

# The Nobel Prize in Physiology or Medicine, 1901-2000

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## Introduction

"...The whole of my remaining realizable estate shall be dealt with in the following way: The capital shall be invested by my executors in safe securities and shall constitute a fund, the interest on which shall be annually distributed in the form of prizes to those who, during the *preceding year*, shall have conferred the *greatest benefit on mankind* ... ; one part to the person who shall have made the most important *discovery* within the domain of *physiology or medicine*; ... The prizes for ... shall be awarded by ... that for physiology or medicine by the *Carolinska Institute* in Stockholm; ... "

This is the exact wording of part of the translation into English of Alfred Nobel's will, which was signed in Paris on 27 November 1895. Together with the statutes of the Nobel Foundation, which were officially approved by the Swedish Government on 29 June 1900, the will constitutes the basis on which the Prize-Awarding Institutions execute their work.

Soon after the will became known to the public it was criticised for legal and other reasons. One complaint was that it was lacking in precision. The will was also contested by the children of Alfred Nobel's brothers, and once a settlement had been reached with the Nobel family, lengthy negotiations and compromises between the executors of the will and the Prize-Awarding Institutions were required before the statutes were approved by the Government. Even though the statutes introduced some practical rules they still left a number of points open for interpretation by the Prize-Awarding Institutions.

The aim of the present essay is to briefly review the Nobel Prize in Physiology or Medicine with regard to selection procedure and the discoveries which have been awarded Nobel Prizes. For information about the scientific work and the biographies of the Laureates, the reader is referred to the series *Les Prix Nobel* which has been published every year since 1901 and most of which is now available online. (Comprehensive reviews covering the periods 1901-1950 and 1901-1960 were published by Liljestrand in 1950 and 1972.)

## Selection of Nobel Laureates

### Selection criteria

The Nobel Prize awarded by the [Nobel Assembly at Karolinska Institutet](#) is commonly referred to as the Nobel Prize in Medicine. The wording in Alfred Nobel's will, however, is *Physiology or Medicine*. It is important to make this distinction since, in the days of Alfred Nobel, physiology was used to describe what is today a number of biological fields. Interpreting the term 'physiology or medicine' in accordance with the intentions expressed in Alfred Nobel's will of 1895, therefore, leaves the Prize-Awarding Institution with considerable freedom to award Prizes in a broad biomedical field as well as in clinical medicine. Although the discussion of what is physiology and what is medicine is likely to continue indefinitely, it is clear that the prize awarder has, on several occasions, applied a broad definition. The prize in 1973 to Karl von Frisch, Konrad Lorenz and Nikolaas Tinbergen "for their discoveries concerning organisation and elicitation of individual and social behaviour patterns" could well be described as a prize in behavioral sciences. The prize in 1979 to Cormack and Hounsfield for "the development of computer-assisted tomography" fits well into the field of applied physics, while the prize in 1983 to Barbara McClintock for "the discovery of mobile genetic elements" could be considered a prize in plant genetics.

The key words in the will are *discovery* and *greatest benefit on mankind*. The essence of these words was thoroughly discussed during the preparatory work with the statutes of the Nobel Foundation. However, in the end no guidelines were provided. As a consequence, it has been up to the Prize-Awarding Institution to interpret how these terms should be applied in the selection of Prize winners. A further complication is that the corresponding wording is different for the two other Prizes within the natural sciences. In physics it is *discovery and invention* while in chemistry it is *discovery or improvement*.

*Discoveries* have been easier to define in the basic sciences than in clinical medicine. On the other hand "greatest benefit on mankind" has often been more obvious in clinical medicine than in basic research. Discovery has been defined as a sudden and significant increase in new knowledge rather than a steady increment of knowledge. As a consequence, awards have been given for scientific breakthroughs of high originality rather than for lifetime achievements. A discussion today of how the Prize-Awarding Institutions interpreted "greatest benefit on mankind" must take into account the knowledge available at the time of the award. Charles Nicolle received the prize in 1928 for "his work on typhus" which showed the role of the body louse in transmission of disease. Thanks to this discovery and simple delousing procedures it was possible to combat epidemics and save hundreds of thousands of lives during World War I. Paul Hermann Müller received the Nobel Prize in 1948 for his discovery of dichloro-diphenyl-trichloromethylmethane (DDT) as an efficient insecticide. During World War II and immediately thereafter, DDT made it possible to master not only typhus epidemics, but also to combat other insect-transmitted diseases, such as malaria. The World Health Organization (WHO) estimates that during the period of its use approximately 25 million lives were saved. Today, DDT is a banned chemical because of its environmental effects on fish and bird reproduction and its tendency to bioaccumulate in other species. However, at the time the prize was awarded, the benefit on mankind was quite obvious. Today, knowing about the disastrous ecological effects that the indiscriminate use of DDT as an insecticide in agriculture has had, the perspective is an entirely different one.

The will also states that the work recognized should have been carried out during the preceding year. This rule has never been possible to follow in the strict sense. First, discoveries have to be made public in print which takes time. Second, they need to be verified by other researchers before becoming generally accepted. To solve this problem, the Prize-Awarders have been pragmatic and have interpreted "preceding year" to mean that the benefit of the discovery has become apparent to the Prize-Awarding Institution during the preceding year. The importance of this flexibility can be illustrated by the following example. Barbara McClintock made her first studies on mobile genetic elements in 1944, i.e. long before the structure of the DNA molecule was established by James D. Watson and Francis H.C. Crick (1953). However, she was not awarded the Nobel Prize in Physiology or Medicine until 1983 (21 years after Watson and Crick). The main reason for this was that when the structure of DNA had been elucidated, and the genetic code had been deciphered by Nirenberg and Khorana (1968), it was obvious that changing even one single nucleotide in DNA could drastically disrupt reading of the genetic information. The scientific community simply found it very difficult to accept mobile genetic elements. Furthermore, it took a long time before it could be shown that mobile, genetic elements is a general phenomenon and not a peculiar trait restricted to maize. Once other scientists had identified mobile genetic elements in bacteria and in insects, and it had become known that transposition of growth regulatory genes was involved in cancer, it was not long before Barbara McClintock was awarded the prize. The same line of reasoning is true for Peyton Rous who made his discovery of tumour viruses in chickens in 1916 but did not receive the prize until 50 years later when the existence of tumour viruses had been confirmed in other animal species.

One reason the will of Alfred Nobel was criticised was that it was too vague. Therefore, in formulating the statutes of the Nobel Foundation and of the Prize-Awarding Institutions, efforts were made to be more specific. A rule was added that *in no case may the prize be divided between more than three persons* (one-third to each Laureate, alternatively one-half to one of the Laureates and one-quarter to each of the other two). This criterion contributes to the exclusiveness of the prize, but it also imposes restrictions. It means that not all worthy candidates can be awarded the prize, and sometimes a whole scientific field has to be dropped because the number of candidates is too large and cannot be reduced to three in a logical and just way. On the other hand, it is not a scientific field that should be awarded but the scientist(s) who have made the most important discovery.

Sometimes an ethical problem arises when the death of a candidate in a combination of four opens the possibility to award the remaining three candidates. According to the statutes the Nobel Prize cannot be awarded posthumously.

The Nobel Prize in Physiology or Medicine has been shared more often during the second half of the twentieth century than during the first half. Between 1901 and 1950, 59 people received the Nobel Prize compared to 113 between 1951 and 2000. The increased tendency to split the prize most likely reflects the growth of the international scientific community after World War II and the fact that the number of people nominated each year has increased. Another plausible reason is that, increasingly, biomedical research is carried out by teams rather than by scientists working alone. But there are at least two other factors to consider. First, both World War I and II occurred during the first half of the twentieth century and Nobel Prizes were not awarded during some of the war years. Second, Jöns Johansson, the only member of the faculty who had worked with Alfred Nobel, was unhappy about the choice of some Prize-winners. For a number of years while on the Nobel Committee, he effectively blocked the awarding of prizes in order to save money to build a Nobel research institute. The task of the institute would have been to assist the Nobel Committee by checking the accuracy of the discoveries claimed by the nominees.

# Karolinska Institutet as a Nobel Prize-Awarding Institution

Karolinska Institutet awards the Nobel Prize in Physiology or Medicine, as stated in Alfred Nobel's will. The task was originally handled by the entire professorial staff, which in 1901 comprised 19 members. The practical work was taken care of by a Nobel Committee comprised of three members, one of whom was the President of Karolinska Institutet and also the chairman of the committee. The first secretary of the Nobel Committee, Professor Göran Liljestrand, was not elected until 1918, and held the position for 42 years. During this period, the prestige of the Nobel Prize in Physiology or Medicine grew. Nevertheless, this long period of control by one person was one of several factors which later prompted changes in the organization.

In 1964, Karolinska Institutet had grown considerably and its research and teaching activities had become much more diversified. Selecting Nobel Laureates in physiology or medicine was the responsibility of a medical faculty which in 1970, counted 61 full professors. In addition, a university reform was planned which would include teachers other than professors (mainly associate professors and senior lecturers) in the faculty. After this reform the medical faculty would have had more than 200 members, thus making it difficult or impossible to conduct the complicated scientific discussions which represent a key element in the selection of Nobel Laureates. Furthermore, a new law was prepared in the 1970s implying that all documents at state institutions and organizations, of which Karolinska Institutet was one, would become open to the public. This would have made it impossible to keep secret the deliberations of the Nobel Committee. Since neither of these changes was considered to be beneficial for the Nobel work, a new organization - the Nobel Assembly - was instituted in 1977.

The Nobel Assembly has very strong connections with Karolinska Institutet but, legally and financially, it is independent of the institute and the state. Its entire budget comes from the Nobel Foundation, which handles all financial matters for the Prize-Awarding Institutions. The Nobel Assembly has 50 members, all of whom are active full professors at the institute. Members resign at the age of 65 years, i.e. when they retire from their positions at Karolinska Institutet. New members are elected by the assembly. A new chairman is elected every year according to seniority.

The Nobel Committee, which is the executive committee of the Nobel Assembly, is made up of five members and an executive secretary. In order to achieve a suitable balance between the need for both continuity and renewal, each committee member can only be elected for 3 + 3 consecutive years. The executive secretary can be elected for a maximum of four three-year periods. The mandates of the members begin and terminate in such a way that only part of the committee is renewed any single year. One of the members is elected chairman for a maximum of three years. After the committee of five has examined the nominations for a given year, an additional 10 ad hoc committee members are elected for a nine-month period. The inclusion of these members ensures that the committee has the necessary expertise to evaluate the work of the nominees who, judging from the nominations, are likely to be the top contenders for the prize in that particular year. The ad hoc members do not have to be members of the Nobel Assembly.

Several meetings between the assembly and the committee are held during the year in order to discuss the candidates nominated and the significance of their discoveries. Therefore, when it comes to the final decision, all assembly members know about the candidates nominated for the prize that year. During the first half of October, a decision is reached by the Nobel Assembly after voting by ballot (simple majority).

## Nominations

The timetable for the prize has remained more or less the same since 1901. Thus, in September the year before the prize is to be awarded, confidential, personal *invitations to nominate candidates* for the prize are sent to 2500-3000 scientists who are members of medical faculties or academies outside Scandinavia. Scientists are invited according to a rotating system. Previous Nobel Laureates in Physiology or Medicine and professors at medical faculties in the Nordic countries have the right to nominate every year. Nominations are made on special forms sent only to those who are formally invited to nominate. The Nobel Committee receives many informal letters with invalid nominations. These are not included among the documents examined by the Nobel Committee.

The fact that it is the international scientific community that nominates the Prize candidates, and the principle that the invitations to nominate are rotated among different academies and individuals, contributes to confidence in the selection procedure and to the prestige of the Nobel Prizes. Furthermore, if someone is nominated several times

over several years by different, independent scientists from different countries, this implies that the discovery made by the candidate has been widely recognized as being important. However, the total number of nominations in any particular year is not considered an important factor in judging the candidacy of a certain nominee. Nominations do not carry over from one year to another. To be considered for a particular year, the candidates must be nominated for that particular year irrespective of whether they have been previously nominated or not.

The deadline for the submission of nominations is 31 January (late incoming nominations are held over to the following year), after which the evaluation of the candidates begins.

All nominated candidates are evaluated by members of the Nobel Assembly and a written protocol is created for each new candidate. Preliminary reports and full reports on the work of individual nominees or, more commonly, groups of nominees, are prepared by members of the Nobel Assembly and by external reviewers. Top candidates are usually examined not once, but over a number of years, and by different reviewers. Each time the reviewer has access to the original nomination and all previous reports. Nowadays, all evaluations are made in English to make it possible for non-Swedish reviewers to access previous documentation. The evaluations have to be delivered before the end of August.

It is very unlikely that a candidate will receive the Nobel Prize in Physiology or Medicine the first year he or she is nominated, although this has happened on rare occasions, e.g. Carrel (1912), Hill and Meyerhof (1922) and Banting and Macleod (1923). It is worth mentioning that Banting and Macleod's first original publication on insulin appeared the year before they were awarded the prize, i.e. in 1922. One of the nominators of Banting and Macleod, Krogh, was almost as close. The discovery for which he was awarded the prize in 1920 was first published in Danish in 1918 and in English in 1919, and he was first nominated in 1919. There are some further examples of Laureates from the first 50 years who got the prize only one or two years after their first nomination, e.g. Domagk (1939), Fleming (1945) and Carl and Gerty Cori (1947). Their discoveries, however, had been made several years earlier.

The boundaries between Physics, Chemistry and Physiology or Medicine are not distinct. Thus, for instance, Röntgen was awarded the Nobel Prize in Physics but his discovery has been tremendously important not only in physics but also in chemistry and in medicine. Other Laureates in Physics have made discoveries which constitute a technological prerequisite for a considerable part of the research made within the biomedical field, especially after World War II. [Schrödinger](#) (Physics 1933) and [Bohr](#) (Physics 1922) played important roles in convincing biologists that life processes could be analysed in terms of atoms and molecules. By doing so they helped to create the field of molecular biology. Delbrück, a physicist who switched to biology, founded phage genetics, and won the Nobel Prize in Physiology or Medicine in 1969.

Laureates in Chemistry have made contributions which might equally well have been awarded a prize in Physiology or Medicine. [Butenandt](#) received the 1939 prize in Chemistry for his work on sex hormones, [de Hevesy](#) was awarded the 1943 Chemistry prize for introducing isotopes as tracers in the study of chemical processes, a technique of great value in biomedical research, while Sanger was awarded two Chemistry prizes for discoveries of great importance in modern biotechnology. In 1958 he received the [Chemistry prize](#) for elucidating the structure of insulin and then in 1980, he received a [second prize](#) for his method of sequencing nucleic acids. Other Nobel Prizes have been awarded for discoveries in the border zone between medicine and chemistry. [Dorothy Hodgkin](#) determined the structure of important biochemical substances by X-ray techniques and received the 1964 Chemistry prize, while [Mitchell](#) (Chemistry 1978) studied biological energy transfer and formulated chemiosmotic theory.

In the field of genetics some discoveries have been awarded prizes in Physiology or Medicine while others have received the Chemistry prize. The former group includes the 1933 prize to Morgan, the 1962 prize to Crick, Watson and Wilkins, and the 1993 prize to Roberts and Sharp. Molecular genetics has been recognized by prizes in Chemistry e.g. those to [Berg, Gilbert](#), and Sanger (1980), [Altman](#) and [Cech](#) (1989), and [Mullis](#) and [Smith](#) (1993).

In order to coordinate the work of the Nobel Committees for Physiology or Medicine and Chemistry, a joint meeting of the committees is held in the spring. This also ensures that a candidate does not receive two Nobel Prizes for the same discovery.

# The Laureates and their Work

During the period 1901-2000 a total of 172 scientists were awarded the Nobel Prize in Physiology or Medicine. Their contributions range from basic to clinical research. The following is a compilation which gives an indication of the nature of the discoveries for which scientists were awarded Nobel Prizes. The prize motivations indicated are not verbatim the official ones but have been shortened to improve readability and overview (comments in parentheses are not part of the official prize sentence). The different prizes have been organized under different headings, but it should be pointed out that one discovery may fit under more than one heading.

<b>Infectious Agents and Insecticides</b>	
<a href="#">Ross</a> (1902)	role of insects as vectors in the infectious cycle (malaria)
<a href="#">Koch</a> (1905)	identification of the tubercle bacillus and other work on tuberculosis
<a href="#">Laveran</a> (1907)	role of protozoa in causing disease (malaria)
<a href="#">Nicolle</a> (1928)	role of clothes lice in the transmission of typhus
<a href="#">Müller</a> (1948)	DDT as an insecticide
<a href="#">Theiler</a> (1951)	yellow fever virus
<a href="#">Enders, Weller &amp; Robbins</a> (1954)	<i>in vitro</i> culture of polio virus
<a href="#">Blumberg &amp; Gajdusek</a> (1976)	new mechanisms for the origin and dissemination of infectious disease
<a href="#">Prusiner</a> (1997)	prions, a new principle of infection
<b>Immunology</b>	
<a href="#">Behring</a> (1901)	serum therapy and its application against diphtheria
<a href="#">Ehrlich</a> (1908)	immunity
<a href="#">Mechnikov</a> (1908)	phagocytosis
<a href="#">Richtet</a> (1913)	anaphylaxis
<a href="#">Bordet</a> (1919)	antigens and antibodies in immune reactions
<a href="#">Landsteiner</a> (1930)	blood groups and blood typing
<a href="#">Burnet &amp; Medawar</a> (1960)	acquired immunological tolerance
<a href="#">Edelman &amp; Porter</a> (1972)	structure of antibodies
<a href="#">Benacerraf, Dausset &amp; Snell</a> (1980)	regulation of immune reactions
<a href="#">Jerne, Köhler &amp; Milstein</a> (1984)	control of the immune system and monoclonal antibodies
<a href="#">Tonegawa</a> (1987)	genetics of antibody formation
<a href="#">Doherty &amp; Zinkernagel</a> (1996)	cell mediated immunity
<b>Chemotherapy/Drug Development</b>	
<a href="#">Domagk</a> (1939)	prontosil (sulphonamides)
<a href="#">Fleming, Chain &amp; Florey</a> (1945)	penicillin
<a href="#">Waksman</a> (1952)	streptomycin, the first antibiotic against tuberculosis
<a href="#">Bovet</a> (1957)	substances that mimic the effects of adrenaline. Substances that paralyse skeletal muscle
<a href="#">Black, Elion &amp; Hitchings</a> (1988)	important principles for drug treatment
<b>Phototherapy and Fever Treatment</b>	
<a href="#">Finsen</a> (1903)	light therapy of lupus
<a href="#">Wagner-Jauregg</a> (1927)	fever treatment of general paralysis

<b>Cancer</b>	
<a href="#">Fibiger</a> (1926)	spiroptera carcinoma illustrating cancer caused by chronic irritation
<a href="#">Rous</a> (1966)	tumour-inducing virus in chickens
<a href="#">Huggins</a> (1966)	hormonal treatment of prostate cancer
<a href="#">Baltimore, Dulbecco &amp; Temin</a> (1975)	interaction between tumour virus and host cell
<a href="#">Bishop &amp; Varmus</a> (1989)	retroviral oncogenes
<b>Classical Genetics</b>	
<a href="#">Morgan</a> (1933)	role of chromosomes in heredity
<a href="#">Muller</a> (1946)	production of mutations by X-ray irradiation
<a href="#">McClintock</a> (1983)	mobile genetic elements
<b>Cell Biology</b>	
<a href="#">Claude, de Duve &amp; Palade</a> (1974)	structural and functional organisation of the cell
<a href="#">Cohen &amp; Levi-Montalcini</a> (1986)	growth factors
<a href="#">Blobel</a> (1999)	the discovery that proteins have intrinsic signals that govern their transport and localisation in the cell
<b>Developmental Biology</b>	
<a href="#">Spemann</a> (1935)	organiser effect in embryonic development
<a href="#">Lewis, Nüsslein-Volhard &amp; Wieschaus</a> (1995)	genetic control of early embryonic development
<b>Molecular Biology/Genetics</b>	
<a href="#">Kossel</a> (1910)	work on protein including the nucleic substance
<a href="#">Beadle &amp; Tatum</a> (1958)	regulation of definite chemical events (one gene-one protein)
<a href="#">Lederberg</a> (1958)	genetic recombination and the organization of the genetic material in bacteria
<a href="#">Ochoa &amp; Kornberg</a> (1959)	mechanisms in the biological synthesis of ribonucleic and deoxyribonucleic acid
<a href="#">Crick, Watson &amp; Wilkins</a> (1962)	molecular structure of nucleic acids and its significance for information transfer in living material
<a href="#">Jacob, Lwoff &amp; Monod</a> (1965)	genetic control of enzyme and virus synthesis
<a href="#">Holley, Khorana &amp; Nirenberg</a> (1968)	genetic code and its function in protein synthesis
<a href="#">Delbrück, Hershey &amp; Luria</a> (1969)	the replication mechanism and the genetic structure of viruses
<a href="#">Arber, Nathans &amp; Smith</a> (1978)	restriction enzymes and their application to problems of molecular genetics
<a href="#">Roberts &amp; Sharp</a> (1993)	split genes
<b>Intermediary Metabolism</b>	
<a href="#">Hill</a> (1922)	heat production in muscle
<a href="#">Meyerhof</a> (1922)	oxygen consumption and the metabolism of lactic acid in muscle
<a href="#">Warburg</a> (1931)	nature and mode of action of the respiratory enzyme
<a href="#">von Szent-Györgyi</a> (1937)	vitamin C and the catalysis of fumaric acid
<a href="#">Cori &amp; Cori</a> (1947)	catalytic conversion of glycogen
<a href="#">Krebs</a> (1953)	citric acid cycle
<a href="#">Lipmann</a> (1953)	coenzyme A and its importance for intermediary metabolism

<a href="#">Theorell</a> (1955)	nature and mode of action of oxidation enzymes
<a href="#">Bloch &amp; Lynen</a> (1964)	cholesterol and fatty acid metabolism
<a href="#">Bergström, Samuelsson &amp; Vane</a> (1982)	prostaglandins and related biologically active substances
<a href="#">Brown &amp; Goldstein</a> (1985)	regulation of cholesterol metabolism
<a href="#">Fischer &amp; Krebs</a> (1992)	reversible protein phosphorylation as a biological regulatory mechanism
<a href="#">Gilman &amp; Rodbell</a> (1994)	G-proteins and their role in signal transduction in cells
<b>Hormones</b>	
<a href="#">Kocher</a> (1909)	physiology, pathology and surgery of the thyroid gland
<a href="#">Banting &amp; Macleod</a> (1923)	insulin
<a href="#">Houssay</a> (1947)	hormones of the anterior pituitary lobe in the metabolism of sugar
<a href="#">Kendall, Reichstein &amp; Hench</a> (1950)	hormones of the adrenal cortex, their structure and biological effects
<a href="#">Sutherland, Jr.</a> (1971)	mechanism of action of hormones
<a href="#">Furchgott, Ignarro &amp; Murad</a> (1998)	nitric oxide as a signalling molecule in the cardiovascular system
<b>Vitamins</b>	
<a href="#">Eijkman</a> (1929)	antineuritic vitamin
<a href="#">Hopkins</a> (1929)	growth-stimulating vitamin
<a href="#">Whipple, Minot &amp; Murphy</a> (1934)	liver therapy in cases of anaemia
<a href="#">Dam</a> (1943)	vitamin K
<a href="#">Doisy</a> (1943)	chemical nature of vitamin K
<b>Digestion, Circulation and Respiration</b>	
<a href="#">Pavlov</a> (1904)	physiology of digestion (conditioned reflexes)
<a href="#">Krogh</a> (1920)	capillary motor regulating mechanism
<a href="#">Einthoven</a> (1924)	electrocardiography
<a href="#">Heymans</a> (1938)	role of sinus and aortic mechanisms in the regulation of respiration
<a href="#">Cournand, Forssmann &amp; Richards</a> (1956)	heart catheterization and pathological changes in the circulatory system
<b>Neurobiology</b>	
<a href="#">Golgi &amp; Ramón y Cajal</a> (1906)	structure of the nervous system
<a href="#">Sherrington &amp; Adrian</a> (1932)	functions of neurones
<a href="#">Dale &amp; Loewi</a> (1936)	chemical transmission of the nerve impulses
<a href="#">Erlanger &amp; Gasser</a> (1944)	highly differentiated functions of single nerve fibres
<a href="#">Hess</a> (1949)	functional organization of the interbrain as a coordinator of the activities of the internal organs
<a href="#">Bovet</a> (1957)	synthetic compounds acting on the vascular system and skeletal muscles (curare)
<a href="#">Eccles, Hodgkin &amp; Huxley</a> (1963)	mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane
<a href="#">Katz, von Euler &amp; Axelrod</a> (1970)	neurotransmitters and the mechanism for their storage, release and inactivation (the concept of synaptic transmission)
<a href="#">Guillemin &amp; Schally</a> (1977)	peptide hormone production in the brain
<a href="#">Yalow</a> (1977)	radioimmunoassays of peptide hormones

<a href="#">Sperry</a> (1981)	functional specialization of the cerebral hemispheres
<a href="#">Neher &amp; Sakmann</a> (1991)	function of single ion channels
<a href="#">Carlsson, Greengard &amp; Kandel</a> (2000)	signal transduction in the nervous system
<b>Surgery</b>	
<a href="#">Moniz</a> (1949)	therapeutic value of leucotomy in certain psychoses
<a href="#">Murray &amp; Thomas</a> (1990)	organ and cell transplantation in the treatment of human disease
<b>Sensory Physiology</b>	
<a href="#">Gullstrand</a> (1911)	dioptrics of the eye
<a href="#">Bárány</a> (1914)	physiology and pathology of the vestibular apparatus
<a href="#">von Békésy</a> (1961)	physical mechanism of stimulation within the cochlea
<a href="#">Granit, Hartline &amp; Wald</a> (1967)	primary physiological and chemical visual processes in the eye
<a href="#">Hubel &amp; Wiesel</a> (1981)	information processing in the visual system
<b>Behavioral Sciences</b>	
<a href="#">von Frisch, Lorenz &amp; Tinbergen</a> (1973)	organization and elicitation of individual and social behavior patterns
<b>Diagnostic Methods</b>	
<a href="#">Cormack &amp; Hounsfield</a> (1979)	computer tomography

## Geographic Distribution

"It is my express wish that in awarding the prizes no consideration whatever shall be given to the nationality of the candidates, but that the most worthy shall receive the prize, whether he be Scandinavian or not" (quote from the English translation of Alfred Nobel's will).

As the contents of Alfred Nobel's will became known, the above sentence was considered unpatriotic and met with considerable criticism. With a perspective of 100 years of prizes, it is of some interest, therefore, to examine the geographical distribution of the recipients (as indicated by the domicile of the Laureates at the time of their awards).

	1901-1925	1926-1950	1951-1975	1976-2000
USA	1	13	32	40
Germany	5	3	3	4
UK	2	7	10	4
France	2	1	3	1
Other	13	12	9	7
Total	23	36	57	56

Practically all Laureates come from or have carried out their work in Europe or North America. After World War II the United States has come to dominate the list. In the 1930s, the rise of the Nazis in Germany and Austria caused many Jewish scientists to flee from Europe to the United States. Among the 32 US scientists who received the Nobel Prize in Physiology or Medicine between 1951 and 1975, nine were born in countries other than the US. Of a total of 172 prize-winners, four are Danish and seven are Swedish. Other small countries have done equally well or better. Switzerland, with a population half that of Sweden and Denmark together, for instance has eight Nobel Laureates. Sweden and Switzerland were not involved in the two World Wars and could continue research relatively



undisturbed while research work in other countries became impossible or difficult. The conclusion, however, is that there is no evidence that the prize-awarder has favored citizens of its own country.

## Criticisms

There are three main types of criticism of the awarding of Nobel Prizes: omissions, mistakes and the failure to recognize the contributions of women. Since there are many prize-worthy candidates but only three who can receive the prize each year, omissions are bound to happen. The failure to award a Nobel Prize to Oswald T. Avery for the discovery of DNA as the genetic material can be used as one example. Avery undoubtedly discovered that DNA is the carrier of the genetic material when he showed that DNA from strains of bacteria with high pathogenicity could transform strains with low to high pathogenicity. His first publication on this topic appeared as early as 1944. Avery was nominated several times between 1932 and 1942 for work on polysaccharide antigens. From 1945 he was nominated every year for his discovery concerning DNA. At the time many scientists thought of DNA, with its four different building blocks, as having too simple a structure to be the genetic material. Instead they favored the idea that proteins, with their 20 different amino acids, were more likely to be the genetic material and did not trust the enzyme digestions used by Avery to remove protein from his preparation of DNA. By the time the scientific community, including the Nobel Committee, had accepted Avery's data, he had passed away.

As far as mistakes are concerned, three examples are often brought up: Banting and Macleod (1923), Fibiger (1926) and Moniz (1949). The prize to Banting and Macleod for the discovery of insulin (1923) was questioned right from the time it was announced. Macleod was the department head and founder of the laboratory where Banting and a young colleague, Charles Best, worked. The discovery was made by Banting and Best at a time when Macleod was away. However, Banting, but not Best, was awarded the prize. This decision has been analysed in a monograph by Bliss (1982). The author arrived at the conclusion that the decision was the best one possible on the basis of what was known at the time. Others have emphasized the difficulties involved in trying to award prizes for discoveries made the preceding year. Incidentally, Best was first nominated in 1950.

The decision to award the 1926 prize to Fibiger for the discovery of the Spiroptera carcinoma has been heavily criticized. Very little was known about cancer-causing mechanisms at the time, and it was not until 40 years later that the next prize was awarded in the area of cancer research. At that time knowledge had accumulated about the genetic code, mutations, tumour viruses and other biological mechanisms involved in cancer.

The prize to Moniz for lobotomy (leucotomy) in 1949 must be seen in relation to the methods available for treating psychotic patients during the early part of the twentieth century. Before surgery was introduced, patients were subjected to very cruel treatments involving straitjackets and cold baths; then came surgical interventions and electric shock treatments. Both techniques became obsolete when neuropharmacology introduced effective drugs to treat psychosis. Today, lobotomy seems unethical but the question is whether it was unethical compared to the alternative methods available at the time of the award.

Only 6 of the 172 Nobel Laureates in Physiology or Medicine are women (Gerty T. Cori (1947); Rosalyn Yalow (1977); Barbara McClintock (1983); Rita Levi-Montalcini (1986); Gertrude B. Elion (1988); and Christiane Nüsslein-Volhard (1995)). This is not surprising, seen in the light of overwhelming male dominance within the biomedical field during the twentieth century.

## Concluding Remarks

The Nobel Prizes awarded for Physiology or Medicine during the past century undoubtedly highlight a number of important discoveries. They do not, however, cover the whole story. There are a number of omissions and also a few prizes which, with hindsight, appear to be mistakes. The prestige of the Nobel Prize, however, comes from the fact that the international scientific community agrees with most of the decisions that have been made.

Alfred Nobel's intention was that the Prizes would make it possible for promising scientists to continue their research without having to worry about their financial situation. It is doubtful whether the prize fulfils this function today. First, the average age at which prize winners receive the prize is relatively high and, second, most of the recipients are already well established scientists when they receive the prize. Furthermore, medical research has gone the same

way as physics and often demands considerable budgets and large research groups. The Nobel Prize, therefore, is not likely to make as big a difference today as it did a hundred years ago.

For the Nobel Assembly, the task of selecting the Nobel Laureates is a very stimulating one and the lectures of the Nobel Laureates are memorable occasions. The announcement of the Nobel Prize-winners in October as well as the award ceremony and festivities in December each year attract international media attention. This presents the Prize-Awarding Institutions with excellent opportunities to explain the achievements of the Laureates, to actively promote greater public understanding of science, and to interest young scholars in biomedical research.

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