SPOTLIGHT ON SCIENCE:





In 2020, science took center stage—what did we know about the virus, how would it affect us, do masks work, and most importantly, how can we develop effective vaccines to help us move on from COVID-19?

Scientific discovery, including the development of vaccines that change the world, is remarkable and often taken for granted. When science gets it right—which is not easy—we quickly move on to the next challenge without taking the time to revel in the wonder that we have achieved.

When you consider the majority of scientific hypotheses are proven wrong—among them many observations and educated guesses about the causes of certain diseases, the health impact of particular foods, and the potential toxicity of medications or medical treatments—it is notable when experiments actually yield the anticipated results.

Accurate research and fact-based science are needed to warn society against unsafe products and practices.

It is even more notable when fact-based scientific evidence contributes to healthier lives and wiser public policy decisions, despite the revolving door of bad actors and misinformation on the internet and in the media that makes it harder for people to discern between real and unwarranted fears.

Accurate research and fact-based science are the strongest defense against unsafe products and practices. What follows are a few historical examples of scientific research "getting it right" for the benefit of humanity.

ASBESTOS

"Asbestos" refers to six silicate-based minerals that form a long, thin, flexible fibrous crystal. Chrysotile, or fibrous serpentine (${\rm Mg_3Si_2O_5(OH)_4}$), is the most common type of asbestos and accounts for 95 percent of all asbestos in commercial use.\(^1\) It occurs naturally worldwide and has been uncovered by archeologists as far back as the Stone Age.\(^2\)

Asbestos resists heat, water, and electricity, which made it a valued resource in developing societies. Egyptian pharaohs were wrapped in asbestos cloth to protect their deceased bodies from deterioration, and its long hair-like fibers were used for the wicks of candles and burning lamps as early as $4000 \, \text{B.C..}^3$

In the nineteenth century, asbestos was celebrated as an effective fire-retardant and electrical insulator. It found many uses in the steam engines, turbines, boilers, ovens, and generators that powered the Industrial Revolution throughout Europe and the United States.⁴ People began to refer to asbestos as a miracle substance. To meet demand, modern production of asbestos began in Italy in 1868, and large scale production began in Quebec in 1878.⁵

Unfortunately, the dangers of asbestos were known and hidden from the public for decades. In 1899, London physician Dr. Montague Murray drew a connection between asbestos exposure and lung damage. Asbestos is easy to breathe in and difficult to destroy. As a result, it can stay in the lungs for decades and cause irreparable damage.⁶

It took a quarter century to make the first diagnosis of asbestosis in 1924. The victim was Nellie Kershaw, an employee of Turner Brothers Asbestos in Greater Manchester, England. Her pathology report indicated lung scarring consistent with a healed tuberculosis infection and extensive fibrosis in which "particles of mineral matter ... of various shapes, but the large majority have sharp angles."

It was determined these particles were asbestos and "the primary cause of fibrosis of the lungs and therefore death." Her death was discussed in the British Medical Journal in 1924. Scientists identified a link between asbestos and lung cancer in the 1930s, but even so, production of asbestos continued with British factories enacting regulations to suppress dust and U.S. factories operating almost entirely unregulated. In

During World War II, more than 4.3 million people worked at shipyards that encountered asbestos materials. In fact, heavy use of asbestos by the U.S. military led to high rates of mesothelioma in veterans from both World Wars.

Between 1940 and 1980, asbestos manufacturing expanded into a multibillion-dollar industry that employed more than 200,000 people. During World War II, more than 4.3 million people worked at shipyards that encountered asbestos materials. In fact, heavy use of asbestos by the U.S. military led to high rates of mesothelioma in veterans from both World Wars. Is

The causal connection between asbestos and mesothelioma was established in the mid-1960s, around the same time the public was made aware that insulation workers

and other civilians with relatively light exposure to asbestos dust—and materials containing asbestos—could later suffer from asbestos-related disease. ¹⁴

This critical information had been known for decades, but was covered up by powerful asbestos companies. In 1929, Dr. Anthony Lanza was commissioned by asbestos industry leaders to explore disease among their factory workers. When Dr. Lanza found high rates of asbestos-related illness, the findings were buried. 15

Dr. Lanza was the assistant medical director at Metropolitan Life Insurance, which was complicit in the cover-up. They were reported to have blocked safety inspections and instructed factories against hanging asbestos warning signs.¹⁶

In the 1930s, private companies Raybestos-Manhattan and Johns Manville manipulated a study to understate the severity of asbestosis. "The less said about asbestos, the better off we are," wrote the president of Raybestos-Manhattan in a 1935 letter to a Johns Manville attorney.¹⁷

Nearly 15 years later, Dr. Kenneth Smith recommended Johns Manville decline to notify its sick workers they had asbestosis. He was later hired as the company's medical director. There are additional reports of companies that refused to show workers their X-ray results if they revealed signs of respiratory disease.¹⁸

Industry leaders were forced to acknowledge the dangers of asbestos after Dr. Irving Selikoff of Mount Sinai Hospital linked asbestos exposure to cancer in the early 1960s, but the damage was done.¹⁹

Roughly 100,000 people in the United States have died from complications associated with asbestos exposure. At one shipbuilding center, case counts of mesothelioma among former workers are seven times the national rate.²⁰

While 67 countries have banned the use of asbestos, production continues in Russia. Attempts to ban asbestos in the United States remain in limbo. In 1991, the 5th Circuit Court prevented the Environmental Protection Agency (EPA) from issuing a ban of asbestos products after research indicated the ban would cost between \$450 million and 800 million. The court noted the EPA could not provide sufficient evidence of the safety of available alternative products.²¹

BLOODLETTING

Bloodletting refers to the removal of part of a patient's blood supply for therapeutic purposes. The practice began nearly 3000 years ago in Egypt, Greek and Roman civilizations, the Middle East, Asia, and throughout Europe during the Middle Ages and the Renaissance.²²

Humans were believed to have four humors: blood, phlegm, black, and yellow bile. Each humor was associated with a particular organ—brain, lung, spleen, and gall bladder. Illness and disease were thought to be the result of an imbalance of these humors.²³

For more than a thousand years, bloodletting was used to treat almost every illness imaginable: acne, asthma, cancer, cholera, coma, convulsions, diabetes, epilepsy, gangrene, gout, herpes, indigestion, insanity, jaundice, leprosy, ophthalmia, plague, pneumonia, scurvy, smallpox, stroke, tetanus, tuberculosis, and more. It was performed before surgery, at the onset of childbirth, and before amputation.²⁴

Bloodletting is believed to have killed King Charles II and George Washington.²⁵ Their deaths, among others, brought the practice of bloodletting under considerable scrutiny and doubt—but it was the development of new medical technology, including the microscope and stethoscope, that finally changed public opinion surrounding the ancient and unproven medical practice.

In the 1800s, this new technology allowed doctors to explore beyond empirical observation, and to move toward pathology and physiology based in research and clinical testing. At the Edinburgh School of Medicine, Dr. Hughes Bennett "grounded his rejection of bloodletting on pathologic concepts of inflammation and pneumonia derived from microscopic studies of inflamed tissues."²⁶

Several studies began to validate the microscope and stethoscope, and led to ground-breaking new medical discoveries and treatments that were rooted in scientific research, not anecdotal experience. This science-driven paradigm shift—led by physicians and biologists across Europe, including Pierre Louis, Robert Koch, Louis Pasteur, and Rudolf Virchow—gradually disproved the usefulness of bloodletting for most ailments.²⁷

While its popularity faded, bloodletting never totally disappeared. It remained a suggested practice in the 1923 edition of the textbook, The Principles and Practice of

Medicine.²⁸ Even now, a modified version of bloodletting is used as a treatment for rare and specific diseases such as hemochromatosis (too much iron in the body) and polycythemia (too many red blood cells or hemoglobin).²⁹

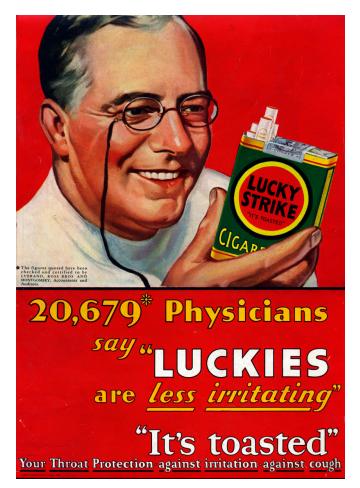
CIGARETTES

Smoking was practiced as far back as the first century BC when Mayans and Aztecs smoked tobacco as part of religious ceremonies.³⁰ Tobacco crossed oceans with explorers like Christopher Columbus, who observed the use of tobacco for medicinal and ceremonial purposes. By the seventeenth century, the practice of smoking had taken hold in Europe.³¹

In the early 1800s, the world was introduced to the "cigarette" (a term coined by the French). It took less than 50 years to begin the mass production—and marketing—of cigarettes worldwide.³²

When the heyday of print and radio advertising began in the 1920s and 1930s, manufacturers jumped on the opportunity to recruit new smokers on a massive scale. Swarms of commercials and advertisements featured images of doctors—in reality, actors—in white coats to persuade the public that smoking was a safe activity with several health and social benefits.

Recognition of cigarette addiction and use of the slang term "coffin nails" can be found in newspapers dating back to the 1800s. ³³ Even so, cigarettes were marketed as a cure-all for many ailments. During the 1890s, Dr. Batty's cigarette brand was sold as a treatment for asthma, hay fever, foul breath, throat ailments, head colds, canker sores, and other lung diseases. ³⁴ Cigarettes were provided by the government in combat rations for both World Wars. ³⁵



A 1930 Lucky Strike advertisement. From the collection of Stanford Research Into the Impact of Tobacco Advertising

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With every concern expressed by medical researchers, the tobacco companies were ready with a counterstrike. In 1930, German researchers made a connection between cancer and smoking but it did not establish a definitive causal relationship. Less than 10 years later, Johns Hopkins University determined that smokers do not live as long as non-smokers, and smoker's cough was a recognized medical condition.³⁷

Lucky Strike responded with advertisements that claimed toasted cigarettes were less harmful and reduced coughing.³⁸ In the 1940s, the R. J. Reynolds Tobacco Company

ran ads that declared, "More Doctors Smoke Camels Than Any Other Cigarette." Philip Morris hired doctors and paid them handsomely to support the tobacco industry and validate their unproven health claims. 40

The rise of lung cancer in the early twentieth century raised even further suspicion about the dangers of smoking, but there was not enough evidence that smoking was the primary cause. ⁴¹ Others theorized that new air pollution due to industrial developments like motor vehicles and factory production might have been additional culprits.

Five large-scale retrospective studies in the 1940s and 1950s provided a link between smoking and lung cancer, but they required people to self-report their smoking habits, which can easily be over or underestimated. In 1952, the American Cancer Society began a ground-breaking new study that recruited a cohort of about 188,000 American men (aged 50 to 69) across 10 states to be interviewed on their smoking habits. They followed-up with these men through 1955. 42

The study found that "men with a history of regular cigarette smoking have a considerably higher death rate than men who have never smoked or men who have smoked only cigars or pipes." Even further, researchers concluded there was enough evidence to establish a causal relationship between smoking and death rates from heart disease and cancer. This was huge, as a cause-and-effect relationship had never been claimed with enough evidence to back it up.⁴³

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Tobacco companies wasted no time fighting back. Leading manufacturers formed the Tobacco Industry Research Council in 1954 to take back the public narrative, and began advertising for filtered and low-tar cigarettes as "healthier" options. 44 They wined and dined medical doctors into recommending cigarettes to patients as a treatment for coughs and other conditions. 45

The American Cancer Society redoubled its efforts with a larger study in 1959 that followed more than one million

men and women.⁴⁶ The data collected by these studies and more provided pivotal evidence for the 1964 report of the Surgeon General, which officially labeled cigarette smoking a cause of cancer on the basis of more than 7,000 studies into the negative health consequences of smoking.⁴⁷

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These findings led to congressional action to require warning labels on cigarette packages and to ban the marketing of cigarettes on radio and television, along with many publicly-funded campaigns to reduce smoking. It also led to age requirement on the purchase of cigarettes and the prohibition of smoking in many enclosed public spaces, including restaurants and airplanes.

[Tobacco] continues to kill more Americans than alcohol, car accidents, HIV, guns, and illegal drugs combined.

Even so, nearly "40 million U.S. adults still smoke cigarettes, and about 4.7 million middle and high school students use at least one tobacco product, including e-cigarettes," according to the Centers for Disease Control and Prevention (CDC). It continues to kill more Americans than alcohol, car accidents, HIV, guns, and illegal drugs combined. 48

COCAINE

Erythroxylum coca is a tropical plant native to Central and South America, and the main source of cocaine. Coca leaves were chewed by Ancient Incas to fight the effects of oxygen deprivation at high altitudes as far back as 3000 B.C..⁴⁹ Other indigenous population of the Andes used coca leaves in religious ceremonies and for increased cognitive performance, hunger reduction, and improved mood and energy. Slave laborers in Spanish mines were given coca leaves for increased productivity.⁵⁰

By 1609, the coca leaf made its way to Europe. "Coca protects the body from many ailments, and our doctors use it in powdered form to reduce the swelling of wounds, to strengthen broken bones, to expel cold from the body or prevent it from entering, and to cure rotten wounds or sores that are full of maggots," wrote Padre Blas Valera. "And if it does so much for outward ailments, will not its singular virtue have even greater effect in the entrails of those who eat it?"⁵¹

European scientists isolated cocaine from coca leaves in the 1850s, and was quickly adopted by the medical community as a local anesthetic and treatment for morphine addiction. ⁵² Sigmund Freud praised cocaine as a treatment for depression and other maladies, and used the drug himself. ⁵³

In his published work, Über Coca, he wrote from his personal experience using the drug, not fact-based scientific research. "You perceive an increase of self-control and possess more vitality and capacity for work. In other words, you are simply normal, and it is soon hard to believe you are under the influence of any drug. ... No craving for the further use of cocaine appears after the first, or even after repeated taking of the drug." 54

Coca was featured in several tonics and elixirs peddled throughout Europe and the U.S. that promised to restore health and vitality. The original recipe for Coca-Cola® used a mixture of cocaine and sugary syrup. ⁵⁵ By the end of the nineteenth century, U.S. manufacturers had sold cocaine in wine, cigarettes, hair care products, powders, and even a mixture to be injected directly into veins.

The pharmaceutical company Parke-Davis advertised that its cocaine drugs would "supply the place of food, make the coward brave, the silent eloquent and render the sufferer insensitive to pain." 56 When the Harrison Nar-

cotics Tax Act of 1914 banned the sale of cocaine in the United States, support for the law was rooted in societal fears and racism—not public health concerns or fact-based science.⁵⁷

Cocaine use spiked in the U.S. during the late twentieth century and cocaine-related deaths quadrupled between 1976 and 1981. A report by the National Institute on Drug Abuse stated nearly ten million people over the age of 11 had reported using cocaine in 1978, more than double the number of users the previous year.⁵⁸

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Studies⁵⁹ have linked prolonged use of cocaine with increased irritability, restlessness, panic attacks, nasal damage, paranoia, tremors, psychosis, and more, people still use the drug—illegally—in the form of cocaine and crack cocaine.⁶⁰ Fentanyl's presence in some cocaine is a rising concern, as it has resulted in higher cocaine-related overdose deaths.⁶¹

LEAD

Lead is a dense, soft, pliable metal that is extracted from galena (PbS). It can also be found in zinc, silver, and copper ores. The original discovery and use of lead predate history, but the first known example of lead used was an Egyptian figurine dating back to 4,000 B.C.. It was used in Egyptian pottery glazes thereafter.⁶²

The Chinese used lead to make coins in 2000 B.C., and the Greeks used lead to protect the hulls of their ships. The Romans used incredibly large quantities of lead (about 80,000 tons/year in the first century AD) for pipes, bath linings, and other structures in their water systems. In the Middle Ages, lead was used as a roofing material throughout Europe.

Throughout history, lead was used in face powders, rouges, and mascaras. It served as a paint pigment,

food seasoning, wine preservative, and moveable type on the printing press. ⁶³ It was in coins, bullets, flatware, goblets, and plates. ⁶⁴ It could be found in gasoline, radiation shielding, underwater power and communication cables, and almost every form of battery or emergency power supply. ⁶⁵

The Romans were aware that acute exposure to lead could trigger madness and even death for those who mined for it. Modern scholars have argued that chronic, widespread lead poisoning was a factor contributing to the decline of the Roman Empire. 66

As Roman aristocrats washed down platters of lead-seasoned food with casks of lead-tainted wine, Julius Caesar was unable to father more than one known offspring. Caesar Augustus was completely sterile. Rome suffered an alarming rate of infertility and stillbirths among upper-class women during this time. 67

It wasn't until the 1950s to the 1970s that Herbert Needleman and Clair Cameron Patterson conducted research into lead and its danger to humans. Patteron's 1965 paper, Contaminated and Natural Lead Environments of Man, revealed the atmosphere contained more than 1000 times the natural amount of lead.⁶⁸

Dr. Needleman produced a series of papers from 1979 to 1996 detailing how lead damages the intellectual development of children and makes those exposed more likely to commit violent crime. He also showed the amount of lead necessary to produce negative outcomes was much less than previously thought. His work was instrumental in getting lead removed from gasoline and paint. ⁶⁹

The lead industry accused Dr. Needleman of scientific misconduct, and denied the charges were in retaliation for his findings. ⁷⁰ In 1978, the manufacturing of lead-based house paint was banned in the United States. Leaded gasoline was banned in 1996. Lead's many other uses continue, though under more regulation. ⁷¹

LYSERGIC ACID DIETHYLAMIDE (LSD)

Chemist Albert Hofmann, working for Sandoz Pharmaceutical company, synthesized LSD for the first time in 1938. He was hoping to develop a compound to reduce postpartum hemorrhage. In 1943, he accidentally in-

gested some of his product and became the first person to go on an acid trip. It was later determined that ingesting as little as 0.000025 grams $(25\mu g)$ can produce intense hallucinations.⁷²

By the 1940s, psychiatrists were interested in LSD for its potential use as a therapeutic agent. It was marketed by Sandoz Pharmaceuticals for this purpose in the 1950s under the brand name Delysid. LSD's use in psychiatric experiments spread throughout America and Europe to explore the drug as a potential treatment for alcoholism, depression, and more. More than 100 articles on LSD appeared in medical journals by 1951, and surpassed 1,000 published articles by 1961.

The U.S. Army and Central Intelligence Agency experimented with LSD as a truth serum in the 1950s and 1960s. Further research was conducted by the U.S. Army to investigate LSD as an incapacitating agent. Researchers found LSD was "capable of rendering whole groups of people, including military forces, indifferent to their surroundings and situations, interfering with planning and judgment, and even creating apprehension, uncontrollable confusion and terror."

Military experiments continued until the United States banned the drug in 1968. Concurrently, Harvard psychologist Timothy Leary was popularizing the drug by encouraging college students to "turn on, tune in, and drop out." Leary was eventually imprisoned for drug-related crimes.⁷⁸

The short and long-term effects of LSD can vary greatly between users. "The days following my LSD use, I was filled with anxiety and extreme depression," reported a frequent user. "Following my first 'trip' on LSD, I would eat it frequently, sometimes up to four or five times per week for an extended period. Each time I would take the drug, mentally I was drifting more and more out of reality. The eventual effect was the inability to feel normal in my own skin."⁷⁹

While LSD may have its dangers, a study conducted in 2019 suggests LSD may have legitimate medicinal value. "LSD is revealed as a potential therapeutic agent in psychiatry; the evidence to date is strongest for the use of LSD in the treatment of alcoholism. Despite the difficulty of designing double-blind clinical trials with this substance, new studies performed under modern standards are necessary in order to strengthen our knowledge, help erase the stigma that still prevails around these substances and open new doors in the future."⁸⁰

MERCURY

Mercury (Hg) is a heavy metal that occurs naturally, though rarely, in the Earth's crust. It exists mostly in nature as mercuric sulfide, also known as cinnabar.⁸¹

Chinese women consumed mercury as a contraceptive 4,000 years ago. It was employed as a medicine and an aphrodisiac as far back as 500 B.C. in both India and China. Be In second-century China, mercury was part of an elixir thought to confer longevity or immortality. Be 3

Mercury was used to treat syphilis in Protestant Europe. In doing so, Paracelsus, Swiss physician and alchemist, formulated mercury as an ointment because he recognized mercury's toxicity when administered orally.⁸⁴

Abraham Lincoln took "blue pills" containing liquid mercury to supposedly promote the flow of bile as a treatment for mood swings, headaches, and constipation. 85 Mercury in its raw, metallic form and as "calomel" (Hg CL) were still being used in the late 1800s to treat venereal disease. 86

In the early 20th century, calomel was being rubbed onto the sore gums of teething babies. Dr. Moffett's Teething Powder advertised that it "Strengthens the Child ... Relieves the Bowel Troubles of Children of ANY AGE" and could "make baby fat as a pig."87



Picture: thestar.com

Mercury's suspected toxic effects were difficult to differentiate from the symptoms of whatever disease the metal was administered to treat. German chemist Alfred Stock published a number of papers on the dangers of mercury including a 1926 essay titled, "Dangerousness of Mercury Vapor."88

Mercury made headlines in Japan in the 1950s when mercury poisoning caused by industrial wastewater sickened more than 2,000 people in Minamata prefecture. This mysterious illness was known as Minamata disease, which later turned out to be mercury poisoning.⁸⁹

The long-term neurological symptoms of mercury poisoning were nicknamed the Mad Hatter's Disease, in reference to Lewis Carroll's 1865 novel, Alice in Wonderland. Hatmakers used to use mercury to cure felt, and many experienced mental and emotional challenges in the waning years of their life due to long-term exposure. 90

Despite the empirical data, several members of the medical establishment supported mercury as therapy well into the twentieth century.⁹¹

RADIOACTIVE PRODUCTS

Henri Becquerel discovered ionizing radiation in 1896 while developing photographic plates using uranyl sulfate (UO_2SO_4) . At the time, it was believed uranium absorbed the sun's energy and released it by emitting x-rays. To Becquerel's surprise, no sunlight was required—uranium emitted radiation on its own due to the spontaneous decay of its atomic nuclei. 92

Marie Curie and her husband Pierre investigated the phenomenon further. Over the next four years they processed large quantities of uranium ore and discovered two radioactive elements (a term coined by the Curies): polonium and radium.⁹³

In the years that followed, "There was this sense that radiation is a very powerful but poorly understood force in the universe, and maybe it's the ultimate healing force," says Cleveland radiation oncologist Roger Macklis, a scholar and historian of radiation quackery. ⁹⁴

Radioactive products became wildly popular, and manufacturers produced countless products claiming to have a positive influence on health. Radium condoms were marketed to have the "strength of iron, energy of radium." Radium suppositories for men purported an increase in sexual performance.

There was radioactive chocolate, hand cleaner, powders, soap, toothpaste, pacemakers, spark plugs, heating pads, water conditioning systems, even a children's toy called the "atomic energy lab." It took several decades to realize and document the mutagenic effects of radiation.

Increased risk of cancer caused by radiation exposure was first recognized by Hermann Joseph Muller in 1927. Muller did a series of three experiments to prove the mu-

tagenic effects of radiation. He bred fruit flies and exposed them to radiation, and counted the mutations in successive generations. Muller received the Nobel Prize in Physiology or Medicine for his research in 1946.⁹⁶

Though Muller's research exposed the mutagenic effects of radiation, the severity of the danger was not truly understood until the 1940s, when several scientists, including Harry Daghlian and Louis Slotin—two physicists involved in the Manhattan Project—died from exposure to radioactive material.⁹⁷

The Hiroshima bomb also caused widespread radiation poisoning, of which Midora Naka, a Japanese actress, was a victim. Her death in 1945 was the first officially documented case of radiation poisoning, though at the time it was referred to as "Atomic Bomb disease." ⁹⁸

THALIDOMIDE

Thalidomide ($C_{13}H_{10}N_2O_4$) was first synthesized in 1954 in West Germany by the Chemie Grünenthal company. 99 It was discovered thalidomide had sedative effects and appeared to be a promising alternative to the barbiturates used as sedatives at the time. Unlike barbiturates that can cause death if given in excessive quantity, an overdose of thalidomide would only cause deep sleep and did not seem to have any toxic side effects. 100

In 1957, thalidomide was produced and promoted for treatment of anxiety, trouble sleeping, tension, and morning sickness among pregnant women. 101 Tragically, the drug had undocumented side effects including severe birth defects and nerve damage. According to the UK's Thalidomide Trust, it was responsible for 80,000 miscarriages worldwide and 20,000 children born with severe physical deformities. 102

The FDA refused approval to market and distribute thalidomide, stating that further studies were needed to confirm its safety and efficacy.

the drug as a sleeping aid. These patients experienced a tingling sensation in hands and feet, followed by numbness and coldness, severe muscular cramps, weakness in the limbs and lack of coordination. These symptoms could improve or disappear, but in many cases the damage proved irreversible.¹⁰³

The FDA refused approval to market and distribute thalidomide, stating that further studies were needed to confirm its safety and efficacy. This reduced the impact of thalidomide in the United States. ¹⁰⁴ After its dangerous side effects became apparent, thalidomide was largely banned worldwide in the early 1960s.

More recently, Thalidomide has been shown to inhibit angiogenesis (the proliferation and growth of new blood vessels) which might be useful in stopping the proliferation of blood cancers. In 1994, Robert D'Amato, a scientist seeking to develop angiogenesis inhibitors, found thalidomide effective in suppressing tumor growth in rabbits. ¹⁰⁵ Further clinical research was conducted by D'Amato and others. Human subjects responded positively to the treatments, and the results were published in the New England Journal of Medicine. ¹⁰⁶

As of 2006, the U.S. Food and Drug Administration accelerated approval for thalidomide in combination with other medications to treat newly-diagnosed multiple myeloma patients. Research is ongoing but indicates this treatment may result in a greater chance of survival.¹⁰⁷

TREPANATION AND LOBOTOMIES

In 1888, Swiss psychiatrist Gottlieb Burckhardt performed the first attempt at "modern" human psychosurgery—operations on the brains of those deemed clinically insane. Targeting what he believed were "association centers" in the brain, he carved a ditch around the motor region of the temporal lobe in hopes of breaking communication between the hyperactive regions of the brain, thus alleviating symptoms and mental distress.¹⁰⁸

Burckhardt performed six surgeries. According to his own report, two patients experienced no changes in behavior, two patients became quieter, one patient died within days of the surgery, and one patient demonstrated noteworthy improvement (this patient later committed suicide). 109

Complications in surviving patients included motor weakness, epilepsy, sensory aphasia, and "word deafness" in which subjects lost the ability to comprehend language, repeat words, and write from dictation.¹¹⁰

Burckhardt nevertheless claimed some success and published his findings. He presented his findings at the Berlin Medical Congress and was immediately met with hostility from his peers. Ultimately, he performed no further operations.¹¹¹

Despite failed results and poor reception, the practice of lobotomies continued into the 1900s. In 1935, Antonio Egas Moniz performed a lobotomy procedure at a Portuguese hospital to treat mental illness, drilling holes into a patient's skull to access the brain. For this work, he received the Nobel Prize in Medicine in 1949. 112



Turning the Mind Inside Out, Saturday Evening Post, 24 May 1941

In 1936, psychiatrist Walter Freeman performed the first prefrontal lobotomy in the United States. He believed "that cutting certain nerves in the brain could eliminate excess emotion and stabilize a personality."113 Freeman found a more efficient, less invasive way to perform the procedure—without drilling holes through the patient's skull.

Freeman created the 10-minute transorbital lobotomy, called the "ice pick" lobotomy, and performed the first procedure at his Washington, D.C. office in 1946. Freeman went on to perform more than 2,500 lobotomies, some of them on display for public viewing.

According to NPR, "As those who watched the procedure described it, a patient would be rendered unconscious by electroshock. Freeman would then take a sharp ice pick-like instrument, insert it above the patient's eyeball through the orbit of the eye, into the frontal lobes of the brain, moving the instrument back and forth. Then he would do the same thing on the other side of the face."114 The Soviet Union banned the surgery in 1950, declaring the procedure to be "contrary to the principles of humanity." It was also banned in Germany and Japan. However, the United States, Britain, and several countries in Scandinavia and Europe continued to perform lobotomies throughout the 1980s.¹¹⁵

A lobotomy that reduced President John F. Kennedy's sister, Rosemary, to a near-vegetative state helped turn public opinion almost entirely against the surgery. 116 But it was never outlawed. Mostly, advancements in surgical procedure and technology allowing for deeper understanding of the human brain rendered the surgical practice of lobotomies obsolete.

X-RAYS

The physicist Wilhelm Conrad Röntgen first discovered X-rays in 1895. Röntgen was testing to see whether cathode rays could pass through glass when he observed a glow emanating from a nearby chemically-coated screen. He named the rays causing the glow "X-rays," as their nature was then unknown to him. 117

Röntgen investigated the unknown rays systematically, publishing his findings two months later. 118 He stumbled upon their medical use when he took a picture of his wife's hand on a photographic plate that using X-rays instead of light —the first photograph of a human body part using X-rays. 119 When she saw the picture, she is reported to have said "I have seen my death." 120

The discovery launched a new era in medical science. For the first time, doctors could see inside a patient and find trauma, or lack thereof, without invasive surgery. The invisible could now be seen.

In 1896, Thomas Edison developed the first mass-produced live imaging device, calling it the "Vitascope," and later the fluoroscope, which became the standard for medical examinations. Edison dropped his research around 1903, shortly before the death of his associate Clarence Madison Dally.



First medical X-ray by Wilhelm Röntgen of his wife's hand

Dally would routinely test X-ray tubes on his own hands, and developed cancer that eventually required the amputation of both arms. In 1904, Dally became the first known death associated with X-ray exposure. 121

Others reported potential hazards of exposure to X-rays, including William J. Morton and Nikola Tesla, noting burns, pain, swelling and blistering. However, it was difficult to prove a direct link between these injuries and X-rays because they took time to manifest and the relationship wasn't immediately obvious. 122

So, the unrestricted commercial use of X-rays continued. From the 1930s into the 1950s, shoe stores in the United States used X-ray-generating fluoroscopes to show customers the bones in their feet for purposes of fitting. 123

It wasn't until the 1950s that suspicion grew surrounding the possible harms of X-ray exposure. G.M. Ardran of Oxford University published a paper in 1956 concerning the risks to radiologists from X-rays¹²⁴, and in 1957, the United

Nations issued a statement that medical professionals had a responsibility to limit exposure to X-rays. 125 Numerous papers followed detailing better ways to limit dosages.

X-rays remain in wide use, but dosages tend to be very small, allowing the benefits of this lifesaving technology while mitigating the risks. There is new concern surrounding the X-ray dosage in CT scans, which deliver a much higher dose—and according to Harvard Medical School, account for 24 percent of the X-ray dosage in the United States. 126

ZANTAC (RANITIDINE)

Ranitidine ($C_{13}H_{22}N_4O_3S$)—known by its generic name "Zantac"—was an antihistamine used to mitigate the symptoms of heartburn and acid reflux. ¹²⁷

Glaxo Holdings Ltd. received approval from the FDA to sell Zantac in 1983. Five years later, it had become the world's best-selling drug and was prescribed to treat ulcers, heartburn, and ongoing treatment of gastroesophageal reflux disease (GERD).

Glaxo's patent for ranitidine expired in 1997, granting competitors an opening to sell generic alternatives. In 2004, the FDA granted Pfizer corporation approval to sell overthe-counter versions of Zantac. Since then, companies like Pfizer, Johnson & Johnson, Boehringer, and Ingelheim Pharmaceuticals have sold Zantac-like products. ¹²⁸ As early as 1983, two Italian medical studies suggested a potential link between ranitidine and N-Nitrosodimethylamine (NDMA), a known carcinogen. The studies noted damage to the cellular DNA of gastric cells. ¹²⁹

Suspicion continued to grow after a 2012 paper revealed how ranitidine could decompose into NDMA in certain contexts. ¹³⁰ In 2019, the online pharmacy Valisure analyzed the composition of a number of medicines it carried, and in doing so, discovered NDMA in an acid reflux baby syrup that contained ranitidine. ¹³¹

As of 2020, the FDA announced that new testing and evaluation prompted by information from third-party laboratories confirmed that NDMA levels increase in ranitidine even under normal storage conditions. Further, NDMA was found to increase significantly at higher temperatures, including temperatures the product may be exposed to during customer use.

The FDA requested all manufacturers withdraw their products containing ranitidine from the market, and advised consumers to stop taking over-the-counter products containing ranitidine immediately and permanently. ¹³²

CONCLUSION

Science, especially settled science, takes time to get right. While suspicions are often the first sign of a potential danger, certainty requires fact-based and time-tested evidence from multiple studies that all produce the same results. We are getting better and faster at achieving this, but the process is not perfect.

For many of these examples, centuries passed before sufficient research was conducted on the impact of these products and practices on the health and well-being of humanity. While the slow and steady nature of the scientific process can be frustrating, the need for speed cannot supersede facts, truth, and accuracy.

Science, especially settled science, takes time to get right. While suspicions are often the first sign of a potential danger, certainty requires fact-based and time-tested evidence from multiple studies that all produce the same results.

When science follows the Mertonian norms—when it is done in the spirit of collaboration and communality, and for the benefit of common scientific enterprise rather than personal gain, and exposed to critical scrutiny before being accepted—it is capable of saving lives, improving the quality of lives, and providing the data to help us make sound public policy, regulatory and judicial decisions.

For every chemical or product that is found to be a danger to society, hundreds more provide an immeasurable benefit. When those in government and the courts are unwilling to give settled science time to settle, one must ask—who stands to benefit?

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