A history of Karl Landsteiner's stature in Nobel Prizes

Sachi Sri Kantha

Karl Landsteiner (1868–1943) was one of the scientific giants of the 20th century. He was awarded the undivided 1930 Nobel Prize in Medicine. As the records of the science Nobel Prize archives had opened for the first 50 years (1901–1951), I found that Landsteiner's trend-setting discoveries received a cumulative 16 nominations from 15 of his peers between 1921 and 1930. Among the 16 nominations, 9 were for an undivided award and ultimately he was recognized by such an award. Landsteiner also functioned as a nominator for the Nobel Prizes in Medicine, Chemistry and Physics between 1926 and 1940. Quite a number of Landsteiner's nominees were eventually awarded a Nobel Prize in Physiology or Medicine (including Thomas Hunt Morgan, Peyton Rous, John Northrop, James Sumner, Wendell Stanley and Herman Muller), or Chemistry (Irving Langmuir, Peter Debye, Adolf Butenandt and Linus Pauling).

That Karl Landsteiner (1868–1943), whose 70th death anniversary passed recently, was one of the scientific giants of the last century has been recorded by quite a number of historians in medicine[1–12]. Alexander Wiener[13], one of Landsteiner's junior co-workers, summarized his senior collaborator's scientific creativity as follows: 'The important discoveries made by this medical genius make up a long list, including the laying of the foundations of immunochemistry, the transmission of poliomyelitis for the first time to experimental animals (rhesus monkeys) thus laying the foundation for its prevention, the development of the complement fixation test for syphilis, and the introduction of dark-field microscopy for its diagnosis, the elucidation of the pathogenesis of paroxysmal hemoglobinuria, the pathogenesis of contact dermatitis and others. Landsteiner is known as the father of blood grouping, because he discovered not only the A, B, O blood groups but also, with Philip Levine MD, the MN types and the P system, while I was fortunate to be associated with Dr Landsteiner in the discovery of Rh factor.'

Rather than regurgitating Landsteiner's exemplary scientific creativity which had been studied previously by others[1–13], for this anniversary note, I focus on (a) how Landsteiner's contributions were evaluated as a nominee for the Nobel Prize in Medicine between 1921 and 1930, and (b) whom Landsteiner chose to nominate for the Nobel Prizes in Medicine, Chemistry and Physics between 1926 and 1940.

Methods

Publicly available databases[14,15] were used to study the records in which Landsteiner was featured as a Nobel Prize nominee and nominator for Medicine, Chemistry and Physics prizes.

Landsteiner as a nominee for the Nobel Prize in Medicine

As shown in Table 1, Landsteiner was nominated for a Nobel Prize in Medicine for six years (1921, 1922, 1923, 1928, 1929 and 1930), cumulatively receiving 16 nominations. From 1921 to 1923, he received single nominations. Then, for the next four years, he did not receive any nomination. Subsequently, his prominence rose in 1928 (4 nominations), 1929 (2 nominations) and 1930 (7 nominations with an eventual award). Among his 15 nominators, Heinrich Wieland (in 1928), Julius Wagner-Jauregg (in 1929) and Christiaan Eijkman (in 1930) were Nobel Prize winners, who had received either the Chemistry prize or

Table 1. Landsteiner as a nominee for the Nobel Prize in Physiology or Medicine

Nominator	Prize year	Motivation for nomination	Prize: split/undivided
Von Gruber	1921	Fundamental studies in agglutination	Split with Rubner
Pettersson	1922	Work on immunity	Undivided
Pettersson	1923	Work on immunity	Undivided
Forssman	1928	Discovery of isoagglutinins	Undivided
Moro	1928	Discovery of isoagglutinins	Undivided
Sachs	1928	Discovery of isoagglutinins	Split with Warburg and Uhlenhuth
Wieland	1928	Discovery of isoagglutinins	Split with O.Warburg
Silberschmidt	1929	Work in infantile paralysis, structure of antigens, blood groups	Split with C. von Pirquet
Wagner-Jauregg	1929	Discovery of isoagglutinins	Split with A. Calmette
C. Eijkman	1930	Discovery of human blood groups	Undivided
A. Fischel	1930	Discovery of human blood groups	Undivided
G. Gaertner	1930	Discovery of human blood groups	Undivided
R. Maresch	1930	Discovery of human blood groups	Undivided
E. Pick	1930	Discovery of human blood groups	Split with E. Steinach and G.H. Whipple
O. Thomsen	1930	Discovery of human blood groups	Undivided
A. Tschermak-Seysenegg	1930	Discovery of human blood groups	Split with Hueppe

the Medicine prize ahead of Landsteiner. Of the 16 cumulative nominations Landsteiner received between 1921 and 1930, 9 were for an undivided award, and ultimately he was recognized by the award.

In the presentation speech for the 1930 Nobel Medicine prize, Hendren[16] placed the vital discovery of Landsteiner in context, as follows:

> 'The transfer of blood from one person to another for therapeutic purposes was first practiced on a considerable scale during the seventeenth century. However, it was found that such blood transfusion involved serious risks, and not infrequently resulted in the death of the patient. Therapeutic application of blood transfusion had therefore been almost entirely abandoned by the time of Landsteiner's discovery. The discovery of the blood groups made it possible, at least in the majority of the cases, to explain the cause of the dangers associated with this therapeutic measure in the past and to avoid them in future. The blood donor must in fact belong to the same blood group as the patient. Thanks to Landsteiner's discovery, blood transfusions have come back into use and have saved a great many lives.'

Landsteiner as a nominator of the Nobel Prize in Physiology or Medicine

Table 2 shows the 16 nominations Landsteiner made for the Nobel Prize in Physiology or Medicine, between 1926 and 1940. He nominated Peyton Rous five times (1926, 1934, 1935, 1936 and 1937) and Thomas Hunt Morgan twice (1931 and 1933) for the undivided prize. Both did receive the Nobel honours; while Morgan received the award in 1933, Rous had to wait 40 years to be honoured in 1966. This 40-year delay was due to the embarrassment faced by the Nobel selection committee in awarding the 1926 Prize for a faulty discovery by Johannes Fibiger[17] for cancer-related research. It should be noted that Rous[18] reported his seminal discovery in 1911 that a chicken sarcoma could be transmitted by cell-free extracts and, therefore was caused by a virus; it took 55 years for the Nobel selection committee to acknowledge this seminal discovery[19], though Landsteiner had the foresight to nominate Rous for five times between 1926 and 1937.

In 1939, Landsteiner made two nominations; John Northrop and James Sumner for a split award as well as Wendell Stanley for an undivided award. Eventually, following the Second World War (and after Landsteiner's death), all three shared the 1946 Chemistry prize. In 1940, Landsteiner nominated Herman J. Muller for an undivided award. Ultimately, the undivided 1946 Nobel Medicine prize was awarded to Muller, 'for the discovery of the production of mutations by means of X-ray irradiation'.

Landsteiner as a nominator of the Nobel Prizes in Chemistry and Physics

Tables 2 and 3 show the 9 nominations Landsteiner made for 7 scientists for the Nobel Prizes in Chemistry and Physics[15], after he became the 1930 Nobel laureate. He made three consecutive nominations (1931, 1932 and 1933) for Peter Debye for the Nobel Prize in Physics. It is interesting to note that among the 7 scientists of his choice, four (Irving Langmuir, Peter Debye, Adolf Butenandt and Linus Pauling) were awarded the Nobel Prize in Chemistry. Langmuir, Debye, Butenandt and Pauling received the Prize in 1932, 1936, 1939 and 1954 respectively.

Discussion

Harriet Zuckerman, who had studied the careers of Nobel Prize-winning scientists in USA, recorded in 1978 that 'Everyone knows about them. Some scientists covet them; others apparently disdain them. No scientist has ever voluntarily turned one down. In a word, the Prizes are unique in the reward-system of science'[17]. As such,

Table 2. Landsteiner as a nominator for the Nobel Prize in Physiology or Medicine

Nominee	Prize year	Prize: split/undivided
Peyton Rous	1926	Undivided
Thomas H. Morgan	1931	Undivided
Harvey Cushing	1932	Split with Levaditi and Uhlenhuth
Constantine Levaditi	1932	Split with Cushing and Uhlenhuth
Paul Uhlenhuth	1932	Split with Cushing and Levaditi
Thomas H. Morgan	1933	Undivided
Peyton Rous	1934	Undivided
Peyton Rous	1935	Undivided
Peyton Rous	1936	Undivided
Felix d'Herelle	1937	Split with Twort and Rous
Frederick Twort	1937	Split with d'Herelle and Rous
Peyton Rous	1937	Split with Twort and d'Herelle
John H. Northrop	1939	Split with Sumner
James B. Sumner	1939	Split with Northrop
Wendell M. Stanley	1939	Undivided
Herman J. Muller	1940	Undivided

Table 3. Landsteiner as a nominator for the Nobel Prizes in Chemistry and Physics

Nominee	Prize year	Prize: split/undivided
Chemistry		
Irving Langmuir	1931	Undivided
Gilbert N. Lewis	1932	Undivided
Max Bergmann	1935	Split with Adolf Butenandt
Adolf Butenandt	1935	Split with Max Bergmann
Max Bergmann	1940	Split with Linus Pauling
Linus Pauling	1940	Split with Max Bergmann
Physics		
Peter Debye	1931	Undivided
Peter Debye	1932	Undivided
Peter Debye	1933	Undivided

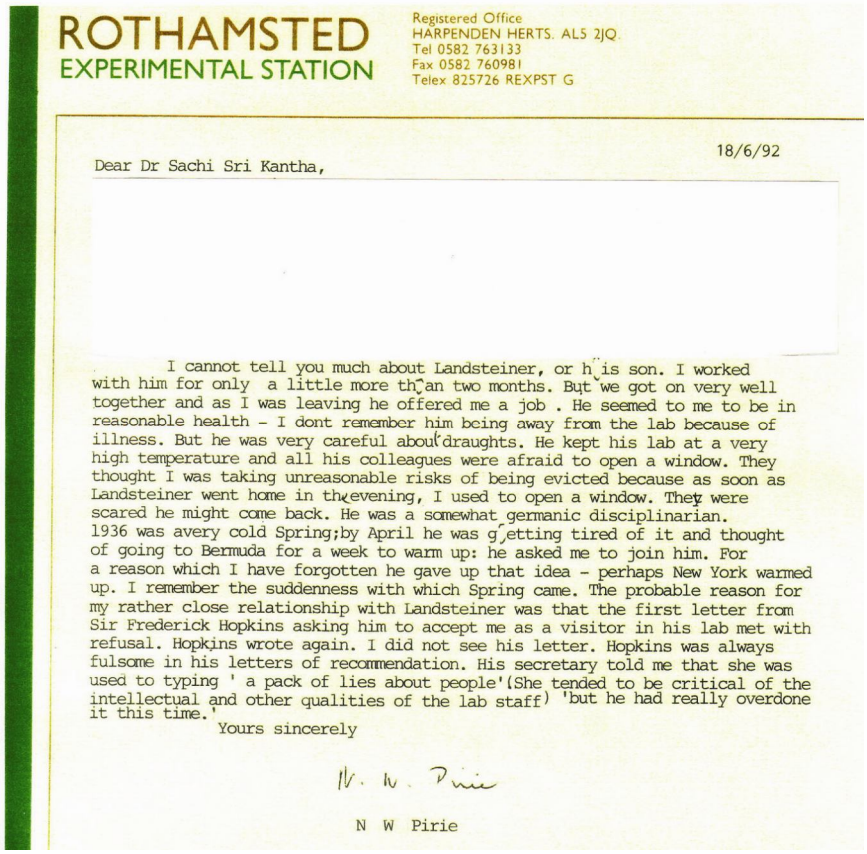
Landsteiner's specific role as a nominee and nominator for the Nobel Prizes in science offers a partial clue to his thinking as well as that of his peers on what they considered as 'excellence in scientific discovery' in the first half of the 20th century. One should remember that during this period, team work (as we understand now!) for a significant discovery was not much in vogue. However, in the second half of the 20th century team work became important and prominent; thus, sharing the spoils of glory turned out to be not easier to decide, even by the selection committees of the Nobel Prizes in science. This had raised serious questions on the nomination and selection processes for the Nobel Prizes since the last quarter of the 20th century[20–24].

However, the nominations of Landsteiner for the Nobel Prizes in Medicine, Chemistry and Physics between 1926 and 1940, and the fact that 10 of his nominees were eventually awarded the Medicine and Chemistry prizes indicate that he was a good evaluator of creativity and eminence among his peers. In this criterion too, Landsteiner and Albert Einstein share a similarity[5]. Einstein's 10 nominees for the Nobel Prizes[15] between 1919 and 1945 (M. Planck, J. Frank, G. Hertz, A. H. Compton, W. Heisenberg, E. Schrödinger, I. Rabi, O. Stern, W. Pauli and C. Bosch) were awarded the Nobel Prize in Physics and Chemistry.

Landsteiner's personality

What sort of a personality, did Landsteiner project for his peers? Bayne-Jones, while delivering his presidential address in 1931 to felicitate Landsteiner's 1930 Nobel Prize in Medicine, recorded, 'Those who have known Dr Landsteiner best have expressed their high appreciation of his rare personal characteristics of simplicity, sincerity, gentleness and charm.[25]' In his obituary note, Michael Heidelberger noted, 'In the laboratory, Landsteiner was the authoritative and energetic director of research; but outside, in his personal contacts, he was diffident, shy and quiet, though his flashes of genial wit were apt to enliven any conversation in which he took part. When he did address a gathering, he was stimulating, inspiring and brief.[26]' In 1992, I communicated with British biochemist Norman Wingate Pirie (1907–1997) to inquire about any specific Landsteiner traits, as Pirie had worked with him for a short while in 1936. Pirie's response in a letter dated 18 June 1992 (Figure 1) was as follows: 'I cannot tell you much about Landsteiner or his son. I worked with him for only a little more than two months. But we got on very well together and as I was leaving he offered me a job. He seemed to me to be in reasonable health – I don't remember him being away from the lab because of illness. But he was very careful about draughts. He kept his lab at a very high temperature and all his colleagues were afraid to open a window. They thought I was taking unreasonable risks of being evicted because as soon as Landsteiner went home in the evening, I used to open a window. They were scared he might come back. He was somewhat Germanic disciplinarian…'. Pirie's letter also indicates that Landsteiner did initially reject the recommendation made by Sir Frederick Hopkins on behalf of Pirie. Subsequently, he did accommodate Pirie, and in 1937 their collaborative work generated one joint publication on serological specificity in pyridine derivatives[27].

Philip Levine, one of Landsteiner's junior colleagues, reminisced in 1961 that though Landsteiner moved to New York from The Netherlands, 'he never completely adjusted himself to life in an apartment house in New York City. Noises he abhorred and in anticipation of neighbours' complaints, he disposed of his piano which, incidentally, he played exceedingly well.[28]' The best description of Landsteiner's personality was provided by Gottlieb[6], under the title 'the melancholy genius'. This account features an unusual group photograph taken during the 1930 Nobel Prize ceremony in which nine of that year's Nobelists (including C. V. Raman) were posing. Landsteiner, seated in the front row, was posing at an awkward 90° angle rather than facing the camera directly. The caption for the figure notes, 'Why he sat in this position for this photograph is obscure'. From the records made by others, one can deduce that one plausible reason could be that Landsteiner was irritated by the alcoholism-induced boorish behaviour exhibited



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Dear Dr Sachi Sri Kantha,

I cannot tell you much about Landsteiner, or his son. I worked with him for only a little more than two months. But we got on very well together and as I was leaving he offered me a job . He seemed to me to be in reasonable health - I dont remember him being away from the lab because of illness. But he was very careful about draughts. He kept his lab at a very high temperature and all his colleagues were afraid to open a window. They thought I was taking unreasonable risks of being evicted because as soon as Landsteiner went home in the evening, I used to open a window. They were scared he might come back. He was a somewhat germanic disciplinarian. 1936 was a very cold Spring; by April he was getting tired of it and thought of going to Bermuda for a week to warm up: he asked me to join him. For a reason which I have forgotten he gave up that idea - perhaps New York warmed up. I remember the suddenness with which Spring came. The probable reason for my rather close relationship with Landsteiner was that the first letter from Sir Frederick Hopkins asking him to accept me as a visitor in his lab met with refusal. Hopkins wrote again. I did not see his letter. Hopkins was always fulsome in his letters of recommendation. His secretary told me that she was used to typing ' a pack of lies about people'(She tended to be critical of the intellectual and other qualities of the lab staff) 'but he had really overdone it this time.'

Yours sincerely

N. W. Pirie

N W Pirie

Figure 1. Letter from Norman (Bill) Pirie, dated 18 June 1992, to Sachi Sri Kantha, on his interactions with Karl Landsteiner in 1936. Details presented in the first paragraph are omitted, because of their irrelevance to this note.

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? Zetterstrom[12] 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, resulting 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