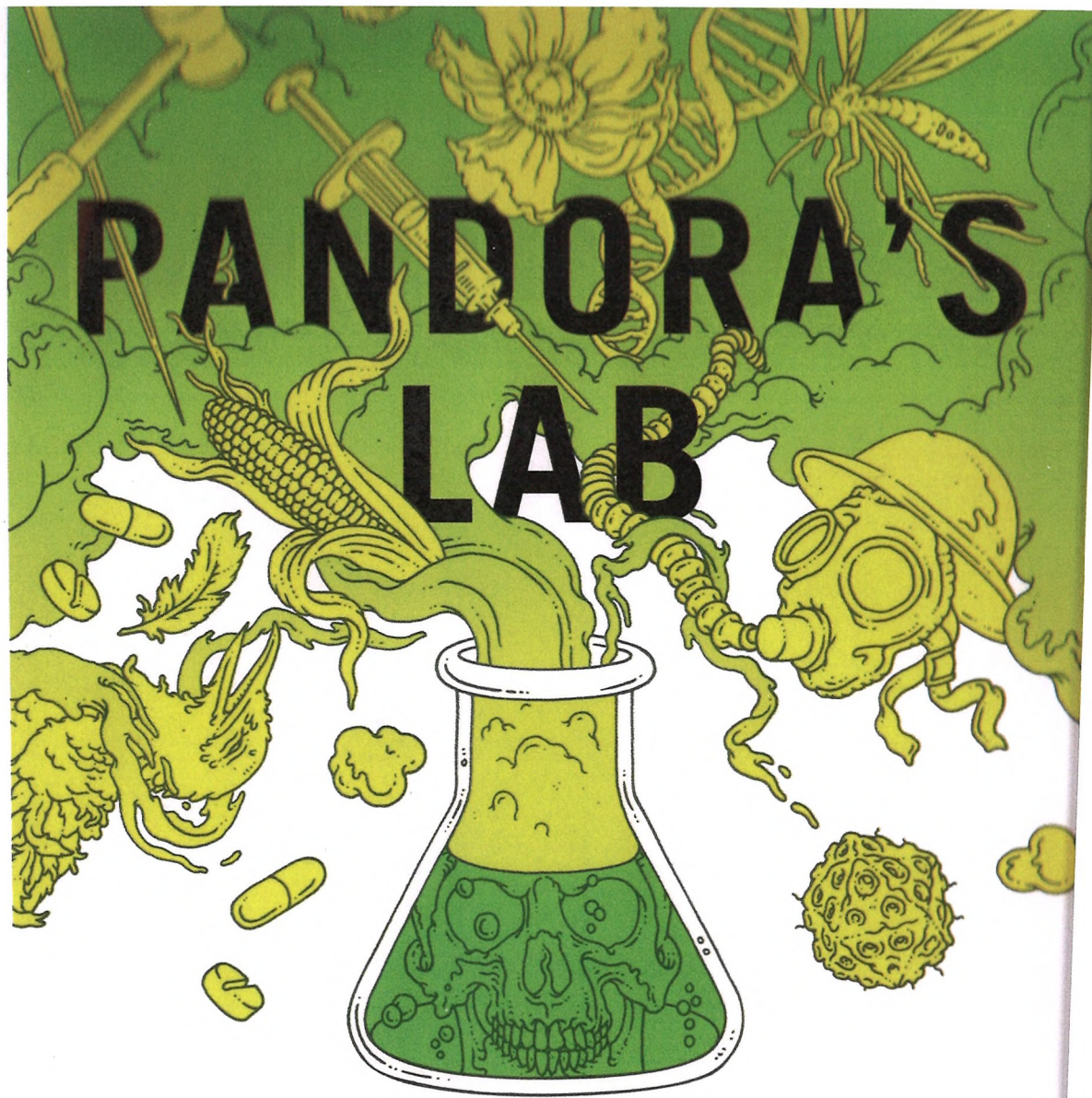




Seven Stories of Science Gone Wrong

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Author of Autism's False Prophets

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PANDORA'S LAB

**Seven Stories
of Science Gone Wrong**

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CHAPTER 8



LEARNING FROM THE PAST

Although it's always easy in retrospect, several lessons have evolved from science's darker past. Let's see what happens when we apply these lessons to a variety of modern-day inventions like e-cigarettes, preservatives, chemical resins, autism cures, cancer-screening programs, and genetically modified organisms (GMOs).

1. It's all about the data.

Truths emerge when studies performed by different scientists working in different environments using different methods find similar results. Ignoring these truths can have disastrous consequences.

On its surface, this lesson would appear to be easy to follow—just look at the data. The problem with data, however, is that there's far too much of it. Every day about 4,000 papers are published in the world's medical and scientific literature. As you would expect, the quality of these studies follows a bell-shaped curve: Some are excellent; some are awful; and most are more or less mediocre. So how is one supposed to separate good data from bad? One way

would be to focus on the quality of the journals. But even that isn't perfect. Excellent, peer-reviewed journals have published claims that excess coffee drinking causes pancreatic cancer; that the measles-mumps-rubella (MMR) vaccine causes autism; and that nuclear fusion—when two small nuclei combine to release energy—can occur at room temperature in a glass of water (cold fusion). All of these observations were later shown to be wrong by other investigators. ("The trouble with the world is not that people know too little," wrote Mark Twain, "it's that they know so many things that ain't so.")

So, if you cannot completely trust observations published in excellent scientific journals, what can you trust?

The answer is that science stands on two pillars: one more reliable than the other. The first pillar is peer review; before a paper is published, experts in the field review it. The process, unfortunately, is flawed. Not all experts are equal and sometimes bad data slip through. The second pillar saves the day: reproducibility. If researchers publish a paper claiming something fantastic (like the MMR vaccine causes autism), subsequent studies will prove it to be correct or not. For example, almost immediately after publication of the claim that MMR caused autism, hundreds of investigators working in Europe, Canada, and the United States tried to reproduce it. They couldn't. Study after study involving hundreds of thousands of children and costing tens of millions of dollars found that those who had received the vaccine were at no greater risk of autism than those who hadn't. Good science had won out.

2. Everything has a price; the only question is how big.

Even the most dramatic, lifesaving, groundbreaking, universally acclaimed scientific and medical breakthroughs—like antibiotics and

sanitation programs—have come with a price. Nothing, as it turns out, is exempt.

The first antibiotic, sulfa, was invented in the mid-1930s. Next came penicillin, which was mass-produced during WWII. Antibiotics have saved our lives. Without them, we would continue to die routinely from pneumonia, meningitis, and a variety of other potentially fatal bacterial infections. In part because of antibiotics, we live 30 years longer than we did a hundred years ago. But aside from the problem of creating antibiotic-resistant bacteria, one consequence of antibiotic use was utterly unpredictable.

In the last decade or so, researchers have been studying something called the microbiome—the population of bacteria that line the surface of our skin, intestines, nose, and throat. Recently, researchers found a role for these bacteria that was surprising. The numbers and types of bacteria that cover our body in part determine whether we will develop diabetes, asthma, allergies, and obesity. More surprising, if we alter the bacteria of infants with antibiotics, we *increase* the risk of these disorders. The lesson is clear. Use antibiotics when you need them, but overuse them at your own risk.

Antibiotics aren't the only dramatic scientific advance that has come with an unanticipated price. Even sanitation programs, which have decreased the incidence of food-borne and waterborne diseases like salmonella, shigella, *E. coli*, and hepatitis A, have unseen risks. Although the incidence of potentially fatal bacterial and viral infections has decreased in the developed world, the incidence of diseases like asthma and allergies has increased—a phenomenon that cannot be accounted for solely by industrialization. The reason for the unanticipated problem with sanitation can be found in an editorial in the *New England Journal of Medicine* titled "Eat Dirt." Children in developing world countries are, from the moment of birth,

bombarded with germs; as a consequence, their intestines often contain parasites and toxin-producing bacteria that are rare in the developed world. Although these infections can cause malnutrition and even death, they make it far less likely that children in developing world countries will develop allergies and asthma. Researchers call this “the hygiene hypothesis.”

The point being that there's always a price to pay. The challenge is figuring out whether a particular technology is worth the price. And we shouldn't grandfather in certain technologies just because they've been around for decades, or even centuries. All technologies should be constantly evaluated. Perhaps the best example is general anesthesia. Although anesthetics have been around for more than 150 years, only recently has it become clear that they can cause problems with attention and memory that can last for years. “No particular anesthetic has been exonerated,” says Roderic G. Eckenhoff, a professor of anesthesiology at the University of Pennsylvania.

3. Beware the *zeitgeist*.

Three current technologies have been victims of the current culture: e-cigarettes, because no one likes the image of a teenager smoking, even if it's not actually smoke; GMOs, because the technology smacks of hubris, our attempt to alter the natural order; and bisphenol A (BPA), because it is a chemical resin that can leach out of plastic baby bottles. All three technologies have been the victims of scientific studies purporting harm. And all three have suffered at the hands of the media. Negative press, however, shouldn't blind us to the evidence.

First introduced into the United States in 2006, e-cigarettes are battery-powered vaporizers that deliver nicotine but don't contain tobacco. The liquid that is vaporized also contains propylene glycol,

glycerol, and assorted candy or dessert flavorings (such as Belgian waffle and chocolate). Only a letter and a hyphen away from one of the most destructive products ever invented (cigarettes), e-cigarettes have been universally condemned by virtually every scientist, physician, and government official responsible for the public's health. And it's not hard to understand why.

First, nicotine is highly addictive and potentially harmful, especially to a developing fetus. It can also cause headaches, nausea, vomiting, dizziness, nervousness, and a rapid heartbeat. Although some brands of e-cigarettes don't contain nicotine, most do.

Next, Big Tobacco companies like Altria, Reynolds, and Imperial make e-cigarettes. Although company executives claim that e-cigarettes are an exit strategy for those trying to quit smoking, they haven't exactly earned the trust of the American public. In 2012, e-cigarette makers spent more than \$18 million on magazine and television ads. Unlike ads promoting cigarettes, which were banned in 1971, companies are free to advertise e-cigarettes. As a result, e-cigarettes have become a \$3.5-billion-a-year industry in the United States, with some predicting that sales will exceed those for conventional cigarettes by the mid-2020s.

Finally, reminiscent of the Joe Camel commercials, some advertisements for e-cigarettes are specifically designed to entice young people. When Julia Louis-Dreyfus was shown smoking an e-cigarette during the 2014 Golden Globe Awards, both Henry Waxman (D-CA) and Frank Pallone, Jr. (D-NJ), called the president of NBC to say that the actress was “sending the wrong message to kids about these products.” Protests by people like Waxman and Pallone have fallen on deaf ears; e-cigarettes have become enormously popular among the young. In 2013, about 250,000 minors who had never smoked a cigarette had tried an e-cigarette. In 2014, an estimated

1.6 million middle and high school students in the United States experimented with them, a dramatic increase from the previous year. Indeed, more than 10 percent of high school students in the United States have tried an e-cigarette. It seems like only a matter of time before this tidal wave of children using e-cigarettes will become a flood of adults smoking cigarettes—and dying from lung cancer as a result. E-cigarettes appear poised to add to the 480,000 deaths and \$300 billion in direct health care expenditures and productivity losses caused each year by cigarette smoking.

For all of these reasons, the American Cancer Society, the American Lung Association, the Centers for Disease Control and Prevention (CDC), the World Health Organization, and the American Academy of Pediatrics all strongly oppose e-cigarettes. And, when I first approached this subject, I assumed that I would end up agreeing with them, wholeheartedly. There was, however, one problem: the data.

Associated with the dramatic rise in e-cigarettes during the past five years, cigarette smoking has declined to historically low levels, including among the young. For example, the CDC reported that although the use of e-cigarettes had tripled between 2013 and 2014, the incidence of cigarette smoking had declined dramatically. In 2005, 20.9 percent of adults smoked cigarettes; by 2014, only 16.8 percent did, a 20 percent drop. Indeed, in 2014, the number of Americans smoking cigarettes fell below 40 million for the first time in 50 years. Further supporting the notion that e-cigarettes were replacing cigarettes, states that had banned the sale of e-cigarettes to minors witnessed an increase in cigarette smoking in that age group. And there is no denying that e-cigarettes are safer; unlike cigarettes, they don't produce tars that cause cancer or combustibles like carbon monoxide that cause heart disease. "People

smoke for the nicotine but they die from the tar," said Michael Russell, a pioneer of nicotine-cessation treatments.

Maybe this is all coincidence. Maybe there are other reasons that cigarette smoking is declining that have nothing to do with the rise of e-cigarettes. But it's too early to condemn e-cigarettes as a gateway product to cigarette smoking when the opposite appears to be true. Time will tell. The point being that the cultural milieu that damns e-cigarettes is irrelevant; only the data are relevant. In August 2015, England's Department of Health recommended e-cigarettes as an effective way to stop smoking. Nine months later, in April 2016, the Royal College of Physicians, an organization of British doctors founded in 1518, supported the Department of Health's decision. British physicians had been influenced by a study in the United Kingdom showing that smokers who used e-cigarettes were much more likely to quit than those who used nicotine patches.

Like e-cigarettes, GMOs have also fallen victim to the zeitgeist.

GMOs are defined as any living organism that possesses "a novel combination of genetic material obtained through the use of modern biotechnology." The key phrase here is "modern biotechnology," because the truth is that we have been genetically modifying our environment since the beginning of recorded history. Using breeding or artificial selection, humans began to domesticate plants and animals around 12,000 B.C.—all for the purpose of selecting for certain genetic traits and all a precursor to modern genetic modification. Nonetheless, for environmentalists, no single act of hubris has been more terrifying than when scientists decided to recombine DNA in the laboratory to modify nature.

Today, the largest use of genetic bioengineering has been in food production. Genetic engineering has allowed crops to resist pests, tolerate extreme temperatures and environmental conditions, and be

free of certain diseases. Genetically engineered crops have also been created to improve nutrient profiles, lengthen shelf lives, and resist herbicides. In the United States, 94 percent of soybeans, 96 percent of cotton, and 93 percent of corn are genetically modified; in the developing world, 54 percent of crops are genetically modified. The consequences, especially for farmers in the developing world, have been dramatic. GMO technology has reduced chemical pesticide use by 37 percent, increased crop yields by 22 percent, and increased profits for farmers by 68 percent. Although GMO seeds are more expensive, the cost is easily offset by reduced use of pesticides and higher yields.

Although many people fear that genetically modified foods might be more dangerous than other foods, careful scientific studies show they have no reason for concern. The American Association for the Advancement of Science and the National Academy of Sciences have both issued statements supporting the use of GMOs. Even the European Union, which has never been particularly supportive of GMOs, cannot ignore the science. In 2010, the European Commission issued the following statement: "The main conclusion to be drawn from the efforts of more than 130 research projects, covering a period of more than 25 years of research involving more than 500 independent research groups, is that biotechnology, and in particular GMOs, are not *per se* more risky than conventional plant breeding technologies."

Although the science is clear, the public remains concerned. A recent Gallup poll found that 48 percent of the American public believed that genetically modified foods posed a serious risk to consumers. Many of those polled wanted foods to contain GMO warning labels so they could know which ones to avoid. This poll showed that not only are we willing to ignore science, but we're also willing to

ignore history. Due to selective breeding and cultivation, the crops we raise today "naturally" have little resemblance to their ancestors. From a practical standpoint, the farmer taking advantage of a chance mutation to cultivate a specific crop is indistinguishable from a choice to create the mutation ourselves. Both have the same mutation.

Genetic modification has also been used to make lifesaving medicines. Insulin used by diabetics, clotting proteins used by hemophiliacs, and human growth hormone used by children with short stature have all been made using genetic engineering technology. Previously, these products were obtained from pig pancreases, blood donors, and the pituitaries of dead people.

Yet those who oppose GMOs persist. Recently, the story of a tomato containing a fish gene made the rounds. The Frankensteinian image galvanized environmentalists to push harder to label GMO foods. Steven Novella, an assistant professor at Yale University School of Medicine, and the creator of the podcast, *The Skeptics Guide to the Universe*, summed it up best: "The real question here is not whether there is a GMO tomato with a fish gene, but who cares?" he wrote. "It's not as if eating fish genes is inherently risky—people eat *actual* fish. Furthermore, by some estimates, people share about 70 percent of their genes with fish. You have fish genes and every plant you have ever eaten has fish genes. Get over it!"

The GMO controversy reached its illogical end in 2015, when New York Assemblyman Thomas J. Abinanti introduced Bill 1706, banning all genetically modified vaccines. Not surprisingly, most vaccines are genetically modified. If not, then people would be injected with the "natural" bacteria or viruses that caused the disease. For example, by genetically modifying poliovirus, we've eliminated polio from the United States and from much of the world. Vaccines have to be genetically modified.

Perhaps no single chemical has suffered from the zeitgeist more than bisphenol A (BPA).

In 1935, the DuPont chemical company launched its slogan, "Better Living Through Chemistry." In 1982, DuPont dropped "Through Chemistry" and later abandoned the slogan altogether in favor of "The Miracles of Science." The word "chemistry" just didn't sit well with the American public. We seem to respond negatively to anything with a chemical name. And bisphenol A certainly fits that bill.

BPA, which was first synthesized in 1891, wasn't commercially available in the United States until 1957, when it was used to make plastics and resins. The chemical found its way into goggles, face shields, bicycle helmets, water bottles, baby bottles, CDs, DVDs, the lining of water pipes, and the lining of metal soup and soda cans. Ironically, BPA wasn't invented to make plastic clear and tough. It was invented as a synthetic estrogen, the hormone primarily responsible for regulating the female reproductive system. But BPA was a weak estrogen—about 40,000 times weaker than other synthetic estrogens—so it was abandoned, only later to be picked up as a plasticizer. What researchers soon discovered, however, was that this weak hormone, although insoluble in water, could leach out of plastic or metal containers. They feared that Americans, including American babies, might unknowingly be ingesting a feminizing hormone.

Concerned that BPA might be harmful, researchers studied its effects on mice and rats, linking it to breast cancer, prostate cancer, early onset puberty, ovarian cysts, obesity, and even attention deficit disorder. Then they started investigating people, finding that 93 percent of adults had traces of BPA in their urine. "If you don't have BPA in your body," wrote one *Time* magazine reporter, "you're not living in the modern world."

Armed with this information, Nalgene, which makes plastic containers, removed BPA from all of its products. Then the FDA banned its use in baby bottles. BPA was now, according to one reporter, "among the world's most vilified chemicals." Similar to the story of DDT, however, the BPA story also soon fell apart.

Initially, researchers had trouble reproducing the animal model studies, especially when using quantities of BPA likely to be encountered by people. A 2004 report from the Harvard Center for Risk Analysis found "no consistent affirmative evidence for low-dose BPA effects." Glenn Sipes, who was a co-author of the study, said, "I've never had a problem saying that we can see biological effects in these low doses. But why are we seeing these studies that can't be repeated? Why do we have to work so hard to try and replicate and show these low doses really have an effect? Why don't [problems with BPA] stand out in black and white?"

In 2011, a review of studies in people found no evidence that low doses of BPA caused harm. The reason that studies in rodents had found that BPA had caused problems was that the rodents had been *injected* with BPA; injection bypassed the liver, which typically inactivates BPA within five minutes. When rodents were *fed* BPA instead of being *injected* with it, those given 40, 400, or 4,000 times the typical human exposure remained healthy.

In July 2014, the FDA stated that, "BPA is safe at the current levels occurring in foods." Similarly, the European Food Safety Authority, which published recommendations about BPA in 2008, 2009, 2010, 2011, and 2015, also continues to state that BPA is safe. Both agencies have set limits for the tolerable daily intake (TDI) for BPA. To exceed this limit, an average adult would have to ingest about 10,000 times more BPA than one would typically ingest in a day: the equivalent of eating more than 500 cans of soup. Nonetheless, today

it's hard to find a water bottle that doesn't proudly proclaim "BPA-free" on the label.

Another reason that we should have been suspicious of the BPA studies is that mice aren't men. All studies of experimental animals should be viewed with caution. For example, in the early 1970s, saccharin was shown to cause bladder cancer in rodents. As a result, all food containing saccharin bore a label warning of its dangers. By 2000, scientists realized that what was happening in rodents wasn't happening in people. The reason was that, unlike humans, the urine of rodents is highly acidic and contains large quantities of calcium phosphate and proteins. For these reasons, rodents fed saccharin formed microcrystals in their urine that damaged the lining of the bladder, causing bladder cancer. None of these events occurred in people. On December 21, 2000, the FDA removed warning labels from foods containing saccharin.

Also, if you're going to say that animal studies predict events in people, then we should stop eating chocolate, which can cause heart arrhythmias and occasionally death in dogs. As it turns out, dogs cannot tolerate even small amounts of a substance in chocolate called theobromine. People, on the other hand, can consume much larger quantities of chocolate without getting sick. (I am living proof of this.)

Animal studies can also be misleading for another reason: They can show that something is valuable even when it isn't. For example, early studies of a vaccine to prevent HIV were promising in experimental mice and monkeys. But studies in people have been far less promising. "Mice lie and monkeys exaggerate," says University of Pennsylvania vaccine researcher David Weiner.

Our fear of anything with a chemical name isn't likely to go away anytime soon. A few years ago the comedians Penn and Teller did an experiment. They sent a friend to a fair in California to get signatures

on a petition to ban dihydroxy-monoxide. Hundreds of people signed the petition, convinced that the chemical was bad for you. *Dihydrox* means two hydrogen (H) atoms and *monoxide* means one oxygen (O) atom. The combination, H₂O, is water. By using a chemical name, their friend was able to convince hundreds of people to ban water from the face of the Earth.

4. Beware the quick fix.

Like lobotomies, mental institutions bursting at the seams with adult schizophrenia patients are a relic of the past. Schizophrenia has become an outpatient disease. So has autism, arguably the most common psychiatric disorder of children. As a consequence, the pressures to find a cure have shifted from psychiatrists working at public facilities to parents living in private homes. Unfortunately, like their counterparts in the past, parents have become desperate, willing to do anything to relieve the suffering. So, although we may think that gruesome, ill-conceived, medieval therapies like lobotomies are behind us, they're not.

Children with autism have been put in hyperbaric oxygen chambers, causing intense, painful pressure on their eardrums and, in one case, death. They've been given intravenous medicines designed to bind heavy metals, causing another child to die when his heart stopped beating. They've been taken to Mexico or other countries for stem cell transplantations. And, perhaps worst of all, they've been subjected to a therapy invented by a former Scientologist turned health evangelist named Jim Humble, who calls himself the archbishop of the Genesis II Church of Health. In his online video, Humble claims to be a billion-year-old god from the Andromeda galaxy.

Humble believes that autism—as well as AIDS, malaria, cancer, and Alzheimer's disease—is caused by worms living in the intestine.

To kill the worms, he invented what he calls the Miracle Mineral Solution or MMS. MMS contains sodium chlorite and citric acid, which combine to form chlorine dioxide, a powerful bleach. MMS, which children swallow or receive as an enema, is now quite popular in the autism community. The problem, apart from the fact that autism isn't caused by worms, is that even small quantities of MMS can cause nausea, vomiting, diarrhea, intestinal bleeding, respiratory failure, hemolysis (when red blood cells in the bloodstream break apart), and, ironically, developmental delay. In October 2015, one U.S. vendor was sent to prison for selling the product. MMS has been linked to at least one death.

Parents who subject their children to MMS often share their stories online. They write about children crying out in pain. They show pictures of the lining of their children's intestines that have come out in their stools, believing, wrongly, that they're worms. They talk about how their children's hair has fallen out. And they talk about how their children have slowly grown more apathetic, losing any previous emotion. How, as they have chronically poisoned their children with an industrial bleach, their children have quieted down, becoming much easier to handle. In essence, how—as had been the case for lobotomies—they have merely substituted one disorder for another. Still, these parents urge each other on. It's working, they claim.

The contrasts between lobotomy and MMS therapy are striking. Lobotomies were endorsed by the American Medical Association, the American Psychiatric Association, and the *New England Journal of Medicine*. MMS therapy has never been endorsed by any professional or medical organization; on the contrary, the FDA has issued a warning against its use. Ice pick lobotomies were invented by a respected neurologist who was a professor at a well-known medical school. MMS therapy was invented by a man claiming to be from a galaxy

2.5 billion light-years from Earth. Frankly, it's much easier to understand how people could lobotomize their children than squirt a powerful industrial bleach into their children's mouths and rectums.

Although it might seem far-fetched, imagine the following scenario: A group of unscrupulous doctors opens a clinic in Switzerland that performs lobotomies for the treatment of autism. The doctors who run the clinic don't call the procedure a lobotomy (that ship has sailed); they call it something else, like the "Fresh Start" procedure. The doctors put up an attractive website that explains how the outpatient procedure takes only a few minutes to perform and involves severing the nerve fibers in the brain that cause autism. They include a few parent testimonials stating that after the procedure their children's language doubled, and then they open their doors. If a man claiming to be a billion-year-old god from another galaxy can get people to line up for a therapy that crosses the line into child abuse, then doctors in some European clinic should expect at least equal success with a quick-fix surgical procedure. It hasn't happened yet, but there is no reason to believe that it couldn't. Desperate to do something, anything, to cure the incurable, we continue to punish the afflicted.

5. The dose makes the poison.

When Rachel Carson wrote *Silent Spring*, she correctly predicted that man-made activities could destroy the environment. Thanks to Rachel Carson, we are now far more attentive to our impact on the planet. Unfortunately, Carson also gave birth to the notion of zero tolerance—the assumption that any substance found harmful at any concentration or dosage should be banned absolutely. If large quantities of DDT (like those used in agriculture) were potentially harmful, then even small quantities (like those used to prevent mosquitoes from

biting) should be avoided. As a result, millions of children died needlessly from malaria.

One recent example of how the concept of zero tolerance has caused harm is thimerosal: an ethylmercury-containing preservative used in vaccines. Because vaccines are injected into babies, no preservative has generated more angst.

Preservatives were first added to multidose vials of vaccines back in the 1930s. The reason was that as the needle penetrated the rubber stopper again and again, bacteria could enter the vial. In the early 1900s, children receiving the eighth, ninth, or tenth dose of a vaccine might be inoculated with bacteria that had inadvertently been introduced into the vial, causing severe and occasionally fatal infections. By adding preservatives containing ethylmercury to vaccines, this problem disappeared. But in the late 1990s the question arose, at what price?

In 1999, some physicians worried that babies and young children might be exposed to too much mercury in vaccines. What happened to thimerosal in vaccines in the 1990s eventually mimicked what had happened to DDT in the 1970s. Exercising caution, thimerosal was precipitously removed from infant vaccines and branded with a scarlet letter. During the year or so when manufacturers were gearing up to produce thimerosal-free vaccines, some, like the hepatitis B vaccine, still contained thimerosal. About 10 percent of hospitals decided not to give thimerosal-containing hepatitis B vaccines; as a result, one three-month-old child in Michigan died of overwhelming hepatitis B virus infection and six children in Philadelphia born to mothers infected with the virus weren't vaccinated, condemning them to the likely development of chronic liver disease (called cirrhosis) or liver cancer later in life. These hospitals had wrongly assumed that the harm from a thimerosal-containing hepatitis B vaccine (which was theoretical at best) was greater than the risk of getting hepatitis B (which

wasn't theoretical at all). Within a few years of the removal of thimerosal from vaccines given to young children, seven studies showed that it hadn't caused harm. The only harm had come from elevating a theoretical risk above a real risk.

It's not hard to understand how this could have happened. Mercury is never going to sound good. (There's no such thing as the National Association for the Appreciation of Heavy Metals.) Large quantities of mercury have clearly been shown to cause harm. Indeed, environmental mercury contaminations caused by a chemical spillage in Minamata Bay, Japan, or by fumigating grain in Iraq damaged hundreds of babies and fetuses. Mercury, however, which is present in the Earth's crust, is hard to avoid. Anything we drink that's made from water on this planet (including breast milk and infant formula) will contain small quantities of mercury. These small quantities of mercury aren't harmful. Only large quantities are harmful. If small quantities of mercury were harmful, we'd have to move to a different planet. Of interest, the quantities of mercury contained in vaccines were far less than those contained in breast milk and infant formulas. And mercury isn't the only heavy metal to which we are routinely exposed. We all have trace quantities of metals like cadmium, beryllium, thallium, and even arsenic in our blood. But at quantities far less than those required to do harm.

Unfortunately, we seem incapable of learning the most important lesson in toxicology: The dose makes the poison. For example, if people drink several gallons of water quickly (as has occurred during fraternity hazings), they might exceed their body's ability to hold onto the mineral sodium. As the level of sodium in the bloodstream drops, it's possible that they could have a seizure. This doesn't mean that water is toxic to the brain. It only means that you shouldn't drink several gallons of it at once. Similarly, a cup of organic coffee

contains acetaldehyde, benzaldehyde, benzene, benzopyrene, benzofuran, caffeic acid, catechol, 1,2,5,6 dibenzanthracene, ethylbenzene, formaldehyde, furan, furfural, hydroquinone, d-limonene, 4-methylcatechol, styrene, and toluene. Many of these substances are known cancer-causing agents or DNA-altering chemicals. Yet no study has ever found that organic coffee causes cancer. That's because the quantities of the chemicals contained in coffee are well within the levels considered safe. Rachel Carson's lesson of zero tolerance doesn't apply to the real world.

6. Be cautious about being cautious.

Rachel Carson taught us caution. Wouldn't it make sense to ban DDT given that at the very least, it might cause harm to people. As we learned, removing it from use caused far more harm than good.

However, one could make a reasonable argument that, regarding BPA, what possible harm could come from removing a plasticizer from a toy. At the time that the FDA banned it from baby bottles and Nalgene removed it from all of its products, it wasn't clear whether BPA was safe. Wouldn't it make sense, then, to remove BPA in the interest of caution—under the precautionary principle? The answer is yes; it was reasonable. But we have to be careful. We have to make sure that in the name of the precautionary principle we aren't doing more harm than good. Although removing a plasticizer from a child's toy was without consequence (and could have been predicted to have been without consequence), the decisions to precipitously remove thimerosal from vaccines (and scaring parents and doctors) or to ban DDT from public health programs (when the only replacements were more expensive and less available) have caused children to suffer needlessly and predictably. The precautionary principle, at the very least, assumes that no harm will come from exercising caution.

Which brings us to arguably the single greatest use of the precautionary principle in modern medicine: cancer-screening programs.

During the past 50 years, doctors and scientists have proven that some cancers can be prevented. Sunblock can prevent skin cancer. The hepatitis B virus vaccine can prevent the most common cause of liver cancer. The human papillomavirus vaccine can prevent the only known cause of cervical cancer. And cessation of cigarette smoking can prevent a common cause of lung cancer. The results of these four strategies are clear.

The definition of cancer, however, is changing—and not for the better. Medical textbooks 20 years ago defined cancer as a “disease the natural course of which is fatal.” No longer. Now we detect cancers that aren't fatal—the kind of cancers that you are more likely to die *with* than *from*. In the process of detecting these nonfatal cancers, we are probably doing more harm than good.

Gilbert Welch, a professor at Dartmouth Medical School, offers the best analogy to our current dilemma. It's a barnyard analogy. Imagine, writes Welch, three animals in a barn that are trying to escape: a bird, a turtle, and a rabbit. When you open the door, they will escape at different rates. The bird, which will invariably fly out before you have time to close the door, is analogous to the kind of cancer that will kill you no matter what you do. Even if you detect the cancer early, it doesn't matter—you'll die from it anyway. It's just too aggressive. The turtle, which is so plodding that it will never effectively escape, is analogous to a cancer that is so slow growing, so nonvirulent, that it will never kill you. You will invariably die from something else first. This is the kind of cancer that you will die with and not from. The rabbit, which can be caught if the door is closed quickly enough, is analogous to the kind of cancer worth detecting. If this cancer isn't detected early, then it will kill you.

And if it is detected early, then the screening test will have saved your life.

Screening tests are valuable only if they are detecting rabbits; if they're detecting mostly turtles and birds, then they won't save lives. Some screening tests, like Pap smears to detect cervical cancer or colonoscopies to detect colon cancer, save lives. Both of these tests are detecting lots of rabbits. For thyroid, prostate, and breast cancers, on the other hand, the value of early screening tests isn't so clear. Atul Gawande, a surgeon at Johns Hopkins University School of Medicine and prolific author, says it best: "We now have a vast and costly health care industry devoted to finding and responding to turtles."

We'll start with thyroid cancer.

In 1999, the South Korean government initiated a large nationwide screening program for the early detection of thyroid cancer. The screening test used was ultrasonography, which sends high-frequency sound waves (higher than those audible to the human ear) into the body. The sound waves then bounce back. Different structures absorb or reflect sound waves differently. As a result of the massive screening program, South Korean physicians detected more than 40,000 new cancers of the thyroid, 15 times more than had been detected before the screening program started. Thyroid cancer became the most common cancer in South Korea. One researcher called it a "tsunami of thyroid cancer."

Virtually all of these South Korean thyroid cancers were treated by completely removing the thyroid, called a thyroidectomy. This procedure, however, comes with a price. At the very least, everyone with a thyroidectomy has to take thyroid replacement hormones for the rest of their lives. And sometimes it's difficult to get the dose right. People suffer from symptoms of too much replacement hormone (sweating, heart palpitations, and weight loss) or too little replace-

ment hormone (somnolence, depression, and weight gain). Worse, because the nerves of the vocal cord travel close to the thyroid gland, some people suffer vocal cord paralysis. Or they suffer from a problem with calcium metabolism because a gland called the parathyroid gland, which regulates calcium, is also nearby. Or they suffer from life-threatening bleeding after the surgery. Initially, South Korean health officials were excited that they had detected all of these cancers before patients had developed any symptoms. Then they looked at the mortality rates from thyroid cancer. No difference. The incidence of death from thyroid cancer was exactly the same before and after the massive screening program. The only tangible outcome was that now tens of thousands of South Koreans had to suffer the side effects of thyroid surgery.

Overdiagnosis and overtreatment of thyroid cancer hasn't been limited to South Korea. In France, Italy, Croatia, Israel, China, Australia, Canada, and the Czech Republic, the rates of thyroid cancer have more than doubled. In the United States, they've tripled. In all of these countries, as had been the case in South Korea, the incidence of death from thyroid cancer has remained the same.

Autopsy studies confirm the problem with trying to screen for thyroid cancer. About one-third of people who have died from other causes also had thyroid cancer at autopsy. Some researchers argue that if the sections of the thyroid examined in these studies had been thinner and more numerous, the percentage of people with thyroid cancer at the time of their death would have approached 100 percent. Which isn't to say that people don't die from thyroid cancer. They do. The death rate from thyroid cancer in the United States is about 1 per 200,000 people. The problem with thyroid cancer is that it's almost all turtles and a few birds. There just aren't enough rabbits to make screening worthwhile.

Next year in the United States, about 60,000 people will be diagnosed with thyroid cancer. Women will outnumber men three to one. Virtually all will have thyroidectomies, and few, if any, will benefit from the diagnosis. If most of these small thyroid cancers don't kill you, then maybe we shouldn't call them cancer.

Screening for prostate cancer has also come under closer scrutiny.

In 1970, Richard Ablin, a professor of pathology at the University of Arizona, discovered the PSA test, which stands for prostate-specific antigen. PSA is an enzyme made by cells in the prostate gland. The purpose of PSA is to break up cervical mucus so that sperm can enter the uterus. Criminologists were the first to recognize the value of PSA, which offered proof for the existence of semen in rape cases, even when the rapist had had a vasectomy or couldn't make sperm. Doctors were the next to realize the potential value of PSAs, using the test to determine whether prostate cancers had relapsed. Then physicians took a step they are now starting to regret—PSA tests were used to *predict* whether someone had prostate cancer. If the level of PSA in the blood was high, then urologists recommended a prostate biopsy. If the biopsy showed prostate cancer, then men either had a total removal of the prostate (prostatectomy) or they had radiation therapy to the prostate. More than 90 percent of men in the United States who have been diagnosed with prostate cancer have had one therapy or the other.

Because of the PSA test, prostate cancer is now the most commonly diagnosed non-skin cancer in the United States. So, what's happened to the incidence of death from the disease? Nothing. The risk of dying from prostate cancer hasn't changed in the last ten years. Indeed, about 50 percent of men more than 60 years old have been found at autopsy to have prostate cancer after they had died from something else; in men more than 85 years old, that number climbs to 75 percent. In

other words, as had been the case for thyroid cancer, men are more likely to die with prostate cancer than from it. Prostate cancer, like thyroid cancer, is mostly turtles and birds.

In 2012, the United States Preventive Services Task Force recommended against PSA-based screening tests for prostate cancer. But not before a lot of harm had been done. High PSA tests invariably lead to prostate biopsies, which can cause pain, bleeding, difficulties with urination, and bloodstream infections requiring hospitalization. And, aside from the psychological trauma of being diagnosed with prostate cancer, therapies for the disease are brutal. Prostate surgeries and radiation commonly cause incontinence and erectile dysfunction. Worse, five of every thousand men will die from prostate surgery. And all for nothing. By 2015, three years after the task force had issued its recommendations, the number of people screened for and diagnosed with prostate cancer had declined; many physicians had gotten the message.

Two years before the task force changed its recommendation, Richard Ablin, the discoverer of PSA, penned an op-ed piece for the *New York Times*. Noting that the annual bill for PSAs was \$3 billion, he wrote, "As I've been trying to make clear for many years now, PSA testing can't detect prostate cancer and, more important, it can't distinguish between the two types of prostate cancer—the one that will kill you and the one that won't. I never dreamed that my discovery four decades ago would lead to such a profit-driven public health disaster."

Mammography screening for breast cancer is also being reevaluated. Although it is clear that mammography, which was first introduced into the United States in the mid-1970s, saves lives; the question is how many and at what cost.

In 2012, Archie Bleyer and Gilbert Welch published a study in the *New England Journal of Medicine* titled "Effect of Three Decades

of Screening Mammography on Breast-Cancer Incidence.” They found that, with the advent of screening mammographies, the incidence of breast cancer in the United States had doubled. For every 100,000 women screened, the number of women diagnosed with breast cancer had increased from 112 to 234. In other words, every year 122 more women (per 100,000) were being diagnosed with breast cancer. At the same time, the number of women presenting with late-stage breast cancer (the kind that often results in death), decreased from 102 to 94 (per 100,000). This meant that only 8 women among 122 appeared to benefit from the screening. Eight. The others were treated with mastectomy, radiation therapy, and chemotherapy without benefit. The authors concluded that, although the incidence of death from breast cancer had clearly decreased during the era of screening mammography, most of that decrease was due to better treatment, not better screening. They also estimated that during the three decades of mammography, about 1.3 million women had been diagnosed with a cancer that would never have killed them. The authors concluded that, “screening is having, at best, only a small effect on the rate of death from breast cancer.”

Another study involving hundreds of countries also cast doubt on the time-honored notion that mammographies save lives. Investigators found that different countries had different rates of screening. In some countries, as few as 40 percent of women were screened; in others, as many as 80 percent were screened. If mammographies were making a difference, then countries that screened more women should have had lower rates of deaths from breast cancer. But deaths rates from breast cancer were the same in both groups of countries. The only difference was that in countries with higher rates of screening, more women had mastectomies, radiation, and chemotherapy.

With no obvious benefit. As a consequence of these and other studies, the recommendations for mammography have changed. Doctors used to recommend that all women between 40 and 74 years of age get a mammogram every two years. Now the United States Preventive Services Task Force recommends screening starting at 50, not 40 years of age. There were just too many noncancers that were called cancers—and women were suffering needlessly as a result.

In February 2015, Christie Aschwanden, a journalist, wrote an editorial in the *Journal of the American Medical Association*. The article was titled, “Why I’m Opting Out of Mammography.” Aschwanden imagined five possible outcomes following the procedure: One, “most likely the scan would turn up nothing suspicious.” Two, “I’d be called back for further testing, perhaps even a biopsy for something that was not cancer,” resulting in “sleepless nights [and] some lingering worry afterwards.” Three, “the mammogram would find a cancer that would have remained innocuous if not detected. If a mammogram found one of these cancers—and right now it’s impossible to definitively differentiate them from the dangerous ones—I would be treated and ‘cured’ for a cancer that was never destined to hurt me.” Four, “the mammogram could find a very aggressive, incurable cancer—the kind responsible for most deaths. In this case, I might be diagnosed sooner, but I’d ultimately die from the cancer anyway, and I’d spend more of the years I had left receiving cancer treatment.” Five, “the mammogram could find a dangerous cancer that’s amenable to treatment, and my life would be saved.” Using data from a recent study, Aschwanden reasoned that the chance that a mammogram would save her life was about 0.16 percent. She concluded that “a mammogram is more likely to ‘cure’ me of a harmless cancer—by subjecting me to life-disrupting and potentially harmful treatments like chemotherapy and radiation—

than it is to prevent me from dying of breast cancer. For me that's a deal breaker."

Until scientists are able to find genetic or biochemical markers that clearly distinguish bad cancers from innocuous ones, we are going to continue to suffer from the overdiagnosis and overtreatment of cancers that aren't really cancers at all. And continue to be told that our lives are being saved when they're not. Today, about 70,000 women every year are diagnosed with breast cancers that would never have killed them. Our overzealous sense of caution has caused a lot of unnecessary fear, anxiety, and debilitating surgeries.

7. Pay attention to the little man behind the curtain.

Today, it's not hard to find people who give medical or scientific advice based on the Wizard of Oz effect. Health gurus all hope that their winning personalities will hide their lack of evidence. And they don't like to be challenged. When little men behind curtains are revealed to be just little men behind curtains, they often cry foul. It wasn't that their claims were wrong, they argue, it was that evil forces were conspiring to defeat them.

For example, in 1998 a British physician named Andrew Wakefield proposed that the combination measles-mumps-rubella (MMR) vaccine caused autism. Thousands of parents in the United Kingdom and the United States withheld the MMR vaccine. As a consequence, hundreds of children were hospitalized and at least four died from measles. The public health and academic communities responded by performing more than a dozen studies. Their findings were clear, consistent, and reproducible. The MMR vaccine didn't cause autism. Andrew Wakefield had been wrong.

Were Wakefield a real scientist—which is to say someone who was open to the possibility that his hypothesis might be wrong—he

would have looked at the mountain of evidence in front of him and stepped aside. But he didn't. Wakefield, as it turned out, possessed something that no scientist should ever possess: a nonfalsifiable hypothesis. MMR caused autism and that was that. So he did what all pseudoscientists do when they are shown to be wrong: He found a bogeyman, claiming that other researchers couldn't reproduce his findings because they had all been unduly influenced by the pharmaceutical industry. Wakefield wanted us believe that thousands of researchers, public health officials, academicians, and pediatricians on several continents were all deeply, hopelessly in the pockets of drug companies. Free of such undue influence, he implied, his theory was unassailable.

Linus Pauling was no different. When his hypothesis that vitamin C could treat cancer was refuted by two excellent studies published in the *New England Journal of Medicine*, he threatened to sue the journal. According to Pauling, the problem wasn't that he was wrong (after all, he was Linus Pauling, the holder of two Nobel Prizes), it was that there was a conspiracy by the medical establishment to defeat him. A medical establishment that had no interest in allowing a product as inexpensive as vitamin C to replace the expensive chemotherapies it had been cashing in on for decades.

If Andrew Wakefield and Linus Pauling's hypotheses were right, then subsequent studies would have shown that they were right. When well-designed studies refuted their claims, they chose to attack those who had found them to be wrong. They did what any good lawyer would do; they argued conspiracy. (The legal aphorism is that when the law is on your side, argue the law; when the facts are on your side, argue the facts; when neither is on your side, attack the witness.) The minute that you hear researchers claim conspiracy, you should suspect that their hypotheses are built on sand. And although their this-is-

what-happens-when-you-speak-truth-to-power lament is appealing, it doesn't mean that it's right. As Norman Levitt, a mathematician and debunker of pseudoscience, famously said, "While Galileo was a rebel, not all rebels are Galileo"—no matter how hard they try to convince you that they are.