



## Allergies: When the Immune System Backfires

### Video Transcript

#### Jellyfishes and dogs

[Andreas J. Bircher]: In 1901, Prince Albert the First of Monaco invited Charles Richet and Paul Portier to use the laboratory on his yacht, Princess Alice The Second. There, they investigated the possibility to develop a vaccine that should protect against the toxins of the jellyfish *Physalia physalis*, also known as Portuguese man o' war.

The idea of the experiment was to inject animals repeatedly with low, non-toxic doses to induce immunity. To the surprise of the scientists, the animals became not less responsive, but developed severe symptoms and some of them even died. After this, Richet and Portier continue to work in Paris with dogs using a similar toxin of the easier available *Actinia* species, *Anemonia sulcata*.

One of their key experiments involved Neptun, a large, healthy male dog. At day one, he was injected a low, non-toxic dose of actinium toxin that was tolerated without reaction. However, 22 days later, the same small dose resulted in very severe symptoms within seconds, and eventually death after 25 minutes. The concept of protective antibodies had been previously postulated by Paul Ehrlich. Inadvertently, Richet and Portier had discovered an antibody-mediated hypersensitivity. Instead of inducing protective antibodies, Immunoglobulin G, short, IgG antibodies, they had sensitised Neptun unknowingly to actinium toxin with the first non-toxic dose. This sensitisation led to the formation of Immunoglobulin E, short, IgE antibodies, which can elicit an allergic reaction. Instead of prophylaxis, that is the protection against the toxin, a new phenomenon, the development of hypersensitivity, had thus been confirmed experimentally.

Richet called this phenomenon etymologically not completely correct, 'Ana-phylaxis', derived from the ancient Greek word phylaxis, meaning guardian. The new term, meaning against protection, was not immediately accepted. Other physicians had previously observed hypersensitivity reactions in patients after the repeated injection of foreign sera to treat infections, for instance, diphtheria. Nevertheless, Charles Richet received the Nobel Prize in Medicine in 1913 for his work on anaphylaxis.

The term anaphylaxis has prevailed and is nowadays used to describe the most severe immediate hypersensitivity reaction. The symptoms involve urticaria, that is rashes on the skin, colicky pain in the intestines, diarrhoea, and asthma. The patient may show also cardiovascular symptoms resulting in an anaphylactic shock. Anaphylaxis is, therefore, potentially fatal. Anaphylaxis can occur in response to almost any foreign substance. Common elicitors are venoms, such as the venom of bees or wasps, food, but also medication. The modern, highly purified or synthetically produced vaccines have become very rare causes of anaphylaxis nowadays.