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Perspective

Who can get the next Nobel Prize in infectious diseases?

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SUMMARY

The aim of this paper is to deliver a perspective on future Nobel prizes by reviewing the features of Nobel prizes awarded in the infectious diseases-related (IDR) field over the last 115 years. Thirty-three out of 106 Nobel prizes (31%) in Physiology or Medicine have been awarded for IDR topics. Out of 58 Nobel laureates for IDR topics, two have been female; 67% have been medical doctors. The median age of Nobel laureates in Physiology or Medicine was found to be lower than the median age of laureates in Literature ($p < 0.001$). Since the Second World War, US-affiliated scientists have dominated the Nobel prizes (53%); however before 1945, German scientists did so ($p = 0.005$). The new antimicrobials received Nobel prizes until 1960; however no treatment study was awarded the Prize until the discovery of artemisinin and ivermectin, for which the Nobel Prize was awarded in 2015. Collaborative works have increasingly been appreciated. In the future, more female laureates would be expected in the IDR field. Medical graduates and scientists involved in multi-institutional and multidisciplinary collaborative efforts seem to have an advantage.

1. Introduction

Appreciation of the scientific achievements made in medicine and infectious diseases is not easy. The most reliable measure of scientific endeavours may be the contribution made to the world's health. This would necessitate years of observation to detect the value of the contribution. Tracking and evaluating the Nobel prizes awarded and the Nobel laureates could be a means of acknowledging scientific developments. Despite some criticisms, the Nobel Prize is considered by many to be one of the most prestigious awards and a worldwide appreciation of specific scientific contributions.

The Nobel prizes have been awarded since 1895, based on the will of the Swedish inventor Alfred Nobel. Nobel prizes are currently awarded in the fields of Physics, Chemistry, Economic Sciences, Literature, Peace, and Physiology or Medicine. The first prize in the field of Physiology or Medicine was bestowed on Emil Adolf von Behring for his work on serum therapy against diphtheria; this Prize was awarded on December 10, 1901, on the fifth anniversary of Alfred Nobel's death.[1] The latest Nobel Prize in Physiology or Medicine, announced on October 5, 2015, was presented to two studies related to the infectious diseases field, which placed a spotlight on this field of medicine.

As of 2015, 106 Nobel prizes in Physiology or Medicine have been awarded to 210 laureates, with 33 of these prizes related to the realm of infectious diseases, clinical microbiology, and immunology. This review focuses on the Nobel laureates and their contributions to the fields of physiology or medicine and infectious diseases. By tracking the Nobel laureates, it was aimed to detail the developments achieved in the infectious diseases-related (IDR) fields over the last 115 years in order to infer information for future scientists.

2. Methods

Data on the laureates, including age, sex, country of birth, affiliation, prize motivation, and whether the prize was shared or not, were retrieved from the official website of the Nobel Prize (http://www.nobelprize.org). The Chi-square test for categorical data and the *t*-test for continuous data were used to analyse the data; statistical significance was set at $p < 0.05$. STATA 13 (Stata Corp, College Station, TX, USA) was used for the statistical analysis.

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3. Results and discussion

The proportion of IDR awards for the Nobel Prize in Medicine or Physiology is 31%. The demographic features of the Nobel laureates with IDR awards and those of the laureates of the separate Physiology or Medicine, Chemistry, Physics, Literature, Economic Sciences, and Peace prizes are presented in Table 1.

Scientists from the USA, UK, and France have been the most frequently represented. France has had a larger share of the Nobel prizes in IDR fields than in Literature, which may be attributed to the Pasteur Institute being awarded a prize five times. Two additional points can be made from these data, including the substantial discrepancy between the sexes of the Nobel laureates in the areas of Physiology or Medicine and Literature ($p = 0.099$). The discrepancy in sex is most prominent in the IDR Physiology or Medicine prizes, with only two female laureates out of 58: Françoise Barré-Sinoussi[2] and Youyou Tu. Laureates with a medical degree have represented 67% of the laureates in the IDR field and 58% of the awardees in Physiology or Medicine. The mean age of Nobel laureates in IDR fields does not differ significantly from that of the Medicine or Physiology Nobel laureates. However, the median age of all Nobel laureates in Physiology or Medicine is lower than the median age of laureates in Literature ($p < 0.001$). Peyton Rous has been the oldest Nobel laureate to receive the Nobel Prize in the IDR field; this was awarded for his work on tumour-inducing viruses in 1966 at the age of 87 years.[3] In the IDR field, Joshua Lederberg won the Nobel Prize at the age of 33 years for his work on the genetic material of bacteria; he was 1 year older than Frederick G. Banting, who was awarded the prize in Physiology or Medicine at 32 years old and who is therefore the youngest Nobel Laureate in Physiology or Medicine. Another interesting fact concerns Ralph Steinman, whose work on dendritic cells was acknowledged with a Nobel Prize. Ralph Steinman was announced to be the 2011 Nobel Prize Laureate in Physiology or Medicine 3 days after his death; the Nobel Assembly at Karolinska Institutet was unaware of this fact at the time of the announcement. Although a decision made in 1974 precluded the awarding of posthumous Nobel prizes, the Board of the Nobel Foundation accepted Ralph Steinman as a Nobel Laureate.

The number of Nobel laureates in the IDR field peaked between 1976 and 1990. Since the Second World War (1945), the leading affiliation has been the USA. The number of Nobel laureates affiliated with institutions in Germany declined abruptly after 1945 (Figure 1). Scientists affiliated with institutions in the USA have dominated the Nobel prizes in the IDR field, with 23 of 43 laureates (53%) after 1945; however, scientists affiliated with US institutions did not win a single prize before 1945 ($p < 0.001$). The number of laureates affiliated with institutions in Germany was also found to be statistically significant ($p = 0.005$), with four laureates before 1945 and only one after 1945; however the number of laureates from the UK has been stable, with four laureates before 1945 and three after. With the announcement of the Nobel Prize in Physiology or Medicine in 2015, scientists in the IDR field affiliated with institutions in Japan and China have been recognized for the first time in Nobel Prize history: Satoshi Ōmura and Youyou Tu.

For analysis, prizes in the IDR field were grouped by topic (Table 2 and Figure 2). Prizes for treatment-related studies

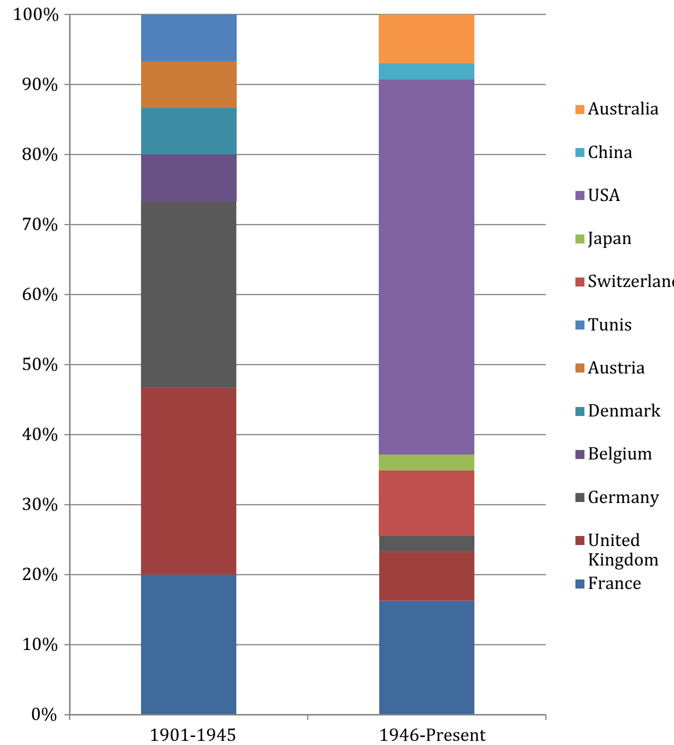

Figure 1. Percentile distribution of the countries of the Nobel laureates' affiliated institutions before and after 1945.

Table 1
Demographic characteristics of Nobel laureates in the infectious diseases-related field and for the individual prizes (Medicine or Physiology, Chemistry, Physics, Literature, Economic Studies, and Peace)

	Infectious diseases-related field (N = 58), n (%)	Nobel Prize in Physiology or Medicine (N = 210), n (%)	Nobel Prize in Chemistry (N = 171[a]), n (%)	Nobel Prize in Physics (N = 200[b]), n (%)	Nobel Prize in Literature (N = 111), n (%)	Nobel Prize in Economic Sciences (N = 76), n (%)	Nobel Peace Prize (N = 103[c]), n (%)
Female sex	2 (3%)	12 (5%)	4 (2%)	2 (1%)	12 (11%)	1 (1%)	16 (16%)
Mean age, years (min–max)	58 (33–87)	58 (32–87)	58 (35–85)	55 (25–88)	65 (42–88)	67 (51–90)	61 (17–87)
Medical doctor	39 (67%)	121 (58%)	13 (8%)	-	-	-	-
Affiliations[d]							
USA	23 (40%)	106 (50%)	79 (42%)	101 (46%)	11 (10%)	62 (78%)	21 (20%)
France	10 (17%)	10 (5%)	10 (5%)	16 (7%)	16 (14%)	2 (3%)	9 (9%)
UK	7 (12%)	31 (15%)	28 (15%)	26 (12%)	11 (10%)	6 (8%)	11 (11%)
Germany	5 (9%)	15 (7%)	27 (14%)	15 (7%)	6 (5%)	0 (0%)	3 (3%)
Switzerland	4 (7%)	8 (4%)	6 (3%)	8 (4%)	2 (2%)	0 (0%)	3 (3%)

[a] 172 prizes have been awarded in the field of Chemistry; however since Frederick Sanger received the award twice, there have been 171 laureates in total.
[b] 201 prizes have been awarded in the field of Physics; however since John Bardeen received the award twice, there have been 200 laureates in total.
[c] 129 Nobel Peace Prizes have been awarded, 103 to individuals and 26 to organizations. For demographic information, the organizations have been disregarded.
[d] For the country of affiliation, the total number is higher than the number of laureates, since some were affiliated with more than one institution at the time they received the prize.

increased regularly up to 1960, corresponding with the discovery of antibiotics; however, a Nobel Prize was not awarded for the treatment of infections until 2015.[4,5] Microbiology, on the other hand, has been the most frequently awarded category throughout the whole century (approximately two of every five IDR Nobel prizes), followed by immunology, which remains a very active field, with the latest contributions made by Ralph Steinman, Jules Alphonse Hoffmann, and Bruce Alan Beutler in 2011. With the recent development of artemisinin and ivermectin against malaria and roundworm infections, respectively, two scientists working on the treatment of parasitic infections received the Nobel Prize in Physiology or Medicine in 2015.[6] Although with the exception of prizes awarded for the discovery of new agents, only one microbiology study was awarded during the first half of the 20th

Table 2
List of Nobel laureates in infectious diseases-related fields

Field	Year	Name	Prize motivation
Epidemiology	1902	Ronald Ross	Work on malaria, by which he has shown how it enters the organism and thereby has laid the foundation for successful research on this disease and methods of combating it
	1928	Charles Jules Henri Nicolle	Work on typhus
	1976	Baruch S. Blumberg D. Carleton Gajdusek	Discoveries concerning new mechanisms for the origin and dissemination of infectious diseases
Virology	1951	Max Theiler	Discoveries concerning yellow fever and how to combat it
	1954	John Franklin Enders Thomas Huckle Weller Frederick Chapman Robbins	Discovery of the ability of poliomyelitis viruses to grow in cultures of various types of tissue
	1969	Max Delbrück Alfred D. Hershey Salvador E. Luria	Discoveries concerning the replication mechanism and the genetic structure of viruses
	1989	J. Michael Bishop Harold E. Varmus	Discovery of the cellular origin of retroviral oncogenes
	2008	Harald zur Hausen	Discovery of human papillomaviruses causing cervical cancer
Bacteriology	1958	Joshua Lederberg	Discoveries concerning genetic recombination and the organization of the genetic material of bacteria
	1965	François Jacob André Lwoff Jacques Monod	Discoveries concerning genetic control of enzyme and virus synthesis
	2005	Barry J. Marshall J. Robin Warren	Discovery of the bacterium *Helicobacter pylori* and its role in gastritis and peptic ulcer disease
Parasitology	1926	Johannes Andreas Grib Fibiger	Discovery of the Spiroptera carcinoma
New agent (prion)	1997	Stanley B. Prusiner	Discovery of prions—a new biological principle of infection
New agent (virus)	1966	Peyton Rous	Discovery of tumour-inducing viruses
	2008	Françoise Barré-Sinoussi Luc Montagnier	Discovery of human immunodeficiency virus
New agent (bacteria)	1905	Robert Koch	Investigations and discoveries in relation to tuberculosis
New agent (parasite)	1907	Charles Louis Alphonse Laveran	Work on the role played by protozoa in causing diseases
Immunology	1901	Emil Adolf von Behring	Work on serum therapy, especially its application against diphtheria, by which he has opened a new road in the domain of medical science and thereby placed in the hands of the physician a victorious weapon against illness and deaths
	1908	Ilya Ilyich Mechnikov Paul Ehrlich	Work on immunity
	1913	Charles Robert Richet	Work on anaphylaxis
	1919	Jules Bordet	Discoveries relating to immunity
	1960	Sir Frank Macfarlane Burnet Peter Brian Medawar	Discovery of acquired immunological tolerance
	1972	Gerald M. Edelman Rodney R. Porter	Discoveries concerning the chemical structure of antibodies
	1980	Jean Dausset Baruj Benacerraf George D. Snell	Discoveries concerning genetically determined structures on the cell surface that regulate immunological reactions
	1984	Niels K. Jerne Georges J.F. Köhler César Milstein	Theories concerning the specificity in development and control of the immune system and the discovery of the principle for production of monoclonal antibodies
	1987	Susumu Tonegawa	Discovery of the genetic principle for generation of antibody diversity
	1996	Peter C. Doherty Rolf M. Zinkernagel	Discoveries concerning the specificity of the cell-mediated immune defence
	2011	Bruce A. Beutler Jules A. Hoffmann	Discoveries concerning the activation of innate immunity
	2011	Ralph M. Steinman	Discovery of the dendritic cell and its role in adaptive immunity
Treatment	1927	Julius Wagner-Jauregg	Discovery of the therapeutic value of malaria inoculation in the treatment of dementia paralytica
	1948	Paul Hermann Müller	Discovery of the high efficiency of DDT as a contact poison against several arthropods
	2015	William C. Campbell Satoshi Ōmura	Discovery of a therapy against roundworm infections
	2015	Youyou Tu	Discovery of a therapy against malaria
Treatment (new antibiotic)	1939	Gerhard Domagk	Discovery of the antibacterial effects of prontosil
	1945	Sir Alexander Fleming Ernst Boris Chain Sir Howard Walter Florey	Discovery of penicillin and its curative effect in various infectious diseases
	1952	Selman Abraham Waksman	Discovery of streptomycin, the first antibiotic effective against tuberculosis

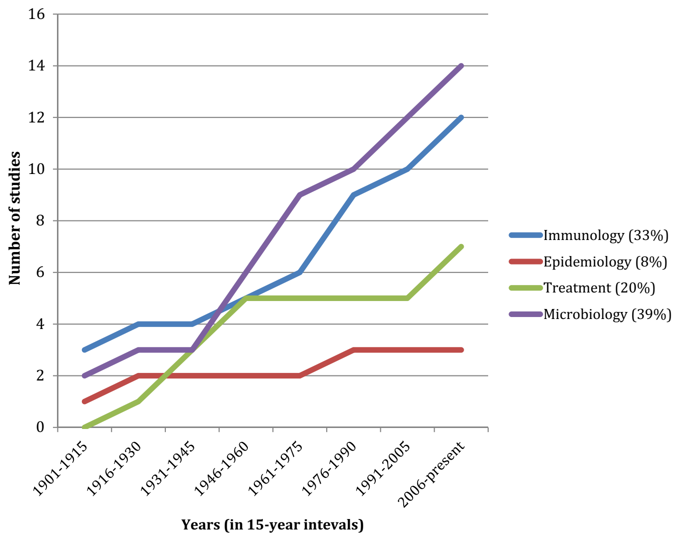

Figure 2. Overview of the infectious diseases-related Nobel prizes with respect to their categories.

century (Johannes Andreas Grib Fibiger,[1] parasitology, 1926), studies in this field increased constantly in the following years, constituting 39% of all IDR Nobel prizes.

After analysis of the data, 10 items related to future perspectives were identified.

(1) Considering the fact that both of the female Nobel laureates were awarded the Nobel Prize within the last decade, it is expected that there will be more female Nobel laureates in the future. The proportion of female Nobel laureates in IDR fields may increase.
(2) Sixty-seven percent of these Nobel laureates have had an MD degree, and the road to the Nobel Prize is always open for those who choose to attend medical school.
(3) The discovery of new microorganisms responsible for prevalent diseases could always result in an award.
(4) The discovery of novel mechanisms of pathogenesis in emerging viral infections that could lead to new treatment options for previously unknown pathways and preventive measures could attract a Nobel Prize.
(5) A surprising infectious aetiology for a health problem with high morbidity, such as dementia, schizophrenia, obesity, inflammatory bowel diseases, and diseases known to be autoimmune in origin could strongly attract a Nobel Prize.
(6) An entirely new antimicrobial molecule that could be a response to the global threat of antibiotic resistance could gain attention.
(7) The first Nobel Prize was given to a study in immunology, and this field is still important. Besides the effective immunization against prevalent infectious diseases, vaccine discoveries against non-communicable diseases such as cancer and obesity would also be attractive.
(8) More than 100 years after the study of Ronald Ross on infectious disease epidemiology, a highly predictive epidemiological tool that includes all of the potential confounding parameters and directly applicable to daily life would be a useful solution that could increase the capacity to combat outbreaks and could attract a Nobel Prize.
(9) Individual Nobel prizes in the IDR field were more common in the first half of the 1900s; however collaborative works from different disciplines have been seen increasingly throughout the years, becoming more common in the second half of the 1900s ($p = 0.002$). The authors' think that collaborative studies from different disciplines, and those that build a bridge between the basic and clinical sciences, will have a greater chance of being awarded a Nobel Prize.
(10) In light of the latest discoveries of new species of microorganisms, studies changing our understanding of their evolution, which could change the taxonomy of microorganisms, may be the focus of a future Nobel Prize.

Finally, these predictions have some confidence limits; within the nature of discoveries, the Nobel Prize could always surprise us with an unpredictable discovery!

4. Conclusions

The 115-year history of Nobel prizes for Physiology or Medicine, mainly in the IDR area, was reviewed. As has started to be seen for the Medicine or Physiology Prize, it is expected that more female laureates will be awarded prizes in the IDR field as well. Despite the higher proportion of PhD degrees than MD degrees, the number of laureates holding an MD degree was strikingly high. The mean age of the IDR laureates was found not to differ from that of all Physiology or Medicine laureates; however, both groups of laureates received their prizes at a significantly lower age than Literature laureates. By focusing on certain countries, an effect of the Second World War on the country distribution of prizes was demonstrated. Immunology studies have continued to garner a high level of interest; prizes for works on new agents are gaining increasing attention. The global trends in scientific studies have increased collaborative efforts, including joint works involving different disciplines.

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