
A meaningful legacy: urologists as Nobel Prize laureates

(Dedicated to the centennial of the Nobel Prize)

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Objective: To review the careers of two urologists among Nobel Prize-winners in medicine, W. Forssmann and C.H. Huggins, and the significance of their contributions.

Material and methods: Investigation was performed based on analysis of collected findings from the biographies of laureates, their scientific publications and the Nobel archive database.

Results: Review revealed that of the 175 scientists and physicians who received the Nobel Prize, just over one half (94) held an MD degree while the remainder were PhD's or other degrees. Of the 94 MD-degreed physicians nine (9.4%) were surgeons. Two of these laureates were urologists- Drs. Werner Forssmann and

Charles B. Huggins, who were awarded the Nobel Prize in 1956 and 1966, respectively. Although Werner Forssmann worked as a urologist for most of his career, early in his surgical training he invented procedures for cardiac catheterization and performed the first procedures on himself in 1929. Charles Huggins identified the role of androgens in prostate cancer progression in 1940, and thus established the principles of hormonal suppressive therapy for advanced disease.

Conclusions: The distinguished accomplishments of these two great urologists exemplify the highest level of excellence in science for the entire surgical and urological community. Furthermore, today's breakthroughs in molecular medicine represent an extremely appealing challenge for the new generation of scientists and clinicians.

Key Words: Nobel Prize laureates, surgery, urology

Introduction

"Earlier discoveries remain useful to us, for they now appear in a new light. Thus we guard ourselves against the mistake which runs all through the history of medicine: that of concentrating dogmatically upon

first one, then another facet of research, instead of standing back to view the whole as a growing entity." W. Forssmann

"Medical research is not complete until the solution which has been achieved impinges on the lives of the people. When one discovers something which prolongs life and relieves suffering . . . it remains a meaningful legacy to the race which will last forever." C.B. Huggins

Once a year for the last century, the hushed reverence of the Hall of Fame of City Hall in Stockholm, Sweden, is shattered by the bustle of preparation for the Nobel Award Ceremony, traditionally held in this most appropriate forum.

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Here, distinguished laureates and honored candidates share their experiences of triumph, luck, misfortune and fame. What is also shared amongst this international scientific community is a continuing endorsement of the integrity of the award. Its prestige is secured by a history of award-winners whose achievements are universally ratified by the scientific world. The Nobel Prize remains a symbol for excellence achieved as well as pursued.

This essay reviews two urologists among Nobel Prize-winning surgeons, Werner Forssmann and Charles B. Huggins, and the significance of their contributions. Indeed, those possessing unique scientific visions deserve to be recognized and honored.

Alfred Nobel's legacy

Alfred Nobel was born in 1833 in Stockholm, Sweden, and was one of the greatest innovators of the 19th century Figure 1. His talent was diverse as his

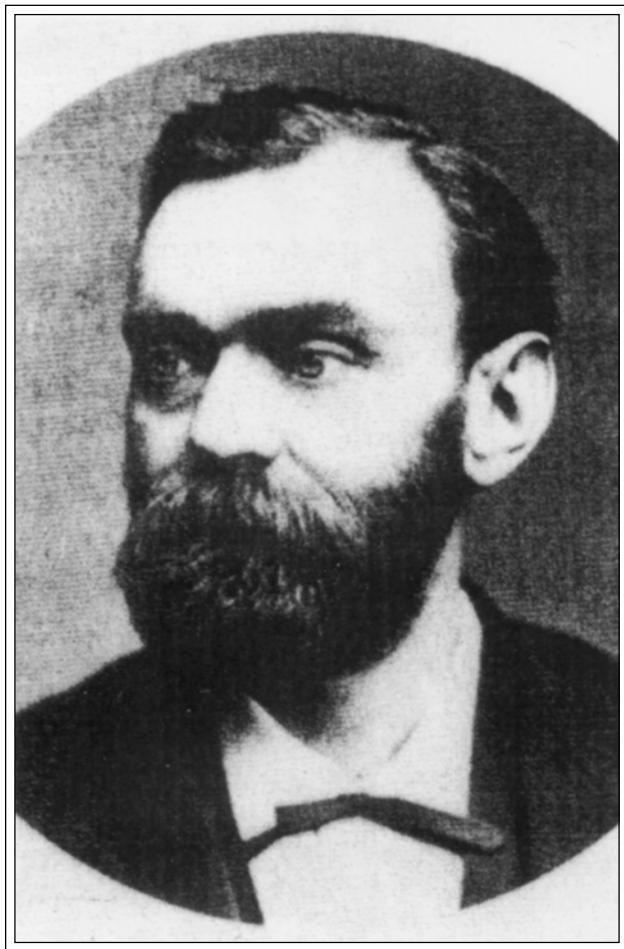


Figure 1. Alfred Nobel at his laboratory.

areas of interest, for instance Nobel was fluent in six languages, authored plays and poetry and was a prolific inventor: his first notable invention was dynamite. He traveled the world over, eventually held 355 patents, and became known as the world's wealthiest philanthropist. In 1895, Alfred Nobel established a system of recognition "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 a person who shall have made the most important discovery within the domain of physiology or medicine [for which] the prizes . . . shall be awarded by [the] Karolinska Institute in Stockholm . . .".¹

There have been 92 Nobel Prizes awarded in the field of medicine since 1901.² The centennial of the Nobel Prize Ceremony sparked numerous special events including a symposium attended by some 170 Laureates as well as a classical concert. This commemoration marked not only the 100th anniversary of Alfred Nobel's legacy but also provided a fitting segue into its second century.

Surgery as the Nobel science

Of the 175 scientists and doctors of medicine who have received the Nobel Prize, just over half (94) have held a Doctor of Medicine degree while the remainder earned PhD's and other degrees Table 1.^{2,3} Of the 94 Doctors of Medicine, nine (9.4%) were surgeons Table 2.³⁻¹¹ Notably, this is the largest number of prize recipients from a clinical field.

The Nobel urologists

The urological community is immensely proud that two of its members—Werner Forssmann and Charles B. Huggins—were awarded the Nobel Prize. Not only were these urologists awarded the highest honor, but their scientific achievements also led to significant advances in surgical medicine over the past century.

TABLE 1. Educational background of Nobel Prize laureates

Scientific degree	Amount of recipients
MD's	84
MD – PhD's	10
PhD's and other	81
Total	175

TABLE 2. Surgeon laureates in medicine and physiology

Year	Surgeon	Original surgical occupation	Country	Awarding area
1909	Emil Theodor Kocher	General surgery	Switzerland	Thyroid disease
1911	Allvar Gullstrand	Ophthalmology	Sweden	Ocular dioptrics
1912	Alexis Carrel	General surgery	France/USA	Vascular surgery
1914	Robert Rabany	ETN	Austria/Sweden	Vestibular disease
1922	Frederick Grant Baunting	Orthopedic surgery	Canada	Discovery of insulin
1949	Walter Rudolf Hess	Ophthalmology	Switzerland	Midbrain physiology
1956	Werner Theodor Otto Forssmann	Urology	Germany	Cardiac catheterization
1966	Charles Brenton Huggins	Urology	Canada/USA	Hormonal blockade of prostate cancer
1990	Joseph E. Murray	General surgery	USA	Kidney and bone marrow transplantation

Werner Forssmann (1904-1979)

Born in Berlin, Werner Theodor Otto Forssmann was the first of the urologists to win the Nobel Prize (Figure 2). During his medical education, Forssmann exhibited extraordinary capabilities in two Nobel areas, physiology and medicine, while he studied cardiac function under the renowned Dr. R. Fick. After graduating from Friedrich Wilhelm University Medical School in 1922, Forssmann completed his formal medical training at the University of Berlin in 1928. The following year, he became a clinical instructor in surgery at the August Viktoria Home at Eberswalde where he hypothesized that, by delivering several pharmacological agents directly into the heart, there would be increased success in the treatment of life-threatening cardiovascular disease. After experimenting successfully on cadavers, Forssmann actually attempted cardiac catheterization on himself (by a percutaneous needle venotomy and ureteral catheter), but this first effort failed when his colleague, fearing possible complications, terminated the procedure. With his second attempt, Forssmann did achieve the passage of a catheter tip into his right atrium, and the findings from these two experiments were published in 1929.¹² Later, building on Forssmann's original experiments from 12 years before, Columbia University's Drs. Andre Frederic Cournard and Dickinson Woodruff Richards, Jr. revived interest in the procedure, eventually winning all three doctors the Nobel Prize.

That same year, after securing a position in the Department of Surgery at Berlin's Charite Hospital,

Forssmann began postgraduate training under one of Germany's leading surgeons, Dr. Ferdinand Sauerbruch. However, this promising collaboration was of short duration due to the diametrically



Figure 2. Werner Forssmann.

opposed working styles of Forssmann and Sauerbruch. Whereas the former challenged his colleagues with open inquiry and innovative techniques, the latter headed a clinic where "an extraordinary inflexibility of thought reigned . . . [as well as] a rigid dogma based upon [his] teachings . . . [where] any divergent opinions were considered heresy".¹³ Sauerbruch terminated Forssmann's employment, harshly dismissing him with the taunt: "You might lecture in a circus about your little tricks, but never in a respectable German University!"¹⁴

For the next few years Forssmann moved frequently, gaining employment and experience at a succession of hospitals. First, he returned to his former place of work in Eberswalde where he successfully performed nine cardiac catheterizations without any complications. In 1931, Sauerbruch invited him to return to Charite Hospital and Forssmann accepted, working there for 6 months without remuneration, as was the custom. Again disenchanted with the working conditions, Forssmann consequently took positions at the City Hospital in Mainz and then joined the staff of the Surgical Clinic at the City Hospital in Dresden. Ultimately, he obtained a position as urologist at the Rudolf Virchow Hospital in Berlin where he developed a passion for urology under the supervision of his chief, Dr. K. Heush. Together, they not only drastically reduced operative mortality within radical prostatectomy from 25% to 2% due to the advanced vascular control by precise ligation of neurovascular bundles bilaterally and improved surgical skill. They also introduced the separate ligation of the vessels for renal pedicle during nephrectomy while strongly criticizing the commonly used practice of ligation en mass.⁶

But this was a politically turbulent time in Germany. The Nazi Party had recently risen to power and Forssmann decided to become a member, a decision that would haunt him professionally in the years to come. Within the party, Forssmann served as a sanitary officer and army surgeon, reaching the rank of surgeon-major. During the war itself, Forssmann served behind the active line of battles on the Eastern Front in East Prussia (Poland, Russia) and the Western Front (Norway) for 7 years. When the war was nearing its end, he attempted to seek refuge in the West, but after swimming across the Elba River, he was captured by the American Army. Interned until the war's end in 1945, he returned home and commenced private practice as an urologist in the small town of the Black Forest. Yet Forssmann's professional reputation, because of his widely known former membership in the Nazi party, was tainted:

despite his many attempts to apologize for his participation in the Nazi movement, the academic community was reluctant to fully endorse his achievements.

Still, Forssmann practiced as an urologist from 1950 to 1958 at Bad Kreuznach. He also traveled broadly, working in Switzerland, England and Argentina as a Visiting Professor where he was distinguished for his discovery in cardiac catheterization. In 1954 Forssmann was awarded the Leibniz medal of the German Academy of Sciences, a prestigious award that earned him the nomination as a Nobel laureate. And despite criticism from the academic establishment and the German press, Dr. Forssmann received notice in 1956 that he had won the Nobel Prize. Forssmann's rare scientific vision, and his unrelenting dedication to surgical excellence, had finally been recognized and honored.

Two years after winning the Nobel Prize, Forssmann was appointed Chief of the Surgical Division of the Evangelical Hospital in Duesseldorf. In the years that followed, Forssmann led a distinguished career; however, regardless of his international and national acclaim and the many honors he garnered over his lengthy career, Dr. Forssmann remained bitter and disillusioned about his rejection by his own nation's scientific community. Werner Forssmann persevered, nevertheless, and continued to practice urology almost up to his death from myocardial infarction in June of 1979.

Charles B. Huggins (1901 – 1997)

The second urologist to win the Nobel Prize was Charles Brenton Huggins Figure 3. Born and raised in Halifax, Nova Scotia, he attended Acadia University in Wolfville, Nova Scotia, graduating with a Bachelor of Arts in 1920. As a graduate student at Columbia University in New York, Huggins studied physical and organic chemistries and later attended Harvard Medical School, from which he graduated in 1924. Three years later, after completing a surgical residency at the University of Michigan, he joined the faculty at the newly formed University of Chicago Medical School. Here he was encouraged to continue developing his background in organic chemistry as support for his special interest in urological research.

In 1929, Huggins was appointed Chief of Urology and Assistant Professor of Surgery at Belling Hospital where he would remain for 25 years. His research laboratory reflected his creative approach and knowledge of organic chemistry helping to define a new discipline known as clinical biochemistry, and

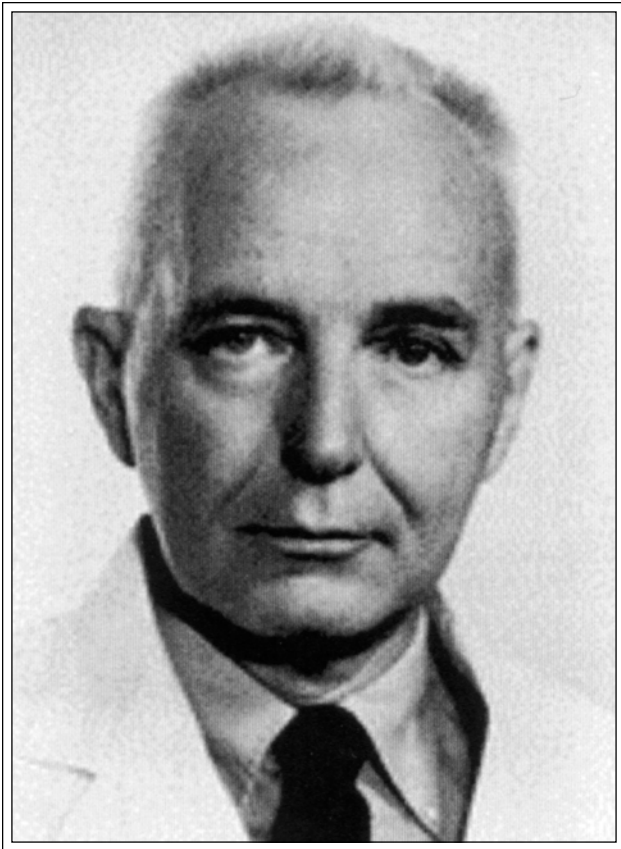


Figure 3. Charles B. Huggins.

his broad range of interest – from urogenital tract functions and tumorigenesis to osteology and its disorders – produced significant discoveries. For instance, he was the first to revise the concept of calcification in canine bladder grafts,⁶ which was conventionally considered a result of tissue incrustation by organic salts derived from the bone, by proving that this phenomenon represented true ossification, that is a transformation of connective tissue into elements of bone.¹⁵

Huggins' early research in prostate cancer identified a relationship between androgens, estrogens and the regulation of hormone-dependent tumorigenesis.^{6,16,17} This discovery would become the underlying principle of modern hormone-therapy as well as chemotherapy of malignant hormone-dependent tumorigenesis. Based on the theory that prepubertal castration most often prevented tumor growth in the prostate gland, Huggins designed an isolated canine prostate model to collect gland secretion Figure 4.¹⁸ His biochemical analysis of the enzyme and hormones present proved an androgenic regulation of prostatic function and its inhibition by estrogens working as competitive antagonists.

In the 1940s, along with his student and future Noble co-laureate, C. Hodges, Dr. Huggins identified a relationship between acid phosphatase levels and metastatic prostatic carcinoma: that castration or exogenous administration of estrogen caused a significant decrease in acid phosphatase cut-off, while androgen-injection caused an increase in this level.¹⁶ The results of bilateral orchidectomy in 24 patients with advanced prostate cancer suggested that in 80% of the cases there was tumor remission, diminished bone pain and weight gain.¹⁷ Four patients survived more than 12 years after castration. Within a few years, Huggins had performed the first bilateral adrenalectomy as a total androgen blockade for the treatment of advanced prostate cancer.¹⁹

Huggins extended his research of hormone-dependent tumorigenesis to breast cancer, realizing that this form of tumor was also related to endocrine function. The recognition of this relationship would lead to the modern use of hormone therapy and

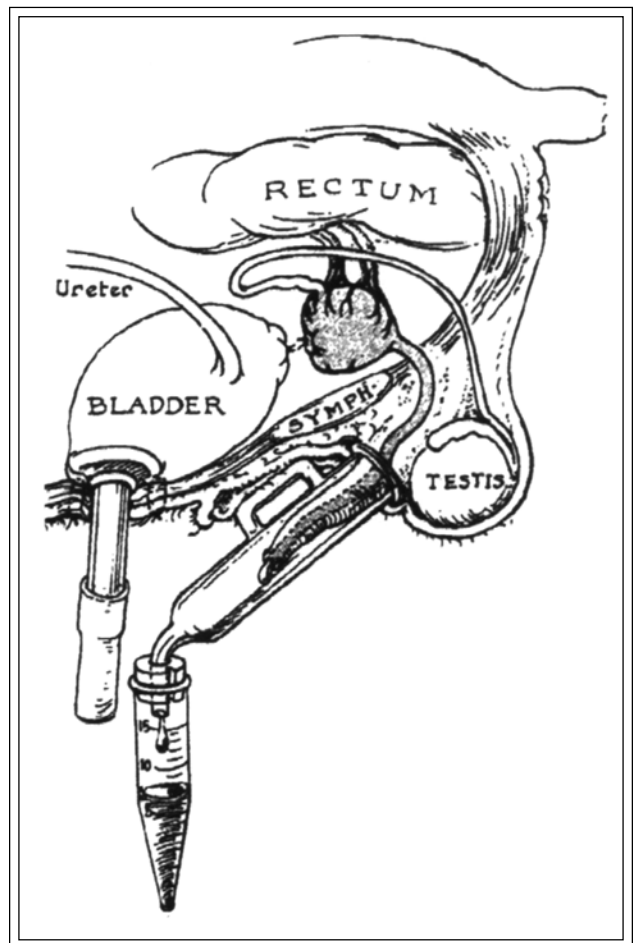


Figure 4. A technique by Huggins to collect the prostatic secretion in canine model.

chemotherapy for advanced carcinoma of the breast. In his continuing research, he established a model for the investigation of breast cancer in rat that remains in use today.²⁰ During his lifetime, Charles B. Huggins was widely recognized for the significance of his discoveries by countless awards and numerous honorary degrees.

Conclusion

The distinguished accomplishments of these two great physicians exemplify the highest level of excellence in science for the entire surgical and urological community. The inspiring biographies of urologists Werner Forssmann and Charles Huggins confirm the skills and experience that surgeons possess to pioneer new discoveries, not only in their own specialty but also in other areas of fundamental and clinical medicine. The fact that more surgeons have won the Nobel Prize in the field of physiology and medicine than have physicians in any other biomedical discipline, signifies the profound importance of the surgical specialty in the development of modern medicine. The time when surgery was defined as an area "extremely limited to the manual skill" is in the past and the future promises discoveries on the novel molecular and gene level. Today's breakthroughs in molecular biology and genetics represent an exciting challenge for clinicians.

Indeed, surgeons are uniquely positioned at the interface between theory and practice, between laboratories, operating tables and bedsides. By definition, excellence in surgery demands immense potential that is realized in a combination of scientific vision, innovation, experience, and self-sacrifice. In the future, surgery as a discipline will deepen and expand its frontiers by employing a multidisciplinary research approach that translates to brilliant technical art. This highly specialized network will forge the link between the disciplines, thus precipitating further discoveries and additional Nobel Prizes in this millennium. □

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