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Allergies: When the Immune System Backfires

Video Transcript

A carriage ride in Central Park

[Andreas J. Bircher]: At the beginning of the 20th century, researchers began to focus on the intricacies of the immune system. In 1902, Richet and Portier discovered anaphylaxis. In 1903, Maurice Arthus observed a phenomenon he named local anaphylaxis. Finally, in 1905, Clemens von Pirquet coined the term 'allergy'. But one big question remained: What soluble factor or which cells provoked the observed effects? This question prompted research.

It was a clinical case that shed first light on it. In 1919, a Greek waiter, HT, then 35 years old, went for a horse carriage ride in Central Park, New York. As he entered the coach, he all of a sudden had difficulties breathing. This led up to a severe asthmatic attack. He was successfully treated with adrenaline. But the next day, when entering the carriage again, he suffered afresh an asthma crisis. Up till then, the waiter had never suffered from asthma or any other symptoms that might have pointed to an atopic condition. In his family, no history of allergies was known. However, two weeks earlier, he had received a blood transfusion to treat what was then called primary anaemia. Today, anaemia is defined as a status in which your organism lacks enough healthy red blood cells to supply the body's tissues with adequate oxygen. The waiter was investigated by Dr Maximilian Ramirez. The physician performed skin tests with a large series of respiratory and food allergens. An extract of horse dandruff that was tested in a high dilution of 1 to 20,000 produced a large wheal. In medical terms, the waiter's test yielded a strong positive result for horse. It turned out that the blood donor suffered from chronic asthma and bronchitis. He had been positively skin tested to horse at the dilution of 1 to 50,000. From these results, Dr Ramirez concluded that the waiter's asthma attacks had their origin in the blood transfusion. According to this analysis, this transfusion had passed anaphylactic reaction bodies – as he called them – to his patient lacking until this point any symptoms of allergy. When, however, the waiter was exposed to horse allergens, he suffered the typical common symptoms of an allergic reaction. The transferred blood did not cause any other untoward effects. And the waiter's allergic condition did only last for several weeks. After that time, it disappeared.

Two years later, an experiment confirmed Dr Ramirez's observation. Its designers were Carl Prausnitz and Heinz Küstner. Heinz Küstner worked at Carl Prausnitz's hygiene institute in Breslau, a city today known as Wroclaw in Poland. Küstner was allergic to fish. Prausnitz was allergic to pollen, but he had never experienced problems when eating fish. In the experiment, they injected a small volume of Küstner's blood serum into the skin of Prausnitz's forearm. They did this in different skin areas using varying dilutions. The next day, they tested fish extract at these skin locations. This provoked positive reactions, but only at the spots where Küstner's serum was present. Thus, they had found proof for a soluble factor that is responsible for a local allergic reaction. The experiment was published in German in 1921. It did not only confirm that the transferable and soluble factor provokes an allergic reaction, it also promoted the Prausnitz-Küstner test, or P-K reaction. It was used to demonstrate and quantify allergen-specific antibodies and became a standard in allergy diagnosis for many years to come. Since it involves the transfer of blood serum, it is no longer used today. With the rise of diseases like HIV or hepatitis passed on by blood, the procedure is too risky. It took more than 45 years until this antibody class could be measured and quantified directly in the blood serum. Discovered by Kimishige and Teruko Ishizaka in 1966, we know it now as fifth class of antibodies, Immunoglobulin E, or IgE.

Let us summarise what we may learn from these discoveries. We do have the observations of Richet, Portier, and von Pirquet on one hand, and the experiences of Ramirez and Prausnitz and Küstner on the other hand. How do they differ? Richet, Portier, and von Pirquet injected a foreign animal-derived protein into a human organism. The immune system then produced antibodies. These, in turn, stimulated an allergic reaction when the organism was exposed another time to this protein. The first introduction of the foreign protein into the body – in other words – resulted in the production of memory B cells producing antibodies targeted towards the intruder. They reacted with the production of either the immunoglobulins IgG or IgE. This principle is called active sensitization. It is also applied in active vaccination. Ramirez, Prausnitz, and Küstner, on the other hand, transferred IgE antibodies into a non-allergic individual as part of a serum. The individual in each case reacted only temporarily allergic to the allergen. This was due to the fact that the individual's plasma cells did not produce the IgE antibodies themselves. Transferred IgE antibodies are used up and degraded after several weeks. Thus, the sensitization, that is called passive, is not permanent. Passive sensitization is rarely used in medicine today. It might be applied in an emergency situation. For instance, if a patient is exposed to rabies without having been vaccinated previously, active and passive vaccination is done in parallel. The passive vaccination provides the patient's organism with antibodies that are directly operational. In the meantime, and induced by the active vaccination, the organism has time to build up sufficient protective antibodies of its own. Done otherwise, the patient might die. IgE circulates only in minute amounts in the blood. For this reason, it took more than 40 years from the first demonstration of transferable factors in allergic reactions until IgE could be quantified. The technique is now established and used in the diagnosis of allergic diseases to complement skin tests.