

by Sinclair Lewis, American literature laureate of that year.

Conclusion

Landsteiner's success in elucidating the mystery behind three (A, B and O) of the four blood groups in 1900–1901 has been attributed to his amazing vitality, stamina and single mindedness and diversity of interests in applying chemical knowledge to a perennial medical problem^{3,28–30}. The fourth blood group AB was reported in 1902 by von Decastello and Adriano Sturli, the latter being an associate of Landsteiner^{29,31}. Why did it take 30 years for the Nobel Prize selection committee to recognize Landsteiner's trend-setting discovery of the blood groups? As revealed in the Nobel medicine prize nomination records (Table 1), he was not nominated for the Prize until 1921. Then, why did it take another 10 additional years? Zetterstrom¹² had inferred that 'some clinical professors on the [selection] Committee underestimated the importance of this discovery'.

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Karl Landsteiner (1868–1943) – a 20th century scientist as the 'Einstein of biomedical science'

Ramesh Maheshwari

Karl Landsteiner (1868–1943) was a 20th century scientist who discovered blood groups and laid down the broad rules of safe blood transfusion: only the blood from a donor which has matching antigens can be transfused into a recipient. This discovery made it possible to save the lives of thousands of war and accident victims from blood loss and of patients requiring blood. Landsteiner was awarded a Nobel Prize at about the same time as Einstein. Both Landsteiner and Einstein were of German descent, their time of work overlapped, and both had almost similar number of publications. Both made discoveries of equal importance in their respective fields of research. Yet, Landsteiner is largely forgotten. Data analysis shows that Landsteiner's scientific acumen which led to the discovery of blood groups was of genius quality and in this year (2013) coinciding with Landsteiner's 70th death anniversary, let him be felicitated as the 'Einstein of biomedical sciences'.

Recently, my attention was caught by a photograph in a newspaper (Figure 1) reporting on the death of a pregnant woman in a local hospital as a result of transfusion of mismatched blood. She was O+ but was transfused B+ blood, re-

sulting in an anaphylactic shock reaction. This tragedy was a poignant reminder of blood groups in humans discovered by Karl Landsteiner (Figure 2) – an Austrian scientist who had laid down the rules of safe blood transfusion from a

donor to a recipient. A biologist-cum-historian-cum-Einstein biographer has compared the productivity of scientists (academic degree, age at the time of publication of the first paper, recognition in research; Nobel Prize) and considers

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Landsteiner on par with Einstein, even though he is forgotten. Here I give an overview on his life and work.

Education and discoveries

Landsteiner (1868–1943) was an experimental scientist born in Vienna, trained (MD, immunochemistry) in Munich and eventually immigrated to USA (The Rockefeller Institute), where he applied his knowledge of chemistry to clinical problems. He mixed blood from different individuals in test tubes or petri dishes and made the discovery that while the blood from certain individuals can be mixed without clumping of the red blood cells, in the case of certain others the mixing results in agglutination of cells. Such a simple experiment led Landsteiner to group the blood from a human population into four major types and lay down the rules of successful transfusion. Blood of type A has antigen A on its red blood cells (RBC). People with blood type A can receive blood from types A and O. Blood type B has antigen B on its RBC. People with blood type B can receive blood from types B and O. Blood type AB has both antigens A and B. People with blood type AB can receive blood from all three blood types A, B and O (universal receiver). Blood type O has no antigen; and hence can receive blood only from another individual with type O blood. However, people with blood type O can donate blood to individuals with the other three blood types (universal donor). Landsteiner thus laid the ground rules of safe transfusion of

blood from a donor to a recipient. I confess that not having access to his original papers in German, this portrayal of Landsteiner will draw some material from textbooks.

Impact

Blood clumping (Figure 3) is an immunological reaction which occurs when the receiver of a blood transfusion has antibodies against the donor blood cells. Landsteiner's findings made it possible to match blood groups and thus blood transfusions to be carried out safely between a donor and a recipient. The matching involves mixing a sample of the recipient's serum with that of the donor's red blood cells and checking if the mixture agglutinates (Table 1), or forms clumps. If agglutination occurs, that particular donor's blood cannot be transfused to that particular recipient. A person can donate or receive blood from another based on the type of antigens present on the surface of the blood cells. This discovery was quickly applied to biomedicine and has saved the lives of millions of wounded victims requiring injection of blood corpuscles. The discovery of four blood groups known as A, B, AB and O has had an impact on genetics (multiple alleles; child-rearing). This blood contains an antibody directed against substance B, found on the red cells of persons with blood type B. Type B blood contains the reverse combination. Serum of blood type AB contains neither antibody, but red cells in this type of blood contain both A and B sub-

stances. In type O blood, neither substance is present on the red cells, but the individual is capable of forming antibodies directed against red cells containing substance A or B. If blood type A is transfused into a person with B type blood, anti-A antibodies in the recipient will destroy the transfused A red cells. Because O type blood has neither substance on its red cells, it can be given successfully to almost any person having 'O' is universal donor. Persons with blood type AB have no antibodies and can receive any of the four types of blood, and AB are called universal recipients.

A melancholy genius

Little is documented on early life of Landsteiner. One commentator has referred to him as a 'melancholy genius'¹. There could be some truth in this. A photograph of the Nobel awardee taken in 1931 shows Landsteiner facing away from the camera. Other awardees, including C. V. Raman wearing his characteristic Indian turban are facing the camera. This pose invites an explanation. Perhaps Landsteiner was lost in thought, contemplating if there is a goal in life greater than a Nobel Prize and a mere photo-op in Stockholm. The year 2013 is Landsteiner's 70th death anniversary. I review Landsteiner's important discoveries in this tribute to him and his place in the library of geniuses.

Selection as a genius

On what basis is Landsteiner regarded a genius comparable to Einstein? Sri Kantha made a list of 24 Nobelists in medicine between 1864 and 1894, who were



Figure 1. A newspaper cutting reporting the death of a woman due to mismatched blood transfusion. Source: *The Hindu*, 5 July 2013.



Figure 2. Portrait of Karl Landsteiner on an Austrian postage stamp. (See <http://www.corbisimages.com/stock-photo/rights-managed/U5523571NP/dr-karl-landsteiner> for a photograph of Landsteiner working in his laboratory.)

Table 1. Landsteiner's tabulation of results on mixing of blood of six apparently healthy men. Plus sign indicates agglutination (clumping).

Serum	Dr St.	Dr Pleen.	Dr Sturl.	Dr Erdh.	Zar.	Landst.
Blood corpuscles of:						
Dr St.	-	+	+	+	+	-
Dr Pleen.	-	+	+	+	-	-
Dr Sturl.	-	+	-	-	+	-
Dr Erdh.	-	+	-	-	+	-
Zar.	-	-	+	+	-	-
Landst.	-	+	+	+	+	-

From this simple blood-mixing experiment, Landsteiner inferred that there are active substances known as isoagglutinins in the serum (liquid portion of the blood) and that they are present in specific distribution. Every serum contains those agglutinins that react with the agglutinogens not present in the red blood cells.

Table 2. A summary of Landsteiner's discoveries (from Sri Kantha²)

Year	Discovery
1900	Demonstration of the existence of different types of human blood (A, B and O groups).
1903	Feasibility of grouping dried human blood stains and the usefulness of such tests in forensic medicine
1908	First to isolate the polio virus and demonstrate the use of monkeys as an experimental model in polio research
1927-1928	Discovery of additional blood groups (M, N and MN) – equally useful as the A, B and O groups, in anthropological research (with P. Levine)
1940	Discovery of Rh-blood groups (with A. S. Wiener)

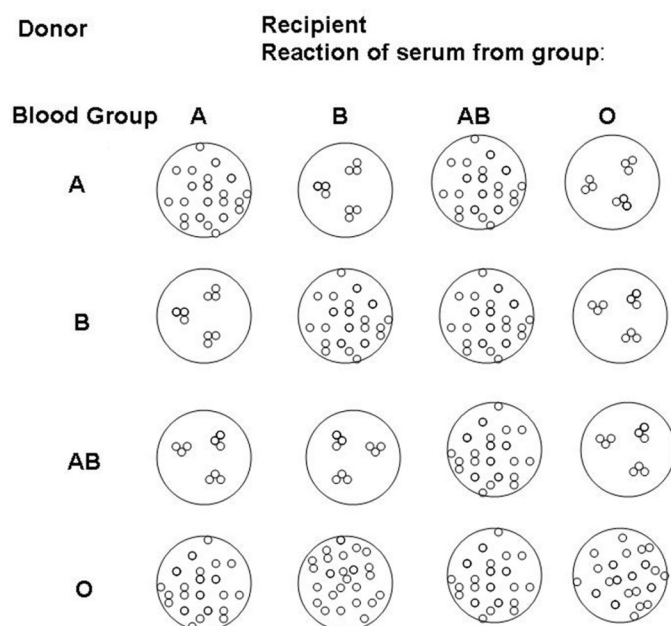


Figure 3. A diagram of Landsteiner's experiment on blood mixing. He collected blood from five of his associates and some of his own blood, mixed equal amounts of serum and 5% red blood cell suspension in 0.6% saline. He noticed that some of the cell suspensions were clumped by the sera of certain individuals, but not of others. Landsteiner inferred that there are active substances known as isoagglutinins in the serum (liquid portion of the blood) and that they are present in a specific distribution. Every serum contains those agglutinins that react with agglutinogens not present in the red blood cells. Among those who were awarded the Nobel Prize in the same year as Landsteiner was C. V. Raman for his discovery of scattering of light by studying the behaviour of crystals.

contemporaries of Einstein². They were grouped under (1) neurology, (2) physiology, (3) pathology, (4) biochemistry, (5) microbiology and (6) surgery. In each of the groups a control was identified for analysing their productivity. Three criteria were applied: (a) the influence of the scientist in multiple disciplines, (b) revolutionary in opening new vistas of knowledge and (c) significant impact to human life. Table 2 gives a summary of the significant discoveries of Landsteiner. The discovery in 1900 of the A, B, O and AB blood groups leading to successful transfusions in humans and saving the lives of countless war victims changed a number of biomedical disciplines such as immunochemistry, anthropology, forensic medicine, genetics and pathology. Successful blood transfusion in humans became routine. Landsteiner remains an unsung hero; probably because he was a melancholy genius¹.

Landsteiner moved from Vienna to Rockefeller Institute (USA), where he continued investigation of blood groups in the human population and on the chemistry of antigens, antibodies and other immunological factors that occur in the blood. He had suggested that because the characteristics which determine the blood groups are inherited, the blood groups could be used to decide instances of doubtful paternity. One of his great contributions was that he introduced chemistry into serology. In 1939, Landsteiner became Emeritus Professor at the Rockefeller Institute. While working in his laboratory, he suffered from a heart attack and died shortly thereafter. Whether or not Landsteiner was a genius some may argue, his discovery of agglutination (specific antigen-antibody reaction), had a great impact on medicine: in use of serology as a utilitarian aid in the identification of macromolecules.

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ACKNOWLEDGEMENT. I thank S. Sri Kantha for providing copies of reference materials that were difficult to access.

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