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Nobel Laureate Surgeons

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Abstract

This is a brief account of the notable contributions and some foibles of surgeons who have won the Nobel Prize for physiology or medicine since it was first awarded in 1901.

Keywords: Nobel Prize in physiology or medicine; Surgical Nobel laureates; Pathology and surgery

Introduction

The Nobel Prize for physiology or medicine has been awarded to 219 scientists in the last 119 years. Eleven members of this illustrious group are surgeons although their awards have not always been for surgical innovations. Names of these surgeons with the year of the award and why they received it are listed below:

Emil Theodor Kocher - 1909: Thyroid physiology, pathology and surgery.

Alvar Gullstrand - 1911: Path of refracted light through the ocular lens.

Alexis Carrel - 1912: Methods for suturing blood vessels and transplantation.

Robert Barany - 1914: Function of the vestibular apparatus.

Frederick Grant Banting - 1923: Extraction of insulin and treatment of diabetes.

Alexander Fleming - 1945: Discovery of penicillin.

Walter Rudolf Hess - 1949: Brain mapping for control of internal bodily functions.

Werner Theodor Otto Forssmann - 1956: Cardiac catheterization.

Charles Brenton Huggins - 1966: Hormonal control of prostate cancer.

Joseph Edward Murray - 1990: Organ transplantation.

Shinya Yamanaka-2012: Reprogramming of mature cells for pluripotency.

Emil Theodor Kocher (August 25, 1841 to July 27, 1917)

Kocher received the award in 1909 “for his work on the physiology, pathology and surgery of the thyroid gland” [1]. He was appointed ordinary Professor of Surgery and Director of the University of Berne Surgical Clinic in 1872 at 31 years of age and he remained there for his entire professional life despite attempts by numerous universities to lure him away.

Kocher was a meticulous surgeon who implemented aseptic techniques, monitored anesthesia and controlled bleeding precisely. Consequently, he reduced the mortality of thyroid surgery from an estimated 75% in 1872 to less than 0.5% by 1912 [2]. An unintended consequence of his meticulous excision of all thyroid tissue was the development of what he initially termed cachexia strumipriva and later renamed cachexia thyreopriva and we now know as cretinism. He reported this to the German society of surgery on April 4, 1883. The Riverdins had previously presented this finding on September 13, 1882 but he refused to accept that he had been preempted [1]. His Nobel lecture is a detailed presentation of every form of impaired thyroid function and in it he also covers parathyroid problems.

Apart from the thyroid gland Kocher investigated hemostasis, surgical infections, antiseptic wound management, osteomyelitis, epilepsy and hernias. He created instruments, described incisions and an intraabdominal maneuver for exposure of the inferior vena cava, duodenum and pancreas. He described a technique to reduce shoulder dislocations and another for draining intracranial cerebrospinal fluid. He studied the damage done by bullets of various calibers and velocities. His

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textbook of operative surgery, Chirurgische Operationslehre, was translated into many languages and six editions of it were published.

He used the money he received for the Nobel Prize to establish the Kocher Institute in Berne.

Alvar Gullstrand (June 5, 1862 to July 28, 1930)

Alvar Gullstrand, a Swedish ophthalmologist, was awarded the Nobel Prize in 1911 "for his work on the dioptrics of the eye". It is extremely difficult to calculate the path that rays of light take through the eye to create an image upon the retina since the layers of the lens refract light to varying degrees and the lens itself also changes its shape. Gullstrand accomplished this feat using advanced mathematics [3]. In 1911 he declined the Physics award in favor of that for physiology or medicine [4].

Gullstrand graduated in 1888, presented his doctoral thesis on the theory of astigmatism in 1890, and was appointed Lecturer in Ophthalmology in 1891 and as the first Professor of Ophthalmology in Uppsala University in 1894. From 1914 onwards he held a personal professorship in physical and physiological optics which allowed him to devote himself to investigating optical system laws of higher order and he researched the use of corrective lenses after cataract surgery.

In 1911 he developed the slit lamp and the reflex free ophthalmoscope that are still in use albeit with some modifications.

He did not believe Einstein's theory of relativity hence, as a member of the Nobel Committee on Physics, he wrote harsh opinions against it in 1921 and 1922 [4]. When Einstein received the award, it was "for his services to theoretical physics and especially for his discovery of the law of the photoelectric effect" even though Arthur Eddington had proven the theory of relativity by then [5].

Alexis Carrel (June 28, 1873 to November 5, 1944)

The 1912 Nobel Prize was awarded to Alexis Carrel "in recognition of his work on vascular suture and the transplantation of blood vessels and organs" [6]. Carrel's interest in vascular surgery appears to have been the result of learning that six surgeons stood around while the French President, Sadi Carnot, bled to death from a stab wound of the portal vein [7]. For most of his career he worked in the United States, first at the University of Chicago and subsequently the Rockefeller Institute for Medical Research, New York. In his Nobel lecture entitled "Suture of Blood Vessels and Transplantation of Organs" [8], he described the techniques he devised. By placing three equidistant initial sutures, still known as the Carrel sutures, he enlarged the opening and enabled precise anastomoses of vessels thus preventing strictures, by using paraffin (Vaseline) in the sutures he prevented postoperative bleeding and by everting the sutured ends of vessels he left no material within the lumen of vessels to form a nidus for clots.

He also developed the Carrel-Dakin method (now known as Dakin's solution) for treating wounds during World War I and with Charles Lindbergh he devised a machine to perfuse organs removed from the body. He performed cardiac valvotomies with Theodore Tuffier and grew sarcoma cells in tissue culture with Burrows. However, there is reason to be skeptical about his immortal chicken heart in tissue culture since it has never been duplicated [9].

In his best-selling book "Man The Unknown" published first in 1935 he expounds on his belief in eugenics, euthanasia for dangerous incurable criminals, clairvoyance, telepathy and the religious miracle he saw at Lourdes [10].

In 1938 the Vichy regime gave him the opportunity to implement his theories by making him the regent of the French foundation for the study of human problems. When France was liberated in 1944, he was placed under house arrest and investigated for being a Nazi collaborator. He died before he could be tried [10].

Robert Barany (April 22, 1876 to April 8, 1936)

Robert Barany, an Otologist, was awarded the Nobel Prize in 1914 "for his work on the physiology and pathology of the vestibular apparatus". While syringing the external auditory canal of a patient for vertigo he noticed that when he used cold water the nystagmus moved in one direction and the direction was reversed if he warmed the water. He surmised it was because the endolymph sank when cooled and rose when warmed [11]. Based upon this observation he designed the experiment he named caloric reaction (now called the caloric reflex test). The test helps diagnose asymmetric function in the peripheral vestibular system thus facilitating surgical treatment for vestibular diseases. In patients with a prior burr hole the dura mater is immediately below the skin at that site. He also studied the effect of cooling those areas of the cerebellum [11].

In 1914 he was a prisoner of war of the Imperial Russian Army so he could only accept the award after being released in 1916. When he returned to Vienna his Austrian colleagues chastised him for not giving enough credit to scientists whose work had preceded his. In his disappointment, he immigrated to Sweden [12].

Frederick Grant Banting (November 14, 1891 to February 21, 1941)

The 1923 Prize was awarded to Frederick Banting and John James Rickard McLeod "for the discovery of insulin". Banting shared his money with Charles Best and McLeod did so with James Collip. Banting's opinion that McLeod had a minimal role in the discovery and should not have received the Nobel Prize was not substantiated [13].

Immediately upon completing medical school Banting reported for military duty and served until he was injured. In 1918 he became an orthopedic resident at the Hospital for Sick Children, Toronto, Canada but he could not secure a staff position at the hospital after residency so he set up a private practice in London, Ontario. To supplement his income, he lectured at the University of Western Ontario and the University of Toronto. He became interested in diabetes and its control with insulin at this time. He obtained insulin from the islets of Langerhans of dogs by ligating the pancreatic duct so that the trypsin producing cells atrophied while the islets remained intact. Later he obtained larger quantities from fetal calves and he began treating patients with insulin in 1922 [14].

He died from injuries received in a plane crash at 49 years of age. To date he is the youngest recipient of the Nobel Prize for Physiology or Medicine [15].

Alexander Fleming (August 6, 1881 to March 11, 1955)

The 1945 Prize was shared by Alexander Fleming with Ernst Boris Chain and Howard Walter Florey "for the discovery of penicillin and its curative effect in various infectious diseases" [16].

Fleming graduated in 1908 and embarked on surgical training. In 1909 he became a Fellow of the Royal College of Surgeons of England [17]. He then became an assistant bacteriologist to Sir Almroth Wright, however, he served during World War I in battle field hospitals on the Western Front in France and he was mentioned in dispatches for major contributions to wound care. After the war he returned to St. Mary's Hospital and remained a bacteriologist for the rest of his life.

He stated that his discoveries of lysozymes and penicillin were both accidental and he credited his co-awardees for the clinical success of penicillin. The paper he published in 1929 [18,19], was forgotten until the British and United States governments funded Boris Chain and Howard Walter Florey to purify and synthesize penicillin in large enough quantities for use in World War II [18]. His relationship with his co-winners soured eventually as the press was enamored with Fleming's accidental discovery and not the later purification and synthesis. Fleming never patented his discovery so it would be available to treat the numerous infections of the time.

Fleming was admitted to the Chelsea Arts Club because of his "germ paintings" in which he brushed pigmented bacteria onto a handkerchief. The colors became visible only when the bacteria proliferated after incubation [20].

Walter Rudolf Hess (March 17, 1881 to August 12, 1973)

In 1949 Walter Rudolf Hess was recognized "for his discovery of the functional organization of the interbrain as a coordinator of the activities of internal organs". Hess started his career as an assistant in surgery, transitioned to ophthalmology and practiced it for four years before becoming a physiologist [21]. He electrically stimulated areas of the brain and recorded the ensuing physiologic responses [22,23]. Once he demonstrated that the diencephalon was the coordinator of activities of the internal organs certain motor disturbances became correctable.

Antonio Caetano de Abreu Freire Egas Moniz also received the award in 1949 "for his discovery of the therapeutic value of leucotomy in certain psychoses", a procedure that was later condemned. Hess and Egas Moniz never worked together and Egas Moniz's work was not based upon Hess' findings but upon the work either of Fulton and Jacobsen or that of Brickner [24].

Werner Theodor Otto Forssmann (August 29, 1904 to June 1, 1979)

Werner Forssmann was awarded the 1956 Nobel Prize along with Andre Frederic Cournand and Dickinson W. Richards "for their discoveries concerning heart catheterization and pathological changes in the circulatory system".

After passing his medical school state examination Forssmann went to the Auguste Viktoria Home in Eberswalde, near Berlin for clinical instruction in surgery. At this time he became aware, that an English parson, the Reverend Stephen Hales, had led a gun barrel from the neck veins into the beating heart of a sheep and also that in a work by Marey there was an illustration of a tube being passed through the jugular vein of a horse into its heart [25]. Believing this would be an extremely valuable technique to study the heart and to instill medicines he approached Richard Schneider a surgeon, family friend and his advisor. Dr. Schneider turned it down as being too risky. Undeterred, Forssmann cajoled a nurse, Gerda Ditzen, into helping him. Through his own antecubital vein, he inserted a ureteral catheter and walked down to the radiology suite too obtain a chest radiograph. When the first radiograph demonstrated the catheter short of the heart, he pushed it in further and confirmed its position in the right atrium with a second film. His report in 1929 caused consternation in German medical circles resulting in his being fired, then re-hired and permitted to instill medicines in a terminal patient only to be fired a second time for "not meeting the scientific expectations of his chief" [26]. Greta Ditzen's fate is a mystery.

A member of the Nazi party he served as a military surgeon during World War II and was taken prisoner of war. After being released he had difficulty finding a position and even worked as a lumberjack. Eventually he practiced as a urologist along with his wife, who was also a urologist. His contribution was only recognized after Cournand and Richards used cardiac catheterization for numerous cardiac conditions [26].

Charles Brenton Huggins (September 22, 1901 to January 12, 1997)

In 1966 Charles Huggins was awarded the prize "for his discoveries concerning hormonal treatment of prostatic cancer" [27]. He proved that contrary to prevailing belief of the 1930s, cancer cells were not autonomous and self-perpetuating. By castrating or administering estrogens to metastatic prostate cancer patients he demonstrated that prostate cancer cells required chemical signals to help them survive and grow [28,29].

In the 1950s he demonstrated that breast cancer in women was also hormone dependent and he had his colleague develop a method to determine the estrogen receptor content of the cancer to pinpoint who would respond to hormonal manipulation [30].

Huggins is quoted as saying "Don't write books. Don't teach hundreds of students. Discovery is our business. Make damn good discoveries" [30].

Joseph Edward Murray (April 1, 1919 to November 26, 2012)

Joseph Murray and E. Donnall Thomas were both awarded the Prize in 1990 "for their discoveries concerning organ and cell transplantation in the treatment of human disease" [31], however, Murray transplanted kidneys while Thomas worked on bone marrow transplantation.

Murray's interest in transplantation immunology was piqued when the US army posted him in a plastic surgery unit where he noticed that skin grafts from unrelated donors were not always rejected immediately. After his army service he trained in general and plastic surgery and then pursued his interest in transplantation.

Until the 1950s human kidney transplants had uniformly poor results. Murphy had the first long-term success with human kidney transplantation when he transplanted a kidney from one twin into his identical twin brother on December 23, 1954 [32,33], at the Peter Bent Brigham Hospital, Boston (now the Brigham Women's and Children's Hospital). As immunosuppressive techniques improved over time, his team progressed to allograft transplants and subsequently transplantation of cadaver organs.

Shinya Yamanaka (Born on September 4, 1962)

Shinya Yamanaka and John B. Gurdon were awarded the Nobel Prize in 2012 "for the discovery that mature cells can be reprogrammed to become pluripotent". Yamanaka identified the genes that are decisive in this process and he reprogrammed skin cells into pluripotent immature stem cells by activating them.

Yamanaka became an orthopedic resident at the Osaka National Hospital after graduation, however, he gave up surgery for basic science research because he felt he lacked surgical skills and also because he believed eradicating diseases was a better goal than treating them after they develop [34].

He moved to the Gladstone Institute of Cardiovascular Diseases in San Francisco where he first worked on the forced expression of APOBEC1 (Apo B mRNA Editing Catalytic Subunit 1) in the liver of mice. One finding led to another until in 2005, with a combination of 4 genes (Oct3/4, Klf4, Sox2, and c-Myc), he generated induced Pluripotent Stem cells (iPS cells) in mice and in 2007 he developed iPS cells from human fibroblasts. This discovery raises the possibility that pathologies can be studied in disease model cells created from patient specific iPS cells [35].

A few other Nobel Laureates listed below had short, unclear associations with surgery since the term surgeon was used rather loosely in the past.

(i) Ronald Ross was awarded the Prize in 1902 for his work on transmission of malaria. His biography at the London School of Hygiene and Tropical Medicine [36], states that he became a Fellow of the Royal College of Surgeons, England in 1879 and then worked as a surgeon on a transatlantic steam ship for about two years while he studied for his licentiate of the Society of Apothecaries to enable him to join the Indian Medical Service. He passed in his second attempt and joined the service in 1881. On the other hand, his Nobel Biography makes no mention of his service on a ship and according to it he was elected a Fellow of the Royal College of Surgeons in 1901 [37].

(ii) Robert Koch was awarded the Nobel Prize in 1905 for his research on tuberculosis. He was a surgeon in the Franco-Prussian war from 1870 to 1872 probably out of patriotism and not an interest in surgery [38].

(iii) Camillo Golgi was the winner in 1906 for his work on the structure of the nervous system. During his internship he was briefly an assistant surgeon at the Novara Hospital, (now the Azienda Ospedaliero Universitaria Maggiore della Carità di Novara) [39]. His role is unclear.

(iv) Fritz Pregl was awarded the Nobel Prize for chemistry in 1923 "for his invention of a method of micro-analysis of organic substances". Ravin (4) claims Pregl "deserted the eye for analytical chemistry". We could not confirm this statement [40].

(v) Charles Scott Sherrington received the award for his work on neurons in 1932. In 1878 he passed the primary examination of the Royal College of Surgeons and the next year he passed the primary examination for Fellowship of the Royal College of Surgeons but that seems to be the end of his involvement with surgery [41].

(vi) George Richards Minot received the award in 1934 for his pioneering work on pernicious anemia. In 1915, as a junior staff member at the Massachusetts General Hospital, Boston, he was appointed as a surgeon in World War I [42]. It is unlikely that he had any choice in the matter.

(vii) In 1981 Torsten Nils Wiesel was given the award for his discoveries on information processing in the visual system. It appears his Fellowship in Ophthalmology at Johns Hopkins University from 1955 to 1958 involved only laboratory work [43].

Conclusion

In this exalted group of eleven, 3 were general surgeons, 2 each were ophthalmologists, orthopedic surgeons and urologists, one was an otologist and another a plastic surgeon. Apart from their obvious intelligence they all had great powers of observation, were logical thinkers and demonstrated a single minded devotion to the task they had undertaken.

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