The History of Vaccines

To the University of Michigan campus in 1955 came hundreds of scientists, hoping to hear the words that would signal the end of polio's long and ruthless reign of terror. Heading the medical men was Dr. Jonas Salk, whose polio vaccine had been tested and carefully evaluated. Then, the historic announcement: the vaccine works! It is safe, effective, and potent. Someday, said Dr. Salk, a vaccine may completely eradicate the menace of polio. Working at Pittsburgh University's Virus Research Laboratory, the 40 year old Dr. Salk labored 3 years, often 16 hours a day…

For as long as we've existed, humankind has had to deal with infectious diseases. We handle some infections better than others. But there have been plenty of examples throughout history where infections have gotten the better of us. Smallpox, influenza, polio – these are just a few examples which have killed countless numbers of people over time. The history of vaccines comes directly out this experience.

I was born in 1953. So, uh, obviously a lot of people don't remember this anymore, but the 1950s was really the peak of significant concern around polio, uh, again in this part of the world. Uh, and, uh, and in fact, uh, you know, when polio, you know, has seasonal peaks, it would tend to peak in the, uh, in the summer and late summer in particular. And, uh, it was not uncommon to see, uh, to see very significant polio cases when in fact those photographs of the iron lungs, you know, where there were unfortunately kids, you know, uh, who, uh, was suffering from actual poliomyelitis oftentimes had to be placed in order to help them breathe.

Dr. Emilio Emini is the director of the tuberculosis and HIV global program at the Bill & Melinda Gates Foundation. He has seen first hand the impact of vaccines in minimizing certain diseases both professionally and personally. Polio peaked in the U.S. in 1952, and at the time the vaccine was actually given on a cube of sugar.

I was in elementary school, I can't remember, I think it was first grade actually. So this would put it in the very late fifties, early, early, early sixties. You've seen these pictures of these children all lined up, you know, get ready to get their oral polio vaccines, you know, which were those little red dots on the, on the sugar cube.

Dr. Emini is referring to one of two kinds of polio vaccines that we have out there. The oral vaccine which was nicknamed the "sugar lump vaccine" and used until 2000. Now, the polio vaccine is given as an injection, at least here in the US, and it's usually combined with other vaccine antigens.

But the striking thing about it, if you look at those pictures, those children were all lined up to get to get the vaccine because, because the alternative was to remain susceptible to polio and poliomyelitis. And that was not considered an acceptable alternative.

Polio was a devastating and widespread illness that lead to permanent disability in children. The United States has been polio-free for forty years, thanks to the effectiveness of this vaccine.

So how did this vaccine — and all vaccines for that matter— come to be? That's what we're talking about today on… The Antigen. I'm your host, Yasmeen Agosti.

So, we won't be able to cover everything in the history of vaccines but we will focus on the highlights. Smallpox is an important one. You may remember the name Edward Jenner from your high school science class, but the history of vaccines actually starts much earlier than that. Here's Dr. Stanley Plotkin. He's a Professor Emeritus of Pediatrics at the University of Pennsylvania School of Medicine, he's developed several vaccines and is now a vaccinology consultant.

The history of vaccines in a way begins before recorded history. That is that in areas of the far East and the middle East, uh, people were using, uh, scabs from smallpox, uh, to inoculate the skin of people who had never had smallpox. And so they essentially developed a mild form of smallpox and were protected against a severe disease and death, which, um, it's estimated that about 30% of all smallpox cases died.

It's estimated that smallpox has killed more than 300 million people before the World Health Organization declared that it had been eradicated in 1980.

As early as the year 1000, there's evidence that people in China were purposefully infecting themselves with smallpox in order to protect against getting the full blown disease. From there the practice of what we call variolation spread west. Variolation is the act of introducing dried pus from a smallpox pustule into the skin of a person to actually protect that protection.

Now, Edward Jenner is the person who is best recognized for smallpox variolation.

But there were others who also did their part to advance this idea. One person worth noting is actually a mom.

An English Lady named Mary Wortley Montagu, was a major advocate for smallpox variolation in the U.K. Lady Mary was the wife of the British Ambassador to Turkey. While living in Turkey she witnessed smallpox inoculations. When she returned to Britain in the early 18th century, she brought with her the knowledge of what she had seen and her experience inoculating her own son.

What is generally true about science is that although, eventually one person or one laboratory succeeds in doing something which is important and obtains the credit for it. Almost always there are multiple people working on the same problem. And, uh, whether, the lab that succeeds, may succeed because of dumb luck, uh, or because of an insight that other people didn't have. But, uh, smallpox obviously was a major, threat killing, uh, literally millions of people. And it just so happened

that, uh, Jenner was the one who did it the most systematically. It is said, and I think confirmed that there were other people. Uh, the, uh, the name of Benjamin Chesty being one who had the same insight into, uh, how the PR, uh, protect against smallpox, but didn't go any further. Uh, so the, the race is won not only by people who start the race, but also more importantly by those who finish the race, uh, by coming up with a practical, uh, product that can be used, uh, to protect people.

As everybody knows, uh, Jenner in England who observed that, um, uh, women who, who, who milk cows were relatively immune to smallpox. And that was because they were exposed to pox viruses from animals. And so he started to use what we think was a horsepox virus, uh, to immunize against smallpox.

Smallpox variolation is commonly seen as the beginning of the modern era of vaccination.

And, uh, that was of course, very successful and became the practice, uh, throughout the developed world. Uh, it quickly spread to the US, uh, there were, uh, people like Cotton Mather, uh, the, the preacher who pleaded in favor of what's called vaccination which, uh, controls smallpox outbreaks. Um, but then nothing much happened for about 80 years until the work of Louis Pasteur and France.

Louis Pasteur is credited with learning how to attenuate – or weaken a germ before using it to make a vaccine. This was a major step forward after smallpox variolation which entirely risk-free.

Now Pasteur started his career as a chemist, but he became interested in biology and notably for example, he worked on diseases of vines that producing grapes. Of course in France, the production of wine is very important and that was a dramatic discovery and help for the wine industry. And he achieved a certain amount of fame for that, which allowed him to start a laboratory in Paris on, uh, other issues.

The history of vaccines is often intertwined with understanding diseases in animals. Like many scientific discoveries, some of Pasteur's work came about due to happenstance, one example was while studying chicken cholera – a highly contagious and serious disease of chickens.

He was working with a disease of, uh, chickens. Uh, and, um, the summer holiday came, uh, during, um, uh, those, this was in the 1880s. And so of course he went off a holiday, um, but then came back in September and, uh, found on the table of his laboratory a culture of the, uh, chicken cholera organism, uh, and tried to induce disease in chickens with that culture, which had worked before. And he observed that the chickens did not become ill. And fortunately, the bulb went off and he realized that the chicken chickens had been protected by the culture that had sat on the laboratory bench all summer. And so then he began to attack the issue scientifically and developed a, uh, an organism that could be injected into chickens that would protect them against the severe disease.

The chicken cholera vaccine was the first laboratory-developed vaccine. A discovery important for poultry farmers no doubt, and as it turns out, for humans too. Louis Pasteur's discoveries didn't stop with chickens.

Uh, and then of course, he turned his attention to human diseases. And as every body will remember, he developed the rabies vaccine because rabies was an important disease in France at that time, uh, and began work on, uh, other pathogens as well. Uh, and of course, other scientists realize the significance of, uh, Pasteur's work.

Towards the end of the 19th century, scientists were working on the next major development in vaccinology – creating inactivated or killed vaccines. Vaccines for typhoid, plague, and cholera were all made at this time.

As vaccinology developed over time, we also learned important things about the immune system, the tetanus and diptheria toxoid vaccines, which were developed in the first half of the 20th century are great examples of this. Both of these bacteria produce toxins, which are primarily responsible for the disease symptoms. So on the one side, you have vaccinology trying to figure out how to inactivate these toxins in order to make toxoid vaccines. And on the other side, you have immunology figuring out that there's something in the blood that can counteract these toxins. And at the time the substance was referred to as an antitoxin, but we later learned that this was in fact antibodies. Flash forward to the 1920s and 1930s where we have the development of several new live attenuated vaccines like tuberculosis and yellow fever. And then we have several more killed whole cell vaccines including typhus, influenza vaccine and pertussis.

Let's talk about pertussis, whooping cough bacterium… and you grow them up in the lab and you kill them by heat or a chemical it so that they can't cause disease.

That's Dr. Sarah Long. She's a pediatric infectious disease specialist and professor of pediatrics at Drexel University College of Medicine. She's taken care of patients with serious infections and help to create important vaccine policies for over 40 years.

You clean them up a bit so that you know you can make this into a reproducible kind of an injection and you inject that. That's what whole cell pertussis vaccine was, and the good part about those kinds of vaccines is that you have lots of, lots of parts of the organism and your body can respond to a thousand antigens or bits and bobbles of the bacterium that can help you when you see it. Uh, it's not just a single thing, it's all the pieces and you can respond to all those pieces. That was the good part about whole cell vaccine. The part that isn't so good is that when they are that incompletely defined, then you very frequently have reactions to them because they're not purified pieces.

In the second half of the 20th century, we continued to learn to make vaccines going from using the entire germ to only specific parts of the germ. These vaccines are known as subunit vaccines. While vaccinology was figuring out how to design new vaccines, the field was also perfecting how to grow the materials needed to make those vaccines.

The major thing that happened just after the second world war was the work of a group in Boston led by John Enders, which was essentially the development of culturing cells from human material or from animals and culture that is taking the cells, putting them into a glass or plastic bottle and allowing the cells to multiply and then injecting those cultures with viruses, uh, which allowed laboratory people to grow viruses in large quantity. And that led to a number of, of vaccines and is of course still a very important, uh, technique. Uh, but um, now we have multiple strategies to develop vaccines, uh, that is, um, by taking the, the agents of disease apart, uh, by cultivating them in different ways, uh, using components, uh, to use the cliche, it's a whole new ballgame as far as vaccine development is concerned.

Long gone are the days of smallpox for relation where you essentially had to go out and find a cow with cowpox before you could get what you needed to make the vaccine.

From 1955 onwards, the list of new vaccines starts to get long. We have even more kinds of live attenuated vaccines like polio, measles, mumps, and rubella. We have even more kinds of killed whole cell vaccines including new versions of polio and rabies vaccines, and then we have a really important advance in the science of subunit vaccines, conjugation.

Originally, certain vaccines were based on the sugarcoat of a bacteria, but a child's immune system wasn't able to respond very well to just this part alone. It wasn't until vaccinology figured out that it had to join the sugar to a protein in order to make the response better. This was done for HIB and meningococcus first and then for pneumococcus.

We heard about HiB in the first episode with Dr. Kathy Edwards, and similar to HiB, prior to the creation of the vaccine pneumococcus or streptococcus pneumonae was a bacteria that afflicted thousands of young children and infants in the US and around the globe.

And then there are those that really, really, really changed the landscape during my time.

And those were conjugate vaccines. Conjugate vaccines like pneumococcal conjugate vaccine or HIB conjugate vaccine, takes a piece of the organism that you want to make the antibodies against, that you want to protect against that we know, if you just gave that by itself, especially children wouldn't respond too well and you chemically hook it to something else that you're really not trying to get an antibody response to, but it makes the immune system behave in a different way when it sees

the part that you care about that's conjugated to it. Well, that was the basis of the pneumococcal in the HiB conjugate vaccine.

There are some other very important aspects to vaccine history we should talk about, like vaccine schedules. Here in the US we have a vaccine schedule that covers the entire lif espan.

And every year we learn more or we have new vaccines, wonderful, that we have to get into this schedule or we have recognized a new burden of disease or a new age group who's the reservoir of disease. Or we have people coming into the country who have had different vaccines, different schedules. But every single year, all year round, and then once a year, the Center for Disease Control with lots and lots of input from experts and in conjunction with the American Academy of Pediatrics and the College of Family Physicians, and the obstetricians and gynecologists when it's relevant, all have representatives who are experts who go through this schedule and change things that have to be changed.

Dr. Long is describing the important work of the Advisory Committee on Immunization Practice or ACIP. This group meets three times a year to determine the best schedule. They include instructions on which vaccines to give at which ages, how many doses and how long to wait between doses as well as who should not receive certain vaccines and why. ACIP provides all of this information on the Center for Disease Control website in easy to understand language for patients, their families and healthcare providers. At the most basic level, the vaccine schedule is designed so that you get certain vaccines at certain times in your life to protect you when you are a greatest risk for getting those diseases.

Now. We know it's very burdensome for doctors to try to remember what the schedules are and there are all kinds of ways now that one can access this and, and um, use computer programs as well as, uh, resources to know who has had what in the past and what they need to be caught up on and what you don't need to give multiple times and where you need to start over or you don't need to start over. And it is all published once a year and I participate in that. Um, uh, as I've been an associate editor of the Red Book of the American Academy of Pediatrics and on, uh, a work group at the Centers for Disease Control, I can't tell you how we try to clarify that, make it as brief as it can possibly be, not change things for the sake of changing things. Um, but trying to make it so that vaccines are used in their optimal fashion so that they're not misused or thrown away. And so they're not used dangerously in people who shouldn't be receiving them. These are very intentioned plans.

Most people first learn about vaccine schedules when they’ve just had a baby. Hepatitis B is usually given at birth and after that, many vaccines are started as part of a series at 2 months of age. It’s

natural for parents to wonder why their babies need so many shots so early in life. Dr. Todd Wolynn, a general pediatrician, and owner of PediatricsPlus in Pittsburgh helps to explain.

Kids are most susceptible in their first year of life in succumbing to these diseases, which is why we see these vaccines being given so early and in a repeated fashion because they boost in the sequences that they're given to get your immune system up to a point where it's sufficient to provide protection. And so by spacing things out, quote unquote using alternative schedules, those only come with risk.

Dr. Long reminds us why we shouldn't forget that immunizations beyond childhood is just as important.

But these go on through your lifetime and there are different things, different organisms that you forget how to respond to. As you get older, your immune system reverts a little bit to being not as clever as it once was and you begin, you begin an end life as extremely vulnerable to infectious diseases. So as we hope to live longer, we will have to have more and more vaccines that we are giving through a lifetime because it's a good payoff for not having these organisms around to have to get reminded of them periodically by an immunization.

Vaccine history has also become highly evolved in terms of monitoring safety.

So the success of these programs depends on the safety of every single one. So we have a trust with the public that we want to protect their children. So there's as much scrutiny if not more scrutiny of the safety events scenes along their development as there is about their effectiveness. And it's something for the safety purposes that's ongoing as long as long as the vaccines are used. So there are multiple systems that are in place where individuals can, uh, report what they think is an adverse event from a vaccine.

And there are, uh, very, very sophisticated systems that then look to see what is the chance that this is what we would call a Sentinel event or a flag that this might be related to the vaccine? Or is it something that would be expected in a population in the same kind of way? The same kind of timing, the same kind of age group that is not related to the vaccine at all to get very early signals. So there's that general system that's called vaccines adverse events reporting system, VAERS. There's, and then there are multiple others that I think of more as adjunctive systems. When you have a particular question about a vaccine.

Um, so that there are multiple ways in which we look at vaccine safety and monitor it all the time.

Vaccine history is incredibly interesting and complex, and hopefully this episode has given you enough to get a sense that the field is now a highly systematic, safe and effective way to protect people against diseases across the lifespan.

Next time on The Antigen, we're focusing on the global health impact of vaccines.

Globally, we've made phenomenal progress on this topic, right? But still today, 5 million children per year die before their fifth birthday of completely preventable causes.

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Talk to you soon.

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