

CHARLES BRENTON HUGGINS NOBEL PRIZE WINNER MEDICINE 1966

Terry Burns, MCIC

Huggins won the 1966 Nobel prize in physiology for discoveries in hormonal treatment of prostatic cancer. He received the award as a co-recipient with Peyton Rous.

Huggins is a native of Halifax, Nova Scotia, Canada and his complete early- life history up to age 19 show he was Halifax grade schools, mostly in Halifax's south-end. He completed his high school in Parrsboro, Nova Scotia, the home of his mother.

After high school, he went to Acadia University for his B.A., then to Harvard Medical School and he graduated in 1924. Dr. Huggins completed his formal education with a surgery fellowship in Michigan, the home of his wife, Emily Wellman, and finally a tour through Europe and Britain to look at some research in a number of fields. Huggins spent his entire medical research career at University of Chicago and between 1972-1979 he was the chancellor of his beloved alma mater in Nova Scotia, Acadia.

Proclaiming Dr. Huggins achievements at the Nobel award ceremony, it was first noted that he had accomplished 'a new type of cancer treatment, one now assisting previously inaccessible patients with the use of nontoxic, natural hormones rather than toxic or radioactive agents with few side effects. In his address, Huggins said that the control of cancer by hormones can be summarized: (1) some cancers differ essentially from the cells they arose in response from a change in the hormone environment; (2) certain cancers are hormone-dependent and these cells die when supporting hormones are removed; (3) certain cancers succumb when large amounts of hormones are administered.

C.B. Huggins a remporté le prix Nobel en physiologie pour sa découverte de traitements par hormones du cancer de la prostate. Il a reçu cet honneur en tant que co-décipiendaire avec Peyton Rous.

Huggins est natif d'Halifax, Nouvelle Ecouse, Canada, où il a complété ses études primaires et une partie du secondaire. Il a terminé son secondaire à Parrsboro, Nouvelle Ecouse, ville natale de sa mère.

Il a poursuivi ses études à l'Université Acadie où il a obtenu le diplôme de Bachelier es Arts. Par la suite, en 1924, il a complété ses études en médecine à l'Université Harvard. Quelque temps plus tard il a complété un stage en chirurgie au Michigan, aux États-Unis, endroit où a grandi sa femme, Emily Wellman. Il a parcouru l'Europe y compris la Grande Bretagne afin d'observer et d'évaluer divers projets de recherche dans une variété de domaines scientifiques.

Huggins a passé toute sa carrière de chercheur médical à l'Université de Chicago. De 1972-1979, il a occupé le poste de recteur à son Alma Mater, l'Université Acadia.

Lorsque on a annoncé les nombreuses réussites du docteur Huggins lors de la cérémonie de présentation du prix Nobel, on a signalé, entre autres, sa découverte de nouveaux traitements du cancer, traitements dont bénéficient certains malades jusqu'alors. Ces traitements consistent d'utiliser des hormones naturelles et non-toxiques plutôt que les agents traditionnels qui étaient radioactifs et toxiques. Il est à noter, de plus, que ces nouveaux traitements ont peu d'effets secondaires.

Dans son allocution, Huggins a déclaré que le contrôle du cancer par hormones peut se résumer ainsi: 1. Certains cancers diffèrent essentiellement des cellules d'où ils proviennent et cela en réponse à un changement dans la composition des hormones qui entourent les cellules. 2. Certains cancers dépendent d'hormones et les cellules en question meurent quand les hormones qui les supportent sont éliminées. 3. Certains cancers meurent lorsque de grandes quantités d'hormones sont administrées.

Introduction

Dr. Huggins' Early Family History in Halifax

Dr. Charles Brenton Huggins, a Nobel prize winner in medicine and physiology for 1966, was born in Halifax, N.S. on September 22, 1901. His father, Charles Edward Huggins, was a pharmacist and most likely also a Halifax native. Dr. Huggins' mother, Bessie Spencer was from Parrsboro, a community in northwestern Nova Scotia. They were married in Parrsboro on June 26, 1900. Young Chas. B.'s brother, Victor, who was also an M.D., practised in Illinois, U.S.A.

Charles Edward Huggins was a professional pharmacist whose drug store was in downtown Halifax at 151/2 Jacob Street. This downtown Halifax street ran from Brunswick St. due east and down the hill to the harbour, and ending at Upper Water Street. Today, the whole Jacob Street area has been replaced by a large high-rise complex called Scotia Square. The Huggins residence was adjacent to the Jacob Street store, on the corner of Poplar Grove and Jacob.

The Huggins family during the time period from 1886 to roughly 1900 had lived in residences on Maynard and Barrington Streets. The family moved to a south-end address of 5 Brenton Place around 1906 when Dr. Huggins began his elementary education at Morris Street School. Dr. Huggins divided his early education between Morris Street and LeMarchant Street schools. Chas. Edward, practised his profession as a pharmacist in Halifax until his death in 1912.

An advertisement in the Halifax city directory of 1895 for Charles Edward's pharmacy described the range of items for sale "Chas. E. Huggins, Chemist, Depot for Army and Navy Blood mixture and Hele-type Cream; Sponges, Toilet Soaps, Perfumery, etc, Jacob cor with Poplar Grove."

Charles Edward Huggins was very much involved in his own professional organization, the Nova Scotia Pharmacy Association. He held the executive position of secretary in 1901, the provincial vice-presidency in 1902 and the presidency in 1903. An informative booklet put out by the Nova Scotia Pharmacy Association summarized the 50 years of pharmacy in Nova Scotia, 1875-1925.

Charles Edward died at the young age of 43 on April 14, 1912 after only 14 years of marriage. He left a family of two young boys and his wife Bessie. Dr. Huggins was only 11 years old and in elementary school. Dr. Huggins' father is interred in Camp Hill Cemetery.

Following the death of C. E. Huggins, the family moved to Parrsboro where Mrs. Huggins family still lived including her sister, Mrs. Clinton (C.V.) Cook, and brother-in-law, Captain C.V. Cook. The two brothers completed both their elementary and high school education in Parrsboro. Dr. Huggins moved quickly through his high school education at Parrsboro because before that in 1914 he was in Halifax in the middle of grade school and by 1916 at age 14 (born September 22) he was at Acadia. The family lived on Spring St. and Dr. Huggins took an active part in the local Baptist Church's Sunday School as a teacher. Some of the information obtained for this period was attained in conversations with former residents of Parrsboro.

Dr. Huggins seems to have enjoyed his years in Parrsboro in 1966, when the announcement of his Nobel Prize was made, he sent a thank you letter to the Parrsboro town council in response to their earlier note of congratulations, in which, in a very exuberant manner, he wrote, "I love Parrsboro."

At other times in his life Dr. Huggins showed similar loyalty to his native province. He especially loves the Annapolis Valley, the home of his alma mater, Acadia University. Possibly Dr. Huggins went to Acadia because it was close to his home and also because it had a Baptist affiliation. Very possibly Charles Brenton got some sort of scholarship assistance because of his excellent academic ability and his close ties with the Baptist religion. At Acadia he had an interest in a wide range of subjects, especially the classics. He enjoyed the classes of Prof. Thompson, whom he respected and was his classics professor. Dr. Huggins came to the profound conclusion that the Latin poets developed a boy's character, and if a scientist could manage his character he could manage cancer research of world calibre. There are many in agreement with him still today who, not just making a verbal consent, believe that a strong liberal arts education is the basis for a successful career in science and medicine. The skills and

knowledge of all types gained from an earlier liberal arts education complement later work in the field of science.

Dr. Huggins graduated from Acadia with his B.A. in 1920 when he was nineteen years old. Dr. Huggins progressed to Harvard Medical School, and in 1924 he received his M.D. In his own manner, he humbly explained his presence at the exalted University by the fact that the admissions office was still lacking a sufficient number of foreign students when he applied. He completed his internship in surgery in Michigan in 1926.

In 1927 he married Emily Wellman of Michigan who was to be his wife for 60 years. As the first major move in Dr. Huggins' early career he was invited to do research at the University of Chicago under the leadership of Professor Dallas B. Phemister.

Huggins was to spend the whole of his professional life at Chicago. In the 20's Phemister sent him to Europe to get some training in urology. Some of the fundamental facts he learned at European and British research labs were that phosphate esters and phosphatases play an important part in the induction of bone marrow and treatment of prostate cancer. During his travels in Europe he learned from Prof. Otto Warburg the essential principle of tumor growth and that tumor cells, unlike normal cells, obtain energy from the combustion of carbohydrates in the absence of oxygen as fuel.

Huggins' Prostate Cancer Research

As early as 1933, Huggins had made many new contributions to our knowledge of the physiology and biochemistry of the male reproductive tract, and this led to an intensive and successful study of the prostate (Talalay, 1965). Measurements of enzymes in blood serum furnished the proof that cancer of the prostate is hormone-responsive (Huggins, 1965). Also, the study of the physiology of prostatic fluid gave us the first understanding of the relationship of the endocrine system to prostatic function. Thus began Huggins' endocrine theory of prostatic carcinoma. In 1940, he announced that treatment consisting of estrogen doses or orchiectomy surgery could give long term regression of the disease. A large number of patients with advanced disseminated prostatic cancer had so responded. He had found that prostate cancer is often not an autonomous process because the cancer grows or shrinks respectively whether androgens are administered or eliminated (Talalay, 1965).

Huggins produced as evidence of his results, relief of pain and regressions of tumors in far-advanced prostatic cancer patients and those beyond help of any therapeutic measures. In some of these patients were included the regression of metastases, and many had returned to active and useful lives (Huggins, 1965). The treatments devised by Huggins have been adopted around the world. The significance of the positive results can not be over-emphasized because prostate cancer is one of the most common types of male cancer, especially among older men. It has been stated that, "humanity owes Charlie Huggins a deep gratitude." (Talalay, 1965). In other words of Talalay (Science, 1966), "the award of a Nobel prize to one who has done so much for the human cancer patient is richly deserved".

Talking about the essentials of his prostate cancer methods, Huggins stated, "The method of proof of a proposition can be of greater interest than that which is proved," i.e. one can look at this as similar to the emphasis that the famous French philosopher Descartes put on method over content. The comparison is based on the fact that Huggins' endocrine treatment of prostate cancer was not reached empirically but from an experiment on prostatic (A fruitful interplay: The University of Charles Huggins

1985) physiology. Therefore, both a method of therapy and its mechanism were in one joint study and as a result a rational chemotherapy of cancer was initiated (Talalay, 1965). Estrogens were the first agents of known constitution (except radioactive agents), which helped substantially with cancer, and estrogens became the first non-toxic substances taken by mouth that were beneficial.

Besides being the first positive results in the clinic, the results spurred a major stimulus to all research on cancer chemotherapy. For the first time a large ray of hope appeared in the treatment of cancers because it had been proven that large metastases could be made healthy by control of the internal environment of the host. The major result clinically has been that the positive effects of estrogens and orchiectomy on cancer of the prostate have been repeatedly demonstrated all over the world. In Huggins' initial series of 20 patients who had large metastases, four lived more than 12 years. The fact that health could be restored to certain cancer patients, by a change in their hormonal states, led Huggins to conclude (Anonymous, 1985), "Two new principles of medicine emerged from these studies: (1) cancer is not necessarily autonomous and intrinsically self-perpetuating; (2) cancer can be sustained and propagated by hormonal function which is not necessarily abnormal in kind or exaggerated in rate, but which is operating at normal or even subnormal levels. (Talalay, 1965 [p. 1139])

In 1939 Huggins had surgically isolated the prostate gland of dogs. By analyzing the quantitative and chemical composition of canine prostatic secretions under different hormonal conditions, (Talalay, 1965) he found that testosterone stimulates the growth and secretory activity of the prostate. He also learned that estrogen, the female sex hormone, inhibits prostate growth.

In 1945 Huggins and two students, C.V. Hodges and W.W. Scot, with the basic problems of prostate cancer in mind, found that testosterone promoted the growth and metastasized the cancer whereas estrogen or castration helped in the reduction of the cancer, but hormone treatment only checked the growth of prostate cancer temporarily (Nobel Prize Winners, 1987). This discovery brought Huggins the 1966 Nobel Prize in medicine. Also, referring to castration, it was a better form of treatment and after seven years the patient was cancer free. In the history of cancer treatment, as early as 1896, Beatson, prior to any concept of hormones, used mastectomy (ovariectomy) to induce the regress of breast cancer in a few women. Any future hope for Dr. Huggins in his field of expertise, hormonal treatment, was not good because mammary cancer rarely responds to such treatment.

A further experiment in 1945 by Huggins came after the failure of antiandrogen measures, and it became clear that the adrenal glands were a source of growth-promoting steroids to maintain the activity of the prostatic cancer after the removal of the testes. This conclusion was reached because both castration and estrogen therapy still required the removal of the testosterone source, the adrenal glands.

He performed the first bilateral adrenalectomy in man in the pre-cortisone era and the results, although minimal, proved to be significant in later development of the cancer therapy (Science, 1966). He replaced the normal function of the adrenal glands with cortisone. Huggins abandoned the cortisone procedure until replacement therapy became available. He found that the hormones formed in the gonads to sustain mammary and prostatic cancers are also formed in the adrenal cortex.

The attitude of Huggins' medical research colleagues around the world toward his success and good judgment, as related to adrenalectomy, is given by Sir Stanford Cade, "His (Huggins') genius in physiological research, his surgical courage, and skill led him to try adrenalectomy in advance of the discovery of cortisone, only to abandon it until replacement therapy became available,..." (Talalay, 1965).

Huggins' major contribution was that he was the first to develop practical processes to suppress aggressively and limit the growth of cancers. However, he was not the first to observe that some cancers of the prostate shrivel when certain procedures are done with the source of the hormones. Huggins prolonged the lives of millions of people through the use of male and female hormones to treat their cancers without surgery. He also used synthetically produced variants of the natural hormones that had little female or masculine effects on either type of patient. To put Huggins' role in perspective, Dr. Rous of the N.Y. Rockefeller University said that he personally had done nothing practical to cause him to be the co-recipient with Huggins of the 1966 Nobel in medicine prize. They worked in the same field, but his successes were not able to be applied as easily as the work of Huggins to the saving of innumerable people.

The first pharmacological estrogen preparation used in the clinical treatment of cancer was diethylstilbestrol. This was the beginning of the chemotherapy of cancer (Huggins, 1965). But, in his research Huggins used phenolic estrogens and orchiectomy with human prostate cancer as with dogs' prostate cancer.

Measurements of phosphates in blood serum proved that cancer of the prostate in man is hormone-responsive. The testing level that Huggins used to come to this conclusion was that he measured the blood levels of an acid-phosphate secreted by prostate and alkaline-phosphatase secreted by bone-forming cells in bone tissue. Both of these substances are in high concentration in the blood of patients with metastatic cancer of the prostate. He concluded that the level of the enzymes in the blood provides a useful index of the cancer's activity and the efficacy of the treatment.

Beginning in 1950, Huggins spent 15 years developing a model for human mammary cancer. It took a long time to induce mammary tumors in animals, and the lesions did not show any susceptibility to hormones. These obstacles prevented any good results in this type of cancer. In the early 1960's he found that a single dose of DMBA (7,15-dimethylbenz(a)anthracene), a polycyclic aromatic hydrocarbon (PAH's), can evoke in a few weeks malignant tumors, many of which are hormone-dependent. The tumors grow or shrink in response to the steroidal balance of the host. They also grow faster during pregnancy and with the injection of progestational steroids. A combination of estrogen and progesterone for a limited time caused permanent regression of one-half of these tumors. Similar regime gave worthwhile relief to some women with disseminated carcinoma of the breast.

A study of the nature, structure, and electronic nature of PAHs show which molecular properties selectively induce mammary cancer. All PAHs' are flat with conjugated double bonds and include special substituents of methyl or amino groups or more aromatic rings. They form colored complexes with electron-acceptors of a charge-transfer type.

Further observations showed that powerful electron acceptors also induce a high incidence of mammary cancer. However, carcinogenicity is not dependent entirely on these factors but also on the size and steric configuration of the molecule is critical. Three types of carcinogenic molecules with similar molecular geometry are certain steroids, carcinogenic hydrocarbons, and hydrogen-bonded base pairs in DNA (Talalay, 1965). Molecular models reveal these similarities very neatly since the molecules fit into a hexagonal box moulded around the base pairs of DNA. The box is not only beautiful but also utilitarian. (AUTHOR'S NOTE: Since Huggins accomplished this work, I suspect that great advances have been made in this area including more precise knowledge of many structural and steric factors, allowing the use of computers with 3-D imagery.) The model suggested that the interaction of PAHs' with nucleotide base pairs may be important in the induction of mammary cancer. To

understand the carcinogenic power of PAHs', we must understand that these hydrocarbons masquerade as hormones or heredity material.

The fact that hormones influence the growth of cancer came initially from the study of tumors of dogs initially, not man, It came and indirectly through a series of observations involving metabolism and endocrinology.

The second quarter of our 20th century found the medical researchers interested in two topics : (1) isolation of steroids; (2) the biochemistry of organic compounds containing phosphorus, an element described as a 'soft atom'. The key to the steroid hormone problem in cancer was the isolation of crystalline estrone from the urine of pregnant women. In the phosphorus field there were important discoveries of hexose phosphates, nucleotides, and high-energy phosphates intermediates.

Remarkably, it was found that spermatote fluid is devoid of acid-soluble phosphorus and free hexose, but human semen contains large amounts of inorganic phosphorus and the carbohydrate, fructose (hexose, ketose). When a human male ejaculates, the environment of the spermatozoa is altered by a sharp rise of fructose and soluble phosphorus. Huggins found (Talalay, 1965) that while seminal vesicles in man are the chief sources of the semen components, unmixed secretions of a human's various sex glands are difficult to obtain.

Conclusion

Huggins has accomplished a great amount both in research and in clinic, and as a result has prolonged many lives. On September 22, 1996, he was 95 years old; that same year was also the 30th anniversary of his Nobel prize in medicine. I strongly urge that all Canadians, all Nova Scotians and all Haligonians should warmly congratulate Dr. Huggins , a native son, on his achievement and feel the association with him as a world-class medical researcher. Dr. Huggins made his first significant contribution to medical research by showing the influence on bone formation. This was in his first year (1927) at the University of Chicago Medical School, and it fueled his commitment to research and discovery for his entire career.

Dr. Huggins left Nova Scotia when he was 20 years old, but he has returned many times especially during the period 1972-79 when he was the Acadia University Chancellor. He has relatives here and has made visits to Parrsboro and Chester over the years.

Throughout the medical world many of the discoveries of Huggins are used and in the many awards he has received we see the degree and magnitude of his life's work. Nova Scotians are extremely proud of their sons and daughters who have risen to a world class status, and I think no event would better exemplify that pride than the day in 1946 when Cyrus Eaton, Dr. Huggins and a clergyman, Rev. A.H.C. Morse, all received honorary doctorates from Acadia. A book by Dr. Allan Marble, who is simultaneously a professor at both Dal and TUNS universities, which is called "Nova Scotians at Home and Abroad" lists many world -level scholars, who are mostly native-born persons including Dr. Huggins.

Dr. Huggins, from my research, is the only person in eastern Canada or east of Quebec who has received a Nobel prize.

To exemplify Dr. Huggins accomplishments in another manner we will list the more important of his many awards:

- (A) 1969- One of 'The 1000 Makers of the 20th Century' Sunday Times, London.
- (B) 1966- Nobel prize in medicine. NOTE. Huggins lab is part of University of Chicago and that institution has collected 24 Nobel prizes over 95 years.

- (C) 1963- Lasker Chemical Research Award- one of the highest awards to be awarded in American medicine; co-recipient with Dr. DeBakey. This award is give for "the highest achievement in the application of biological science to human welfare."
- (D) 1943- C.L. Mayer Award from National Academy of Sciences; First recipient.
- (E) 1936 and 1940- twice received gold medals from AMA.
- (F) 1909- Emil Kocher was the only other surgeon to receive a Nobel prize up to 1966.
- (G) 1963- Another award the very next day after award (c) from American College of Surgeons

It was an honorary fellowship from the American College of Surgeons. He received this award because he "rightly earned the highest distinction which can be bestowed by the Surgeons of Canada and the United States". Besides these awards, Dr. Huggins was the first to pioneer many different and effective medical procedures :

- (A) 1927- Demonstrated the direct influence that heat had on blood formation in the bone.
- (B) 1938- Focused on cancer of the prostate; discovered the hormone dependency of prostate cancer and found the first effective treatment of the disease.
- (C) Discovered that androgens stimulated cancer, whereas castration or estrogens slowed it down; found that cancer can be dependent on hormones for metabolism ; his major contribution on prostate cancer was that orchiectomy or small doses of phenolic estrogens relieved pain and reduced size of the tumor; an alternate treatment was the use of synthetic or natural estrogens.
- (D) Created a method of treatment of breast cancer which included the removal of the adrenal glands; this was, in 1951, an advance in treatment.
- (E) Devised a much quicker method to develop breast tumors in lab animals; the PAH type-molecule, DMBA, induced breast cancer while ovarian hormones suppressed DMBA-type cancers.
- (F) Seven sorts of hormone-responsive cancers of humans and animals have been treated across the world by this system including : cancers of the prostate, breast, endometrium, thyroid, lymphatic system, kidney, and seminal vesicle. Huggins also worked in the following areas and made original contributions; bone formation, bone marrow, serum enzymes, protein chemistry.

Huggins has accomplished a great deal in the area of clinical physiology, and he has a large number of 'firsts' in medicine to his credit. But equally intriguing is his philosophy, for his very successful life, which included such principles as, "It is a pleasant vocation to do experiments while teaching young people how to find new and beautiful things- how to do elegant science." (Huggins, 1965).

Another quote explains his love of science and details the qualities of science which make it mysterious and interesting: he stated that Science is pre-set to give only the truth" (Huggins, 1965). As many young graduate science students have found out, Huggins describes such students as very hard workers , full of enthusiasm, and the full bloom of these characteristics is limited to the age range of 18-32.

He is famous for the statement, "Discovery is our business." The adjective "our" tells the fact that the only economic procedure is by working entirely as a group. Also, two other rules for the effective use of student research time are that the overall objective is that no one is responsibility-free, and that these years are excellent ones to learn science.

Huggins continues and tells us that a researcher must be able to recognize an essential problem, and that usually a talented student has such as an inborn ability. A noble problem is one which gets things moving during its period or time. What problems a researcher spends his time on do not need to be dictated by the requirements of the people, but certainly for the good of mankind a medical problem should have priority. This was said by a man who fell in love with medical research and who regarded science as the art of our age. Huggins' Nobel award was the first for cancer research by 1966.

Although many different directions can be taken, the problem in science is solved in only one way, and this direction is simple and comprehensive. The only possibility of success in research is to look at science being ruled by a combination or duumvirate of idea and technique (or substance and accident, essence and form).

Finally, Huggins gives some sensible advice related to the time to make a decision to set the problem aside. He says that the law of diminishing return is one good criteria on, and he also compares Heisenberg's principle concerning the lack of ability to know both the position and velocity of an electron with the fact that when the researcher starts to get close to a final answer the solution becomes evasive. This is a good indicator that it is time to move on.

Dr. Huggins has worked very hard for 70 years, but his objective over this long time was not to amass a fortune of money but to do research, "Research is not work to me. It is my pursuit and pleasure." (Medicine on the Midway Fall, 1985) He worried that too many doctors have an objective of high income, and this distracts them from research.

(NOTE FROM AUTHOR: Everyone talks about coincidences in their lives, but I think I met the absolutely extreme example when doing research for this paper . In one of the Dalhousie professional school libraries I had a chat with the librarian, and the net result of our conversation was for me to learn that she was working in University of Chicago on the very October day in 1966 when Dr. Huggins heard the news. She also assisted Mrs. Huggins manning the telephones.)

Acknowledgements

Although this is a relatively short paper, I do have a need to thank a number of people for their very direct assistance. I will list them simply alphabetically:

First, the help of Dalhousie Killam, Pharmacy, and Medical (Tupper building) libraries, public libraries at Woodlawn, Alderney Gate, Spring Garden Road, and the Public Archives. Second, the combined help of the library, Archives of Acadia University and the collection of Dr. Huggins materials at Acadia were significantly beneficial.

Individuals who have helped:

- 1) Dr. Alan Marble - TUNS and Dal; Dr. Marble read and edited the manuscript.
- 2) His Worship the Mayor of Halifax - Mr. Walter Fitzgerald : for preparing a plaque which was sent to Dr. Huggins prior to his 95th birthday recognizing his relationship to his home town-Halifax, Nova Scotia.
- 3) Mr. Lamont Larkin- Lamont's enthusiastic support in scientific projects that I have been involved with him goes back over 20 years.
- 4) Mr. Al MacInnis, Toronto and Ms. Betty Osborne, Dartmouth for their combined efforts with the french form of the abstract.
- 5) Mr. Don Moore, M.Sc. - a loyal & supportive colleague.

References

- 1000 Movers of the 20th Century - General reference.
Halifax City Directories, 1886-1914 Huggins, C.B. 1965. Propositions in Hormonal Treatment of Advanced Cancers. JAMA, June 28, 192, 1142-1144
Medicine on the Midway Fall 1985, University of Chicago, A fruitful interplay: The University and career of Charles Huggins, 17-20.
Talalay, Paul 1965. The Scientific Contributions of Charles Brenton Huggins. JAMA, June 28, 1965, 192,1137-1140.
Nobel Prize Winners, 1987 ed., Wilson Co.
Notable 20th Scientists p. 975-977.
Marble, E. Allan 1977. Nova Scotians At Home and Abroad.
Parrsboro Record, October 12, 1966 and November 5, 1966.
Science, October 21, 1966, 154, 362-366.
Who's who in America, 1972-73, J. Kerr 110.

(AUTHOR'S NOTE The Burns family's great-grandfather, John Burns, who is buried in Holy Cross Cemetery on South Park St. and is (our 4th generation relative) in Halifax resided at 151/2 Brunswick St. during the exact period that the Chas. Edward Huggins family was at 151/2 Jacob St., that was roughly, 1880-1895. These two residences were about 3-4 blocks apart north-south on Brunswick St.)