BIOGRAPHY BIOΓΡΑΦΙΑ

Ludwik Hirszfeld (1884–1954) – Pioneer of blood type testing Significance for organ transplants

Proper selection of the organ to be transplanted requires a series of tests and determines the effectiveness of the treatment. The selection is preceded by a series of tests performed between the donor and recipient: pre-selection according to blood group, human leukocyte antigens (HLA), panel reactive antibody (PRA) and crossmatch. Of course, the first condition is the compliance of blood types between the donor and the recipient. In 1901, Karl Landsteiner discovered that human blood had different properties and distinguished three blood groups: A, B, and C. In 1910–1911, Emil von Dungern and Ludwik Hirszfeld discovered the Mendelian inheritance of blood types. Their division into four basic groups A, B, AB and O has been used since 1928. The same researchers found subtypes A1 and A2 within type A. Ludwik Hirszfeld (1884–1954) was born in Warsaw and studied medicine in Würzburg. In 1907, he received a doctorate at the University of Berlin and moved to the Cancer Research Centre in Heidelberg and, in 1911, to the University of Zurich. As a volunteer in World War I in Serbia, he fought a typhus epidemic. In 1918–1919, with his wife Hanna, he researched and described the uneven distribution of blood type features that reflects the diverse evolutionary adaptations of humans. In the 1920s, he co-founded the National Institute of Hygiene in Warsaw. During World War II, he spent two years in the Warsaw ghetto, where he fought infectious diseases, typhus and tuberculosis. After the war, he headed the Department of Medical Microbiology at Maria Skłodowska-Curie University in Lublin. In 1945, he worked in Wrocław as the Head of the Department of Microbiology. He died in Wroclaw. Ludwik Hirszfeld was an outstanding medical doctor, researcher and community activist. The importance of Hirszfeld's contribution to our knowledge of the blood type system was confirmed by Karl Landsteiner in his Nobel Address, by choosing Hirszfeld to the Presidency of the Blood Group of the Second International Congress of Blood Transfusion in Paris in 1937 and by naming after him the Institute of Immunology and Experimental Therapy of the Polish Academy of Sciences in Wrocław.

1. INTRODUCTION

Beyond doubt, the ultimate solution for those suffering from end-stage renal disease is renal transplant. The first attempts at transplanting kidneys date back to the early 20th century, yet for a long time the success of the surgery depended on the then-unknown mechanisms of transplant rejection. A good, yet sorry example is made by a series of unsuccessful organ transplants resulting from the lack of knowledge about the mechanisms of immune response after the introduction of a foreign tissue or organ ARCHIVES OF HELLENIC MEDICINE 2020, 37(Suppl 2):63–67 ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2020, 37(Συμπλ 2):63–67

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Ludwik Hirszfeld (1884–1954) – Πρωτοπόρος των εξετάσεων τύπου αίματος. Μεγάλης σημασίας για τις μεταμοσχεύσεις οργάνων

Περίληψη στο τέλος του άρθρου

Key words

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into the system. Nowadays, the selection of organs to be transplanted is preceded by a series of tests performed between the donor and recipient: pre-selection according to blood group, human leukocyte antigens (HLA), panel reactive antibody (PRA) and crossmatch. The first and fore-most condition for correct selection is matching for ABO blood groups.¹ The discovery of blood groups is owed to the research carried out by the Austrian Karl Landsteiner, working at the Anatomical Pathology Department at the University of Vienna. It was in 1901 when he divided blood into three groups, depending on its properties: A, B and a

third one, today known as group 0. One year later, in 1902, Sturli and von Decastelo described the fourth and rarest of them all - group AB. In 1930, for his discoveries, Landsteiner received the Nobel Prize in the field of physiology and medicine. In 1910-1911, Emil von Dungern and Ludwik Hirszfeld from the Cancer Research Centre in Heidelberg, Germany discovered and described Mendelian inheritance of blood type and introduced the marking of blood groups A, B, AB and O, which was officially accepted in 1928. They also discovered subgroups A₁ and A₂ within the A type.²⁻⁴ Being representatives of Western Europe, Karl Landsteiner and Emil von Dungern are very well known to readers of English and German-language publications. So remarkable was the significance of these discoveries that the presentation of the third one, Ludwik Hirszfeld from Eastern Europe, seems necessary.

2. LIFE

Ludwik Hirszfeld was born on 5th August 1884 in a Polonised Jewish family (fig. 1). His parents were Stanisław, a merchant and industrialist and Jenny nee Ginsberg. The Hirszfelds were strongly rooted in Polish culture. Ludwik's uncle was a chemist and a community activist and his sister's husband, Władysław Sterling, was a renowned Polish neurologist. Due to financial problems, the Hirszfelds moved to the city of Łódź where, in 1902, Ludwik graduated from a secondary school, majoring in Arts and Humanities. Followed on from that, he went to Germany which, at that time, was one of the most popular destinations for young Poles



Figure 1. Ludwik Hirszfeld (photo courtesy of the National Digital Archive in Warsaw).

wishing to study at a university. First, he studied medicine in Würzburg and then in Berlin, where he obtained the title of doctor of medicine. Then, in 1907, the young doctor moved to the Cancer Research Institute in Heidelberg, to be taken on as an assistant in the Parasitology Department and then in Serology. This is where he came into contact with Emil von Dungern; their cooperation, in 1910, resulted in the establishment of blood types and the principles of their inheritance. The following year, Hirszfeld moved to the University of Zurich, Switzerland where he was habilitated in the field of hygiene and the science of immunity. In Zurich, he also investigated the issue of endemic goitre in Switzerland and worked as a full-time associate professor, lecturing on infectious diseases and serology.⁵⁻⁷

After the outbreak of World War I, in 1915 he volunteered to go to Serbia where he was shortly joined by his wife. During his visit to the Balkans, he was involved in fighting a huge epidemic of typhus typhoid in the town of Valiewo. Extraordinary measures having been applied, the epidemic was brought under control. In stunningly primitive conditions, Hirszfeld managed to set up a small scientific centre there. Before the end of the war, the Hirszfelds were evacuated out of Serbia with the retreating army, as part of the hospital formation. The daunting route led through the Albanian mountains from where they made a sea crossing to Italy and finally managed to get back to Switzerland. There, for a while, Hirszfeld continued his work on the application of kitchen salt in patients with haemorrhagic shock only to move to Corfu, Greece where his wife, Hanna, ran her own department and he conducted statistical research on the incidence of major blood groups among different races and nations.8,9

After the end of World War I, the Hirszfelds returned to Warsaw, Poland, where Ludwik became Director of the Serum Research Department of the Department of Bacteriology and Experimental Medicine of the emerging National Institute of Hygiene, headed by Ludwik Raichman, the founder of UNICEF. In Warsaw, Hirszfeld also lectured on bacteriology and immunology at the Free Polish University, in the Medical and Pharmaceutical Departments of the University of Warsaw and at the School of Hygiene (fig. 2).

After the outbreak of World War II, due to his origin, he could not continue working in the National Institute of Hygiene and, in 1941, he and his family were transferred to the Warsaw Ghetto. There, he fought the typhoid fever epidemic with the use of a typhoid vaccine smuggled out of Lviv by another Polish researcher, Rudolf Weigel. He was also involved in underground university teaching. In August 1942, the Hirszfeld family managed to get out of the ghetto

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Figure 2. Ludwik Hirszfeld (photo courtesy of the National Digital Archive in Warsaw).

and were hiding under a changed name in many places in German-occupied Poland. After the war, Hirszfeld was one of the organisers of Maria Skłodowska-Curie University in Lublin, being the head of the Department of Medical Microbiology and simultaneously acting as the university's Vice Rector. However, the following year, in August 1945, he arrived in Wrocław to organise the Medical Department of the University of Wrocław, since 1950 known as the Medical Academy, where he headed the Department of Microbiology and, for one year, held the position of Dean. In 1954, he became head of the Blood Group Department of the Institute of Immunology and Experimental Therapy of the Polish Academy of Sciences, which today is named after him. He died of a heart attack on 7 March 1954 in Wrocław and was buried in the cemetery of St. Lawrence. Professor Ludwik Hirszfeld's wife was Hanna Kassmann, after World War II professor of paediatrics at the University of Warsaw and later Medical University in Wrocław. The Hirszfelds had one daughter, who died in 1943 at the age of 23.^{10,11}

3. WORK

Ludwik Hirszfeld's scientific achievements are impressive. The most important publications include papers written together with Emil von Dungern on Mendelian blood group differentiation A, B, AB, O adopted worldwide in 1928, as well as the discovery of subgroups within type A. In 1917, he described erythrocyte sedimentation (ESR), independently of Edmund Biernacki. Working with his wife in 1918–1919, he described the uneven distribution of blood group features that reflect diverse adaptations of the human species in the course of evolution. In 1919, he presented the bacteria of paratyphoid, which he had discovered, today named *Salmonella hirszfeldi*. Also important is his work on serological conflict between mother and foetus, as well as in the field of forensic medicine and genetics.¹²⁻¹⁴

He also wrote four books: *Konstitutionsserologie und Blutgruppenforschung* (fig. 3), *Blood groups in biology, medicine and law* (fig. 4);^{15,16} *Affiliation in the Light of Blood Grouping*, and *General Immunology*. His autobiography *The Story of*



Figure 3. The title page of the book *Konstitutionsserologie und blutgruppenforschung (Constitution Serology and Blood Group Research).*



Figure 4. The title page of the book Grupy krwi w zastosowaniu do biologii, medycyny i prawa (Blood Groups in Biology, Medicine and Law).

One Life, first published in 1946, and later renewed several times, sheds a lot of light on Professor Ludwik Hirszfeld. For his scientific achievements, in 1950, he was a Noble Prize nominee. He also received numerous awards, including honorary doctorates at the Universities of Prague (Czechoslovakia) and Zurich (Switzerland). He was also an honorary member of the Academy of Sciences in New York (USA). He was awarded numerous Polish and foreign state decorations.

Paweł Kisielow presented crucial Hirszfeld's characteristics with the following words: "[...] for many he remains an icon of science, not only Polish. He embodies a large-scale scholar, researcher, teacher, doctor, community activist, organiser and humanist of well-earned international fame. His reputation was earned thanks to his wide array of talents and original scientific discoveries and concepts which greatly added to the development of a number of branches: immunogenetics, haematology, microbiology and immunology of neoplastic diseases, forensic medicine, transfusiology and, above all, research on blood types [...]". On the other hand, research on blood types had a significant impact on the development of transfusion medicine and transplantology, including kidney transplants. The authors of this study strongly agree with the opinion presented by the author of the above-cited publication.¹⁷

ΠΕΡΙΛΗΨΗ

Ludwik Hirszfeld (1884–1954) – Πρωτοπόρος των εξετάσεων τύπου αίματος. Μεγάλης σημασίας για τις μεταμοσχεύσεις οργάνων

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Η σωστή επιλογή του προς μεταμόσχευση οργάνου απαιτεί σειρά εξετάσεων και καθορίζει την αποτελεσματικότητα της θεραπείας. Η επιλογή προηγείται από μια σειρά εξετάσεων που διεξάγεται μεταξύ του δότη και του λήπτη: προεπιλογή σύμφωνα με την ομάδα αίματος, τα αντιγόνα ανθρώπινων λευκοκυττάρων (HLA), τα αντισώματα αντιδραστικής ομάδας (PRA) και τη διασταύρωση. Φυσικά, η πρώτη προϋπόθεση είναι η συμβατότητα των τύπων αίματος μεταξύ του δότη και του λήπτη. Το 1901, ο Karl Landsteiner ανακάλυψε ότι το ανθρώπινο αίμα είχε διαφορετικές ιδιότητες και διέκρινε τρεις ομάδες αίματος: Α, Β και Γ. Το 1910–1911, ο Emil von Dungern και ο Ludwik Hirszfeld ανακάλυψαν τη μεντελική κληρονομιά των τύπων αίματος. Η διαίρεσή τους σε τέσσερις βασικές ομάδες Α, Β, ΑΒ και Ο χρησιμοποιείται από το 1928. Οι ίδιοι ερευνητές βρήκαν υποτύπους Α1 και Α2 εντός του τύπου Α. Ο Ludwik Hirszfeld (1884–1954) γεννήθηκε στη Βαρσοβία και σπούδασε Ιατρική στο Würzburg. Το 1907, έλαβε διδακτορικό δίπλωμα στο Πανεπιστήμιο του Βερολίνου και μετακόμισε στο Κέντρο Έρευνας για τον Καρκίνο στη Χαϊδελβέργη και το 1911 στο Πανεπιστήμιο της Ζυρίχης. Ως εθελοντής στον Α΄ Παγκόσμιο Πόλεμο στη Σερβία, καταπολέμησε μια επιδημία τύφου. Το 1918–1919, με τη σύζυγό του Hanna, διερεύνησε και περιέγραψε την ανομοιόμορφη κατανομή των χαρακτηριστικών του αίματος που αντικατοπτρίζει τις ποικίλες εξελικτικές προσαρμογές των ανθρώπων. Στη δεκαετία του 1920 συνίδρυσε το Εθνικό Ινστιτούτο Υγιεινής στη Βαρσοβία. Κατά τη διάρκεια του Β΄ Παγκοσμίου Πολέμου, πέρασε δύο χρόνια στο γκέτο της Βαρσοβίας, όπου καταπολέμησε μολυσματικές ασθένειες, τύφο και φυματίωση. Μετά τον πόλεμο, ηγήθηκε του Τμήματος Ιατρικής Μικροβιολογίας στο Πανεπιστήμιο Maria Skłodowska-Curie στο Λούμπλιν. Το 1945 εργάστηκε στο Βρότσλαβ ως Επικεφαλής του Τμήματος Μικροβιολογίας. Πέθανε στο Βρότσλαβ. Ο Ludwik Hirszfeld ήταν εξαιρετικός ιατρός, ερευνητής και ακτιβιστής της κοινότητας. Η σημασία της συμβολής του Hirszfeld στη γνώση μας για το σύστημα τύπων αίματος επιβεβαιώθηκε από τον Karl Landsteiner στην Απονομή του Νόμπελ, επιλέγοντας τον Hirszfeld στην Προεδρία της Ομάδας Αίματος του Δεύτερου Διεθνούς Συνεδρίου Μετάγγισης Αίματος στο Παρίσι το 1937 και δίνοντας το όνομά του στο Ινστιτούτο Ανοσολογίας και Πειραματικής Θεραπείας της Πολωνικής Ακαδημίας Επιστημών στο Βρότσλαβ.

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Λέξεις ευρετηρίου: Ludwik Hirszfeld, Μεταμόσχευση οργάνου, Τύπος αίματος

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