Why curiosity is the key to science and medicine

Subtitles and Transcript about 17minutes

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Posted Dec 2016
Rated Informative, Inspiring

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Science. The very word for many of you conjures unhappy memories of boredom in high school biology or physics class. But let me assure that what you did there had very little to do with science. That was really the "what" of science. It was the history of what other people had discovered. What I'm most interested in as a scientist is the "how" of science. Because science is knowledge in process. We make an observation, guess an explanation for that observation, and then make a prediction that we can test with an experiment or other observation.

A couple of examples. First of all, people noticed that the Earth was below, the sky above, and both the Sun and the Moon seemed to go around them. Their guessed explanation was that the Earth must be the center of the universe. The prediction: everything should circle around the Earth. This was first really tested when Galileo got his hands on one of the first telescopes, and as he gazed into the night sky, what he found there was a planet, Jupiter, with four moons circling around it. He then used those moons to follow the path of Jupiter and found that Jupiter also was not going around the Earth but around the Sun. So the prediction test failed. And this led to the discarding of the theory that the Earth was the center of the universe.

Another example: Sir Isaac Newton noticed that things fall to the Earth. The guessed explanation was gravity, the prediction that everything should fall to the Earth. But of course, not everything does fall to the Earth. So did we discard gravity? No. We revised the theory and said, gravity pulls things to the Earth unless there is an equal and opposite force in the other direction. This led us to learn something new. We began to pay more attention to the bird and the bird's wings, and just think of all the discoveries that have flown from that line of thinking. So the test failures, the exceptions, the outliers teach us what we don't know and lead us to something new. This is how science moves forward. This is how science learns.

Sometimes in the media, and even more rarely, but sometimes even scientists will say that something or other has been scientifically proven. But I hope that you understand that science never proves anything definitively forever. Hopefully science remains curious enough to look for and humble enough to recognize when we have found the next outlier, the next exception, which, like Jupiter's moons, teaches us what we don't actually know.

We're going to change gears here for a second. The caduceus, or the symbol of medicine, means a lot of different things to different people, but most of our public discourse on medicine really turns it into an engineering problem. We have the hallways of Congress, and the boardrooms of insurance companies that try to figure out how to pay for it. The ethicists and epidemiologists try to figure out how best to distribute medicine, and the hospitals and physicians are absolutely obsessed with their protocols and checklists, trying to figure out how best to safely apply medicine. These are all good things. However, they also all assume at some level that the textbook of medicine is closed. We start to measure the quality of our health care by how quickly we can access it. It doesn't surprise me that in this climate, many of our institutions for the provision of health care start to look a heck of a lot like Jiffy Lube.

The only problem is that when I graduated from medical school, I didn't get one of those little doohickeys that your mechanic has to plug into your car and find out exactly what's wrong with it, because the textbook of medicine is not closed. Medicine is science. Medicine is knowledge in process. We make an observation, we guess an explanation of that observation, and then we make a prediction that we can test. Now, the testing ground of most predictions in medicine is populations. And you may remember from those boring days in biology class that populations tend to distribute around a mean as a Gaussian or a normal curve. Therefore, in medicine, after we make a prediction from a guessed explanation, we test it in a population. That means that what we know in medicine, our knowledge and our know-how, comes from populations but extends only as far as the next outlier, the next exception, which, like Jupiter's moons, will teach us what we don't actually know.

Now, I am a surgeon who looks after patients with sarcoma. Sarcoma is a very rare form of cancer. It's the cancer of flesh and bones. And I would tell you that every one of my patients is an outlier, is an exception. There is no surgery I have ever performed for a sarcoma patient that has ever been guided by a randomized controlled clinical trial, what we consider the best kind of population-based evidence in medicine. People talk about thinking outside the box, but we don't even have a box in sarcoma. What we do have as we take a bath in the uncertainty and unknowns and exceptions and outliers that surround us in sarcoma is easy access to what I think are those two most important values for any science: humility and curiosity. Because if I am humble and curious, when a patient asks me a question, and I don't know the answer, I'll ask a colleague who may have a similar albeit distinct patient with sarcoma. We'll even establish international collaborations. Those patients will start to talk to each other through chat rooms and support groups. It's through this kind of humbly curious communication that we begin to try and learn new things.

As an example, this is a patient of mine who had a cancer near his knee. Because of humbly curious communication in international collaborations, we have learned that we can repurpose the ankle to serve as the knee when we have to remove the knee with the cancer. He can then wear a prosthetic and run and jump and play. This opportunity was available to him because of international collaborations. It was desirable to him because he had contacted other patients who had experienced it. And so exceptions and outliers in medicine teach us what we don't know, but also lead us to new thinking.

Now, very importantly, all the new thinking that outliers and exceptions lead us to in medicine does not only apply to the outliers and exceptions. It is not that we only learn from sarcoma patients ways to manage sarcoma patients. Sometimes, the outliers and the exceptions teach us things that matter quite a lot to the general population. Like a tree standing outside a forest, the outliers and the exceptions draw our attention and lead us into a much greater sense of perhaps what a tree is. We often talk about losing the forests for the trees, but one also loses a tree within a forest. But the tree that stands out by itself makes those relationships that define a tree, the relationships between trunk and roots and branches, much more apparent. Even if that tree is crooked or even if that tree has very unusual relationships between trunk and roots and branches, it nonetheless draws our attention and allows us to make observations that we can then test in the general population.

I told you that sarcomas are rare. They make up about one percent of all cancers. You also probably know that cancer is considered a genetic disease. By genetic disease we mean that cancer is caused by oncogenes that are turned on in cancer and tumor suppressor genes that are turned off to cause cancer. You might think that we learned about oncogenes and tumor suppressor genes from common cancers like breast cancer and prostate cancer and lung cancer, but you'd be wrong. We learned about oncogenes and tumor suppressor genes for the first time in that itty-bitty little one percent of cancers called sarcoma. In 1966, Peyton Rous got the Nobel Prize for realizing that chickens had a transmissible form of sarcoma. Thirty years later, Harold Varmus and Mike Bishop discovered what that transmissible element was. It was a virus carrying a gene, the src oncogene. Now, I will not tell

you that src is the most important oncogene. I will not tell you that src is the most frequently turned on oncogene in all of cancer. But it was the first oncogene. The exception, the outlier drew our attention and led us to something that taught us very important things about the rest of biology.

Now, TP53 is the most important tumor suppressor gene. It is the most frequently turned off tumor suppressor gene in almost every kind of cancer. But we didn't learn about it from common cancers. We learned about it when doctors Li and Fraumeni were looking at families, and they realized that these families had way too many sarcomas. I told you that sarcoma is rare. Remember that a one in a million diagnosis, if it happens twice in one family, is way too common in that family. The very fact that these are rare draws our attention and leads us to new kinds of thinking.

Now, many of you may say, and may rightly say, that yeah, Kevin, that's great, but you're not talking about a bird's wing. You're not talking about moons floating around some planet Jupiter. This is a person. This outlier, this exception, may lead to the advancement of science, but this is a person. And all I can say is that I know that all too well. I have conversations with these patients with rare and deadly diseases. I write about these conversations. These conversations are terribly fraught. They're fraught with horrible phrases like "I have bad news" or "There's nothing more we can do." Sometimes these conversations turn on a single word: "terminal."

Silence can also be rather uncomfortable. Where the blanks are in medicine can be just as important as the words that we use in these conversations. What are the unknowns? What are the experiments that are being done?

Do this little exercise with me. Up there on the screen, you see this phrase, "no where." Notice where the blank is. If we move that blank one space over "no where" becomes "now here," the exact opposite meaning, just by shifting the blank one space over.

I'll never forget the night that I walked into one of my patients' rooms. I had been operating long that day but I still wanted to come and see him. He was a boy I had diagnosed with a bone cancer a few days before. He and his mother had been meeting with the chemotherapy doctors earlier that day, and he had been admitted to the hospital to begin chemotherapy. It was almost midnight when I got to his room. He was asleep, but I found his mother reading by flashlight next to his bed. She came out in the hall to chat with me for a few minutes. It turned out that what she had been reading was the protocol that the chemotherapy doctors had given her that day. She had memorized it. She said, "Dr. Jones, you told me that we don't always win with this type of cancer, but I've been studying this protocol, and I think I can do it. I think I can comply with these very difficult treatments. I'm going to quit my job. I'm going to move in with my parents. I'm going to keep my baby safe." I didn't tell her. I didn't stop to correct her thinking. To shift that blank to where it should be. The experiment wasn't whether or not she could comply with this very difficult protocol. She was trusting in a protocol that even if complied with, wouldn't necessarily save her son. I didn't tell her. I didn't fill in that blank. But a year and a half later her boy nonetheless died of his cancer. Should I have told her?

Now, many of you may say, "So what? I don't have sarcoma. No one in my family has sarcoma. And this is all fine and well, but it probably doesn't matter in my life." And you're probably right. Sarcoma may not matter a whole lot in your life. But where the blanks are in medicine does matter in your life.

I didn't tell you one dirty little secret. I told you that in medicine, we test predictions in populations, but I didn't tell you, and so often medicine never tells you that every time an individual encounters medicine, even if that individual is firmly embedded in the general population, neither the individual nor the physician knows where in that population the individual will land. Therefore,

every encounter with medicine is an experiment. You will be a subject in an experiment. And the outcome will be either a better or a worse result for you. As long as medicine works well, we're fine with fast service, bravado, brimmingly confident conversations. But when things don't work well, sometimes we want something different.

A colleague of mine removed a tumor from a patient's limb. He was concerned about this tumor. In our physician conferences, he talked about his concern that this was a type of tumor that had a high risk for coming back in the same limb. But his conversations with the patient were exactly what a patient might want: brimming with confidence. He said, "I got it all and you're good to go." She and her husband were thrilled. They went out, celebrated, fancy dinner, opened a bottle of champagne. The only problem was a few weeks later, she started to notice another nodule in the same area. It turned out he hadn't gotten it all, and she wasn't good to go. But what happened at this juncture absolutely fascinates me. My colleague came to me and said, "Kevin, would you mind looking after this patient for me?" I said, "Why, you know the right thing to do as well as I do. You haven't done anything wrong." He said, "Please, just look after this patient for me." He was embarrassed — not by what he had done, but by the conversation that he had had, by the overconfidence.

So I performed a much more invasive surgery and had a very different conversation with the patient afterwards. I said, "Most likely I've gotten it all and you're most likely good to go, but this is the experiment that we're doing. This is what you're going to watch for. This is what I'm going to watch for. And we're going to work together to find out if this surgery will work to get rid of your cancer." I can guarantee you, she and her husband did not crack another bottle of champagne after talking to me. But she was now a scientist, not only a subject in her experiment.

And so I encourage you to seek humility and curiosity in your physicians. Almost 20 billion times each year, a person walks into a doctor's office, and that person becomes a patient. You or someone you love will be that patient sometime very soon. How will you talk to your doctors? What will you tell them? What will they tell you? They cannot tell you what they do not know, but they can tell you when they don't know if only you'll ask. So please, join the conversation.

Thank you.