Charles Richet: When Our Defenses Turn Against Us (1913)

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Boulogne-sur-Mer, 1902. The August sun beat down on the harbor, but inside the floating laboratory of the*Princesse Alice II*, a yacht turned research center, the air was icy. Charles Richet, a man with a thick mustache and piercing gaze, watched intently as his colleague Paul Portier injected a tiny dose of sea anemone venom into a dog named Neptune. "We just want to see how he reacts," Portier murmured, adjusting his fogged-up glasses.

Neptune, a grayish mixed-breed dog, wagged his tail indifferently. Minutes later, there was no sign of pain. Richet jotted in his notebook: "Initial dose tolerated." But what happened the next day left them breathless. When Portier injected an*even smaller*amount of the same venom, Neptune collapsed. His legs trembled, his breathing became a death rattle, and in less than five minutes, the dog lay dead. Richet stared at the body, his heart pounding. "This makes no sense," he whispered. "How can a smaller dose kill when the first one did nothing?"

That question would haunt him for years. Richet, a man of many talents—physiologist, writer, even playwright—had stumbled upon something that defied everything medicine thought it knew about the human body. This wasn't the first time science had encountered this mystery. In 1839, French physician François Magendie had described how a dog that survived a dose of snake venom died after receiving a second,*even smaller*dose. In 1894, bacteriologist Emil von Behring, a future Nobel laureate, had noticed that some animals died when re-exposed to diphtheria toxins. But no one had connected the dots. No one, until Richet.

The most chilling case reached his ears in 1905. A young woman named Jeanne, 22, was admitted to Saint-Louis Hospital in Paris with a red rash covering her body. Doctors diagnosed hives, but when they administered a rabies serum—a common practice at the time—her body rebelled. Her throat swelled shut, her blood pressure plummeted, and she died within hours. The autopsy showed no sign of infection or poison. Only one detail stood out: Jeanne had received a dose of rabies seruma *year earlier*. Could her own body have killed her?

Richet began collecting stories like this. A child who died after eating a single egg, though he'd tolerated them before. A man who nearly lost his life after taking an aspirin, when he'd taken it without issue in the past. Each case followed the same terrifying pattern: the first exposure to the substance did nothing. The second, even in tiny doses, could be lethal. "It's as if the body learns to hate," Richet wrote in his journal. But how? And why?

In his lab, Richet and Portier repeated the experiment with Neptune over and over, using different substances: jellyfish venom, horse serum, even egg proteins. The results were always the same. Something in the animals'—and humans'—bodies changed after the first exposure. Something made them*hypersensitive*. But what was that "something"? And how on earth could a defense mechanism turn into a deadly weapon?

The Experiment That Changed Everything

Charles Richet was not a man who gave up easily. If something intrigued him, he pursued it with the tenacity of a bloodhound. And what he had seen in Boulogne-sur-Mer in 1902 intrigued him like nothing before. So, back in Paris, he turned his laboratory into a factory of questions. What if they used other substances? What if they tried different animals? What if the time between doses was key?

In 1903, Richet and Portier published their first findings in the journal*Comptes Rendus de l'Académie des Sciences*. The title was dry and technical: "On the anaphylactic action of certain venoms." But what they described was anything but boring. They had discovered that, in certain cases, the body

didn't just*fail to defend itself*against a second exposure to a substance—it*overreacted*, as if it had developed an irrational hatred for something it had previously tolerated. Richet coined a term for this phenomenon:**anaphylaxis**, from the Greek*ana*-(against) and*phylaxis*(protection). "It's as if the body mistakes a friend for an enemy," he wrote.

But why?

The Wrong Clue (and the One That Mattered)

At first, Richet thought he was dealing with a phenomenon of "cumulative intoxication." Perhaps the venom stayed in the body and, when combined with the second dose, reached lethal levels. But experiments disproved this. If they injected the venom once and waited months before the second dose, the effect was the same: rapid death. It wasn't accumulation. It was*memory*.

So, what did the body remember? Richet tried substances that weren't poisonous: horse serum, egg whites, even milk. The results were identical. A dog that received an injection of horse serum could tolerate it without problems. But if weeks later it received another dose, even a tiny one, the animal went into shock. "It's not the venom that kills," Richet concluded. "It's the*body's reaction*to the venom."

The key came from an unexpected place: the work of a German scientist named Emil von Behring. In 1890, von Behring had discovered that the body produced substances called**antibodies**to fight infections. These proteins, he explained, attached to germs like keys in locks, marking them for destruction by the body's defenses. Richet wondered: what if antibodies didn't just attack germs but also harmless substances? What if, in some cases, that response became so violent that it damaged the body itself?

The Case That Confirmed It: The Boy Who Couldn't Drink Milk

In 1906, Richet received a letter from a doctor in Lyon. The physician described the case of a 5-year-old boy named Louis, who had developed a red rash and difficulty breathing after drinking a glass of milk. His parents swore Louis had never had problems with milk before. But the doctor noticed something strange: three months earlier, Louis had received an injection of diphtheria antiserum*made from horse blood*. Could it be related?

Richet traveled to Lyon immediately. There, in the boy's bed, he saw something that chilled him: Louis's reaction was identical to that of the dogs in his laboratory. The swelling, the redness, the difficulty breathing. "It's anaphylaxis," he told the doctor. "His body mistook milk for something dangerous." But why?

The answer lay in antibodies. Richet theorized that, upon receiving the horse serum, Louis's body had produced antibodies against equine proteins. But those proteins were similar enough to cow's milk

proteins that, when Louis drank milk, the antibodies attacked them by mistake. It was as if Louis's immune system had developed a "false positive," mistaking a harmless food for a deadly invader.

The Definitive Experiment

To test his theory, Richet designed a bold experiment. He took a group of guinea pigs and injected them with a small dose of horse serum. He waited two weeks, long enough for their bodies to produce antibodies. Then, he injected a second dose, but this time directly into the heart. The results were dramatic: the guinea pigs died within minutes, their lungs filled with fluid and their blood vessels collapsed. "It's as if the body drowns in its own defense," Richet wrote.

But the most shocking discovery came next. If he injected horse serum into guinea pigs that had*never*-been exposed to it, nothing happened. Only the guinea pigs that had received the first dose died. "The body isn't born hating," Richet concluded. "It learns to hate."

The Nobel Prize and the Legacy of an Uncomfortable Discovery

In 1913, Charles Richet was awarded the Nobel Prize in Medicine for his discovery of anaphylaxis. But the recognition didn't make him happy. "I've discovered something terrible," he confessed to a friend. "The human body isn't an invincible fortress. It's a castle with glass walls: strong until something hits it in the wrong place."

His work changed medicine forever. Today, we know that anaphylaxis is just one of the many ways the immune system can turn against us. Allergies, autoimmune diseases like type 1 diabetes or multiple sclerosis, even some drug reactions, follow the same principle: the body mistakes the harmless for the dangerous and attacks itself.

But Richet also left an unanswered question: why did this mechanism evolve? Why did the human body, in its infinite wisdom, develop a defense system that sometimes becomes lethal? Some scientists believe anaphylaxis is a "design flaw," a side effect of an overzealous immune system. Others argue that, in nature, this mechanism may have served to protect organisms from parasites or toxins that required multiple exposures to be deadly.

Either way, Richet's discovery reminds us of something fundamental: medicine isn't a science of certainties, but of questions. And sometimes, the most important answers come from the most terrifying mistakes. As Richet said in his Nobel acceptance speech: "Nature doesn't give us easy answers. It gives us mysteries. And it's our job to unravel them, even if they scare us."

Final Reflection: When the Body Becomes the Enemy

Today, more than a century after Richet's discovery, anaphylaxis remains a reminder of how fragile the line between defense and destruction can be. Every year, thousands of people die from allergic reactions to food, insect stings, or medications. And yet, we still don't fully understand why some bodies decide that a peanut or a dose of penicillin is a deadly threat.

But there's something hopeful in this story. Richet didn't discover anaphylaxis because he had all the answers, but because he asked the right questions. And in a world where medicine sometimes seems like a science of protocols and certainties, his story reminds us that great advances are born from curiosity, observation, and, above all, the willingness to face the unknown head-on.

The next time someone says, "It's just an allergy," remember Charles Richet and Neptune, the dog that died from a dose too small. Remember that sometimes the greatest danger doesn't come from outside, but from within. And that, in the struggle to understand the human body, the heroes aren't always those with all the answers, but those who dare to ask the most uncomfortable questions.