Nobel Prize Winners

in Medicine and Physiology 1901-1965

BY THEODORE L. SOURKES

Revision of earlier work by Lloyd G. Stevenson

From Pavlov to Monod,
here are the men who have led the fight
against disease in the twentieth century
and the stories of their victories – told
in their own words

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Nobel Prize Winners in MEDICINE and PHYSIOLOGY

1901-1965

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FROM THE PREFACE TO THE FIRST EDITION

A HALF-CENTURY OF ACHIEVEMENT IN MEDICAL SCIENCE IS reflected in the awards of the Nobel Prize for Physiology and Medicine. One-fifth of the interest on Alfred Nobel's fortune is to be given annually "to the person who shall have made the most important discovery" in this domain. Winners are selected by the Caroline Medico-Chirurgical Institute in Stockholm. Each Nobel laureate is judged to have made a personal contribution of first-rate importance. Behind and around him there is always a constellation of scientists who have taken part in the same work. Their preliminary researches have made it possible, or their subsequent efforts have made it more fruitful. The winner of the Prize is therefore not only a discoverer in his own right, but a representative—by virtue of his outstanding contribution—of those who have worked toward the same or a similar goal. The configuration of the heavens may be roughly indicated by mapping the principal stars, but the sky would be dim indeed without the rest.

In the following pages each Prize Winner is represented, first, by a short biographical sketch; second, by a passage in which he describes the Prize discovery in his own words; and third, by a brief editorial explanation of the meaning and importance of the work. For the most part the quotation is an excerpt from the Nobel Lecture delivered in Stockholm at the time of the presentation of the Prize.

These Lectures are given to general audiences and should therefore be suitable for general readers, as many of them are. Unfortunately this is not always the case. When the Lecture has been very technical in form, some less complicated version of the same story has been sought for elsewhere in the author's works. Sought for, but not always found. Happily there are only a few cases—Professor Gullstrand's is one—in which the very nature of the discovery requires that the reader should have extensive background knowl-

edge before he can hope for a competent understanding. These few instances must be left to those who can grasp them. The majority of the discoveries are easy to comprehend in outline. No more than this is aimed at here.

Occasionally, too, the Prize Winner has grown bored with his own discovery long before reaching Stockholm—he may have described it already fifty times—and has chosen to talk about something else. Pavlov and Florey are examples: both of them preferred to speak of more recent work. Again, a modest laureate may devote most of his time to expounding the related discoveries of other scientists. In all such cases it is obvious that the Nobel Lecture would have been an unsuitable choice for the present purpose. Actually most of these Lectures are precisely what is needed. Sometimes, too, the choice has been determined by the way in which the work of one Prize Winner can be linked with that of another: as they are here represented, Sherrington's physiological discovery leads on from an anatomical finding by Golgi; there are also other examples. . . .

Lloyd G. Stevenson, M.D.

October, 1952

PREFACE TO THE SECOND EDITION

SINCE 1901 THE NOBEL PRIZE has been awarded on 56 occasions to 90 scientists working in the broad area encompassed by the term "physiology and medicine." This new edition incorporates much of the material in the original volume as well as new chapters covering the period from 1951 to 1965. The text of the first edition has been revised to bring biographies up to date; the descriptions of the Prize-winning work have in a few cases been changed through selection of different material from the laureate's writings; and, as before, the assessments of the significance of the work take into account the new perspectives that current progress in science and medicine have brought. An appendix, in which the Nobel laureates are listed by the subjects of their research, has been added; together with the index, it may be of assistance to the general reader as well as to teachers who use the book for didactic purposes. Although I have revised some material, I have also preserved extensive sections from the original volume and, in many cases, have retained complete chapters. I worked with the conviction that, in the interests of the reader, Dr. Stevenson's fine exposition had best be tampered with as little as possible.

It is my great pleasure to thank Dr. Stevenson, now Professor of the History of Science and Medicine at Yale University, who generously handed over to me the fruit of his earlier labour. His suggestion that I undertake the preparation of a new edition of *Nobel Prize Winners in Medicine and Physiology* led me into a fascinating project which, through the pressure of teaching and of laboratory research, necessarily became a part-time avocation during the last two and one-half years.

Theodore L. Sourkes, Ph.D.

Montreal, May 1966

CONTENTS

Nobel Prize Winners in MEDICINE and PHYSIOLOGY

1901-1965

1901

EMIL VON BEHRING

(1854–1917)

"For his 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 death."

BIOGRAPHICAL SKETCH

EMIL ADOLF (VON) BEHRING WAS BORN IN DEUTSCH-EYLAU, Germany, in 1854 and studied in Berlin. He entered the Army Medical Corps and was lecturer in the Army Medical College, Berlin, in 1888. The following year he became assistant in Robert Koch's Institute of Hygiene. In 1891, when Koch became chief of the new Institute for Infectious Diseases, von Behring accompanied him. Meantime (1890) he had published his important papers on serum therapy. The consequences in medical practice were sensational and von Behring was soon famous. In 1894 he accepted the chair of hygiene in Halle, but a year later transferred to a similar position in Marburg. He received many distinctions and several monetary prizes. In Marburg he established works for the manufacture of antitoxins and a remedy for the tuberculosis of cattle. He died in 1917.

DESCRIPTION OF THE PRIZE-WINNING WORK*

"As already proved by Löffler, then Roux and Yersin, there are animals naturally immune to diphtheria; I have confirmed by my own investigations that this is true of mice and rats, and that these animals tolerate, without appreciable damage to their health, inoculations with cultures which have a sure and deadly effect on much larger animals, such as the guinea pig, rabbit, and wether. . . .

"Furthermore, one can make animals immune which were originally very susceptible to diphtheria. . . .

"1. One of the immunization methods, which I can show to be very reliable on the ground of my own research, has been described exactly by Prof. C. Fränkel [1861-1915; an assistant of Koch's who became professor of hygiene at Halle and did much original work in bacteriology and immunology]. . . . It depends on the use of sterilized cultures, and with the help of this method one can make guinea pigs nonsusceptible in 10-14 days to inoculations that are certain death to normal guinea pigs. . . .

"2. [Von Behring next describes a method of his own, using in place of the sterilized cultures of Fränkel cultures weakened by the addition of iodine trichloride in small amounts. A feeble culture was succeeded by a more active one. Finally a fully virulent culture was tolerated.]

"In both the methods just mentioned, immunity is brought about by the metabolic products bred by diphtheria bacilli in cultures.

"3. But it is also possible to produce immunity through the same metabolic products engendered from diphtheria bacilli in the living animal organism. If one investigates animals dying of diphtheria, one finds an extremely abundant transudate in the pleural cavity. . . .

"In more than 50 separate cases investigated, this transudate never contained diphtheria bacilli; but it possesses properties poi-

* Translated from Emil von Behring, " Untersuchungen über das Zustandekommen der Diphtherie-Immunität bei Thieren," *Deutsche medizinische Wochenschrift,* Vol. 16 (December 11, 1890), pp. 1145-1148.

sonous for guinea pigs. The degree of toxicity is not always the same. . . .

"Those [few] guinea pigs which survive an injection of [10 to 15 c.c. of] transudate . . . are regularly sick for a long time; [here follows a description of their symptoms].

"Now when I awaited the complete recovery of those animals which displayed the symptoms just described to a pronounced degree, then . . . I could establish that they endured without harm inoculations that would kill healthy animals in 3 to 4 days. . . .

"4. An[other] immunization method, one not hitherto employed, can also be traced to the operation of the metabolic products of the diphtheria bacilli.

"*It consists in first infecting the animals and then doing away with the deleterious effect through therapeutic management.* [This was exceedingly difficult. Of the many drugs tried, most were useless. Mention is made, however, of certain compounds which appeared to have cured infected guinea pigs, notably iodine trichloride. Behring reported that treatment with this drug prior to infection did no good.]

"5. [It was reported that prior treatment with hydrogen peroxide seemed to confer some immunity. This alleged success had nothing to do with immune products resulting from the metabolism of bacilli.]

"All five of the methods of immunization against diphtheria thus far described are in my opinion not practicable—at least in the form I have given them—for humans.

"But from the scientific viewpoint, and . . . for the understanding of the occurrence of diphtheria immunity, they are capable of affording us worth-while service.

"That is to say, immunity having somehow occurred—and I do not exclude natural immunity—all diphtheria-immune animals have certain characteristics in common which distinguish them from non-immune animals.

"First of all, the living immune animals, as a whole, not only possess protection against infection with the living diphtheria bacilli but are also protected against the deleterious effect of the poisonous substances formed by the diphtheria bacilli in cultures and in the animal body.

"I have undertaken the proof of this in various ways. First I tried it with the solution of an albuminous substance which I separated from old cultures with acidified alcohol; however, I was unable to remove the acid from the resulting preparation without impairing the poisonous effect; I also think it no easily soluble problem . . . to separate other precipitating agents from the precipitate produced. But for the purpose in question I scarcely needed to go after the diphtheria poison, or, perhaps more correctly, the diphtheria poisons; filtrates of old cultures afforded me all I wanted.

"Using my cultures grown in alkaline bouillon, with 10 c.c. normal alkali per liter, I found that after 10 weeks they contained so much poisonous substance that, having been rendered germ-free by filtration, they already called forth characteristic symptoms of diphtheria poisoning with a dose of 1 c.c. in medium-sized guinea pigs; these symptoms did not entirely disappear for 3 to 4 weeks. Furthermore, 3 to 4 c.c. were enough to kill larger guinea pigs in 3 to 8 days . . .

"Now all guinea pigs with established diphtheria immunity . . . endured 3 to 5 c.c. without any discernible disease symptoms or local reaction whatever; on the other hand, guinea pigs that had still not quite recovered from an infection proved to be only very little more poison-resistant than they normally would be. . . . *It is very noteworthy that the immunity can be lost again through the subcutaneous injection of considerable and repeated quantities; this happens with all the more certainty, the less the immunity has been 'established.' At all events, guinea pigs under the influence of the poisonous, germ-free diphtheria culture fare as before against diphtheria infection under unfavorable conditions.*

"The first thought to arise could be this, that the resistance to poison here described depends on 'habituation,' as in the case of alcoholics, morphine addicts, arsenic eaters. . . .

"But such an interpretation is at once controverted by the fact that animals which have never had anything to do with diphtheria poison also possess diphtheria poison resistance.

"If we start out again with the 10-week culture rendered germ-free, then, calculating on the basis of body weight, it is deadly for guinea pigs in the ratio of about 1:100; but mice endure the poison