About 80 percent do not change or actually regress over the next three years.

With early detection, he said, “our net has become so fine that we are pulling in small fish as well as big fish.” Now, he said, “we have to identify which small fish we can let go.”