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### Dr. Rino Rappuoli on the hard truth about vaccines

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Discussed: The era of 50-year lifespans, the attitudes in low-income countries, mandatory vaccination policies, and vaccine-hesitant doctors



#### Dr. Rino Rappuoli

Dr. Rino Rappuoli is something of a legend in vaccine science. He is a pioneer of reverse vaccinology, a method of creating vaccines in which the genome of a virus is sequenced to determine how to fight it. In the late 1990s, he and a team of scientists used this method to create the first successful Meningococcal B vaccine. Within five years, they had uncovered a "goldmine of new vaccine antigens."

More recently, Dr. Rappuoli, who is also the chief scientist and head of external research and development at GlaxoSmithKline vaccines, has been helping develop a vaccine for RSV, the leading cause of infant mortality in many low-income countries and one of the leading causes of newborn hospitalizations in high-income countries. Scientists have tried and failed consistently since the 1960s to develop such a vaccine, the most recent failure coming only months ago. But with this latest vaccine winding its way through clinical trials—itself the product of a new method called X-ray crystallography—Dr. Rappuoli is optimistic they have finally addressed the source of the perennial failures.

"Every 10 years or so we get a new technology that allows us to conquer new diseases," he said. "Five years ago we were able to do things that were impossible five years previous, and in five to 10 years we'll be able to do things that we can't even dream about today."

He spoke with the *Medical Post* about the growing problem of vaccine hesitancy, what vaccines have done for modern societies, and how doctors can best speak to patients about vaccines.

## Q: Your career has taken you to a lot of different countries. How are attitudes toward vaccines different in different countries, say in Europe versus the U.S. versus Canada?

I would say that all high-income countries have something in common. About 80% of the population is okay with vaccines. They believe they're safe and necessary. Then, about 15% to 18% can be pushed in one direction or the other. Then you have 1% to 8% who, depending on the countries, are absolutely against it. This includes people who are opposed for religious reasons, or sometimes they'll have a child with autism and they believe that that is due to the vaccine. It is not true, but it's impossible to convince them otherwise. So you have these three categories, and the one we need to focus on is the 15% to 18%, because these are usually more educated people. Sometimes they are also doctors.

#### Q: Oh, so doctors sometimes fall in the 15% to 18%?

Yes, sometimes they do. I believe that all we need to do is a little more education. Right now during medical school they'll maybe spend one or two days on vaccines.

#### Q: What do you think is the single greatest misconception about vaccines?

Just a century ago, life expectancy in the U.S., Europe and Canada was less than 50 years. We've gained 30 to 35 years largely from conquering infectious disease. You've got smallpox, diphtheria, tetanus, pertussis, measles, all those kinds of things, and nobody remembers. I was talking even today to a beautiful group of very bright young people, and I was telling them about diphtheria. You've never seen diphtheria. It's gone. There are no cases during the last 60 years in high-income countries, but in 1900 in Germany, in one year, it caused 50,000 deaths. In the United States, in 1920, it caused 15,000 deaths.

#### My mother did not need to be convinced about vaccines because she saw I had schoolmates with polio.

In Venezuela, there's a political and economic crisis and the healthcare system has broken down. It used to be like all the other, high-income countries, free of diphtheria for many decades. But during the last three years, it came back. They've had more than 2,000 cases and more than 400 deaths. That's something we should probably talk about. These are things we thought we had conquered. If we don't vaccinate, they're going to come back.

There is a recent report from the <u>Wellcome Trust</u> where they interviewed 140,000 people worldwide about vaccines and about vaccine hesitancy. They found a huge difference between high-income and low-income countries. In low-income countries, where they still see the diseases, more than 90% of the people trust vaccines completely. But in both sets of countries, people trust their doctors. So, if the doctor encouraged their patient to be vaccinated and spent time educating them, people would listen. If the doctors are hesitant, they are not going to get vaccinated.

### Q: So this is interesting to me. You've come across doctors in your career who are themselves vaccine hesitant. Do you have any idea how many are?

No, but it's pretty low. It depends on the degree of hesitancy. No doctor would say having a vaccine is bad. But the influenza vaccination is a good example. We know the influenza vaccine is not 100% effective. Sometimes it's 60%, or 80%, or 40% effective, depending on the year. If a doctor makes a comment that doesn't show full confidence, people are going to see that as a negative. I've never seen a doctor say they are against vaccination, but I've seen doctors who don't show sufficient support.

I went to my family doctor recently (great guy, great doctor) to get caught up on some vaccines I had missed when I was little. And as he was explaining the risks, he made a joke about the polio vaccine. He said, "I used to tell patients that the likelihood of getting Guillain-Barré is about the same as the likelihood of Donald Trump getting elected. I can't use that joke anymore." And normally I'd be totally onboard with a bit like that, but I didn't really know what to do with the information. I was thinking to myself, "Okay, so am I more likely to get Guillian-Barré than polio or what?" I can imagine it's that sort of thing that would put more vaccine-hesitant people on edge.

Doctors have a very difficult job when parents come in with a precious newborn because obviously the first thing that the parents want is assurance that the vaccine is not going to do any harm to their new baby. This is a very difficult conversation because the doctor has to inform them that there's no drug in this world that is without risk, and vaccines have a very low risk.

Still, that job is much easier today than it used to be. There are no more vaccines that pose severe risks. I mean, with most of them, there may be fever, swollen arm, a bit of pain, these kind of things, but it's not like when the oral polio vaccine could cause the poliomyelitis itself (although even then it was rare). When parents come in, having read about the claims that vaccines could cause autism or other things, doctors need to be very well-prepared. I think helping doctors talk to parents requires a lot of social science, knowing which words you can use, how you need to be transparent at the same time confident.

We need to solve the problem in the long term by spending time with the new generation of doctors. Today, we still tell the same stories about vaccines that we were telling to my mother when I was a child. But my mother did not need to be convinced about vaccines because she saw I had schoolmates with polio.

#### Q: Do you think that involves, for lack of a better word, scaring people?

What's happening today is: we don't vaccinate for a while, we get outbreaks, people get scared, and vaccination rates go up again. That's not very efficient. I mean, children should grow up with the knowledge that vaccines changed our world. I think if they grew up knowing that, it just becomes part of their values—they don't need to be scared.

## Q: What's your position on mandatory vaccination as a matter of policy? Do you think it is a good or bad thing?

Mandatory vaccination is very effective. In Italy the vaccination rates were dropping, the hesitancy was there, and then two years ago they passed a law where they made it compulsory, and that had two effects. One, vaccination rates rose back to 95%. I mean, unprecedented really in a year—very, very effective. Second, the proportion of people who were vaccine-hesitant was basically cut in half. That's because people think that if they're not compulsory, then the government or public health doesn't really believe in them. If they're compulsory, it sends a clear message that they must be important. So, mandatory vaccination policy is effective and it reduces hesitancy. On the other hand, it exacerbates a smaller group of people—the 1% to 8%—who will become more vocal, but that's okay. Now, to have to mandate something that educated people understand is a good thing, I believe that represents a failure of our society.

Edited for length and clarity.