Karl Landsteiner (1868-1943)

Karl Landsteiner studied blood types in Europe and in the United States in the late nineteenth and early twentieth centuries. Landsteiner won the Nobel Prize in Physiology or Medicine in 1930 for detailing immunological reactions in the ABO blood group system. The ABO blood group system divides human blood into one of four types based on the antibodies that are present on each cell. Landsteiner's work with blood types led physicians to safely perform blood transfusions and organ transplants. Additionally, Landsteiner researched the Rh blood factor, a protein marker on the surface of blood cells and that can impact pregnancy.

Karl Landsteiner was born on 14 June 1868 in Baden bei Wien, an upper middle class suburb just outside the city of Vienna, at the time belonging to the Austro-Hungarian Empire, that later became part of Austria. He was the only child of Fanny Hess and Leopold Landsteiner, a legal scholar, journalist, and founder of The Daily Presse. In 1874, Landsteiner's father died from a heart attack. At the age of twelve, Landsteiner attended the Staatsgymnasium, a public high school in Linz, Austria, as an honors student.

In 1885, Landsteiner entered the Vienna Medical School in Vienna at the age of seventeen and studied anatomy, zoology, blood chemistry, and organic chemistry. In 1888, he took a break from his studies to complete a year of mandatory military service. In 1890, Landsteiner and his mother converted from Judaism to Catholicism, just before Landsteiner graduated with his medical degree in 1891 at the age of twenty-three.

After graduating, Landsteiner began his post-doctoral studies in the laboratory of Ernst Ludwig, where he studied cancer of plasma cells, responsible for making antibodies. An antibody is a protein used by the immune system to identify and neutralize bacteria, viruses, and other foreign objects. Antibodies work by recognizing and attaching to little protein markers of the surfaces of cells called antigens. Between 1891 and 1896, Landsteiner worked in different laboratories across Europe. Landsteiner worked with Eugen von Bamberger in Munich, Germany, on hypertrophic pulmonary osteoarthropathy, a condition associated with lung cancer and later worked with Arthur Hantzsch and Roland Scholl in Zurich, Switzerland.

In 1896, Landsteiner obtained a position as the second assistant of Max von Gruber at the Institute for Hygiene at the Vienna General Hospital in Vienna. Landsteiner became involved in a debate that would set the course for future research on immunological reactions between his mentor von Gruber and Paul Ehrlich, the director of the Frankfurt Royal Institute for Experimental Therapy in Frankfurt, Germany. Ehrlich argued that the antigen-antibody relationship was one-to-one, such that antigens antibodies fit each other like a lock and a key. Von Gruber, on the other hand, theorized that an antibody worked best with the antigen that was used to produce it, but that the same antibody would work, though less effectively, with other antigens. The opposing theories led to a debate between von Gruber and Ehrlich. Landsteiner conducted an experiment that supported von Gruber's theory. In 1897, while working with von Gruber, Landsteiner published his first paper about a clumping reaction in blood serum, a process called agglutination, and its relationship to immunity.

In 1897, Landsteiner accepted a position at the Institute of Pathological Anatomy in Vienna, where he worked on cadavers. Over the next ten years he performed nearly four thousand post-mortem examinations and published over seventy-five articles on his observations. Fifty-two of these articles discuss blood chemistry. Landsteiner described the agglutination reactions that occur when blood from one individual is brought into contract with the blood of another individual. Landsteiner relegated his observation of agglutination to a footnote in a paper he wrote in 1900, but he expanded upon this observation the following year in in his paper ”Agglutination of Normal Human Blood.”

Landsteiner observed a pattern of antigen reactions that occurred when he combined blood serum from different individuals. Landsteiner observed that antigens on the outside of blood cells differed between individuals. If blood from what he called the A or the B group was introduced into a host of the opposing group, the host body would trigger an immunological reaction. Landsteiner found that this reaction caused the invading antigen carrying blood cell to burst. Large accumulations of burst cells created clumps that could clog small blood vessels (capillaries) and perhaps cause shock or death. Initially, Landsteiner recognized three different blood types: A, B, and C. The C-blood type was later more commonly called type-O. In 1902, one of Landsteiner's students found a fourth blood type, AB, which triggered a reaction if introduced into either A or B blood. In 1930, The Health Committee of the League of Nations in Geneva, Switzerland, formally adopted the Landsteiner nomenclature (A, B, AB, and O) in his honor, the naming convention that was still used up through the first decades of the twenty-first century.

Landsteiner's blood typing system had an immediate impact on forensic and surgical sciences. In 1902, Landsteiner and Max Richter, who worked at Vienna University Institute of Forensic Medicine in Vienna, described a method of using blood evidence gathered from the scene of a crime to aid in the investigation. Using this system, scientists could determine whether a blood sample contained A-antigen, B-antigen, both A- and B-antigen, or neither antigen (type-O). If a suspect's blood had a different antigen than the sample left at the crime scene, investigators could conclude the sample could was not from that particular individual. However, roughly fifty percent of the population has O-type blood and less than five percent has AB-type blood. So, if a sample and a suspect had matching blood types, investigators could not make a positive identification. The ABO system also enabled doctors to perform safe blood transfusions. Reuben Ottenberg at the Mt. Sinai Hospital in New York, New York, completed the first successful blood transfusion based on Landsteiner's blood type theory in 1907. During World War I, blood transfusions saved tens of thousands of lives. Later, the ABO blood grouping made it possible to successfully complete the first organ transplants by reducing the chance that a body rejected incompatible transplants.

In 1908, as the head of the pathology department at the Imperial Wilhelminen Hospital in Vienna, Landsteiner showed that polio is a viral disease. Together with his assistant Erwin Popper, Landsteiner conducted an autopsy of a boy who had died of polio. To determine whether bacteria or a different agent had caused the polio, Landsteiner collected some of the boy's spinal fluid and strained it through a filter fine enough to trap bacteria. He then cultured this filtered particles and found that no bacteria grew there. To determine if the infected spinal fluid material was infectious, Landsteiner injected it into rabbits, mice, and guinea pigs, but none of the animals became sick. Landsteiner and Popper injected the filtered spinal fluid into two Old World rhesus monkeys (http://eol.org/pages/327960/overviewMacaca mulatta), and they found that both died within two weeks. Landsteiner performed autopsies on the rhesus monkeys that revealed spinal cord lesions like those observed in human polio victims. Because Landsteiner and Popper had eliminated bacteria as a potential cause of the infection earlier in the experiment, they concluded that a virus must have caused the infection. Landsteiner proposed that it could be possible to create a polio vaccine. However, it took forty-seven years until Jonas Salk at the University of Pittsburgh School of Medicine in Pittsburgh, Pennsylvania, developed and successfully administered the polio vaccine in 1952.

During World War I, Landsteiner performed blood transfusions on many injured soldiers. In 1916 and at the age of forty-eight, Landsteiner met and married Leopoldine Helene Wlatso. A year later, they had to their only child, Ernst. Because of economic difficulties in post-war Austria, Landsteiner and his family moved to Netherlands in 1919. Landsteiner soon obtained a job at the Catholic R.K. Hospital in The Hauge, Netherlands, performing routine tests on urine and blood. During his stay in the Netherlands, he published twelve papers about immune responses triggered by changes in small fat or sugar molecules.

In 1923, the Rockefeller Institute for Medical Research in New York City, New York, offered Landsteiner a position to research immunity and allergies. Landsteiner accepted and moved with his family to the US. Most biographers report that Landsteiner's move to the US was very difficult for him. He disliked the fame that came with his status as an authority on immunology and avoided invitations to speak publicly, preferring instead to stay in his laboratory. Landsteiner became a US

citizen in 1929, and he won the Nobel Prize in Physiology or Medicine in 1930

Landsteiner continued researching until the end of his life and compiled a comprehensive summary of his contributions to medicine in his 1936 book Die Spezifitat Der Serologischen Reaktionen (The Specificity of Serological Reactions). Landsteiner retired in 1939 at the age of seventy-one, but he continued to work as an emeritus professor. Along with his assistants, Philip Levine and Alexander Wiener, Landsteiner further studied new blood factors.

In the late 1930s and early 1940s, Landsteiner studied rhesus monkeys and found that the presence or absence of a particular factor could affect the compatibility of mixed blood, even if the blood came from two organisms with the same blood type. Landsteiner called this the Rh-factor, named after the rhesus monkeys he had used for such research. The Rh-factor became a part of Landsteiner's blood typing system, indicated by a positive or negative qualifier after the blood group, for example O+ or AB-. With the Rh-factor identified, researcher could better study and explain newborn hemolytic disease, a condition that arises when an Rh negative woman gives birth to second-born Rh positive fetus. During her first Rh positive pregnancy, an Rh negative mother develops Rh positive antibodies that can cause her body to attack the second Rh positive fetus.

Landsteiner also analyzed blood chemistry and defined genetic differences between individuals in regard to blood type. This also proved to be important for forensic scientists who used blood groups to exclude suspects suspected of leaving blood at the scene of a crime.

Towards the end of his life, Landsteiner turned his attention to the study of malignant tumors to find a treatment after his wife developed thyroid cancer. Karl Landsteiner died from a heart attack on 26 June 1943.

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