

# Sir UN Brahmachari: His life & his science

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Sir Upendranath Brahmachari was a physician-scientist best remembered for his fight against kala-azar and for discovering urea stibamine, a cheap and effective drug to combat the dreaded disease. This great medical scientist was born on 19<sup>th</sup> December 1873 in a small village called Sardanga near Purbasthali in the East Burdwan district of Bengal during the days of the British Raj. U.N. Brahmachari's family lineage can be traced back to the time of Sri Chaitanya Mahaprabhu, some 500 years ago. The extremely rare family surname 'Brahmachari' originated from Keshav Bharati, who had initiated Sri Chaitanya into 'sannyas'. He had also given 'Deeksha' to his elder brother, Gopal Mukhopadhyay, who subsequently renounced his family surname and became known as Gopal Bharati Brahmachari Thakur. With time, 'Bharati' and 'Thakur' were dropped, and only the first name and 'Brahmachari' remained. This is how the surname, 'Brahmachari,' originated, and U.N. Brahmachari was the 9<sup>th</sup> generation originating from Gopal Brahmachari.

## His Early Life

U.N. Brahmachari's father was Dr. Nilmani Brahmachari, a respected physician of Purbasthali. He worked with the Eastern Railways and was based in Jamalpur, now in Bihar. Young Upendra studied at the Eastern Railways Boys School in Jamalpur. His mother, Saurabh Sundari Devi, was a homemaker. He married Nani Bala Devi in 1898 at the young age of 25 years. They had two sons – Phanindra Nath Brahmachari and Nirmal Kumar Brahmachari (Figure 1).

## His College Education

After passing with credit from the Eastern Railways Boys School in Jamalpur, he joined Hooghly College in Chinsurah (Figure 2). This college was established in 1836 by Muhammad

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Mohsin. Subsequently, in its centenary year, the college was renamed Hooghly Mohsin College in honor of its founder. It was from this college that, in 1893, U.N. Brahmachari obtained his B.A. degree with double honors in Mathematics and Chemistry. He stood first in Mathematics, for which he was awarded the Thwaites medal.

The following year, he obtained his master's degree in Chemistry from Presidency College (Figure 3). This heritage college was established in 1817 when it was called Hindoo College. Much later, in 1855, it was renamed as Presidency College of Bengal. It was upgraded to the status of a university in 2010. His educational attainments, with a solid foundation in Chemistry, stood him in good stead in his quest for a cure for kala-azar during his later years, culminating in the discovery of urea stibamine.

## His Medical Education

Despite being a brilliant student of Chemistry, U.N. Brahmachari switched tracks and joined Calcutta Medical College to study Medicine (Figure 4). This college was established in 1835 and was originally known as Medical College Bengal. It was the first medical college in all of Asia and came into existence 22 years before the University of Calcutta, which was established in 1857, the same year as the 'Sepoy Mutiny'. After coming under the purview of the

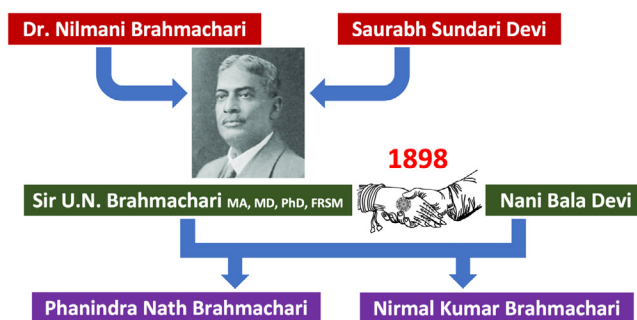


Figure 1: Sir U.N. Brahmachari's family tree



Figure 2: Hooghly College in the 19<sup>th</sup> century

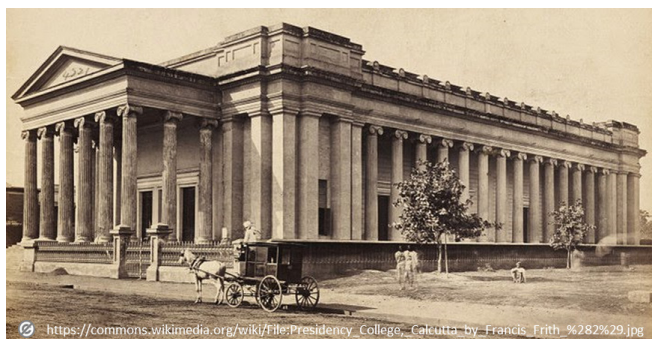


Figure 3: Presidency College in the 19<sup>th</sup> century

University of Calcutta, the name was changed to Calcutta Medical College. He completed his Licentiate in Medicine and Surgery (LMS) here in 1899, standing first in Medicine and Surgery, for which he received the Goodeve and McLeod Medals, respectively. In the meantime, in 1898, he tied the knot with Nani Bala Devi.

In 1902, he was awarded his MD degree from the Presidency General Hospital in Calcutta. This medical institution was established way back in 1707. In those days, the teaching, research, and hospital wings were all under one roof. It was only after independence in 1957 that these became separate entities. The teaching and research wings became known as the Institute of Postgraduate Medical Education and Research (IPGMER), while the hospital was named Seth Sukhlal Karnani Memorial (SSKM) Hospital after its largest benefactor.

Even before being awarded his MD, he had been appointed at the Dacca Medical School as a Teacher of Physiology and Materia Medica and Physician. So, he had commenced his research simultaneously in Dacca and Calcutta. Hence, this was a busy time for him as he was shuttling back and forth between Dacca and Calcutta. During this time, he primarily focused on various aspects of hemolysis, for which he was awarded his PhD within two years of his MD in 1904. The title of his thesis was *Studies in Haemolysis*.

### His Medical and Research Career

The person who inspired U.N. Brahmachari the most and encouraged him to enter into medical research was Sir Gerald Bomford. He was the Principal of Calcutta Medical College when U.N. Brahmachari was doing his LMS and MB. From that time, Sir Bomford noticed the spark in him to excel in medical research. If it hadn't been for Sir Bomford, he



Figure 4: Calcutta Medical College in the 19<sup>th</sup> century

would probably have been just another physician and not a renowned physician-scientist. Sir Bomford offered him the position at Dacca Medical School, where he worked from 1901 to 1905. Here, he came in contact with Sir Robert Neil Campbell, who further encouraged him to pursue a research career side-by-side with his medical career.

In 1905, he returned permanently to Calcutta and joined the Campbell Medical School (now Nil Ratan Sircar Medical College & Hospital) as a Teacher of Medicine and First Physician. He spent the lion's share of his medical career here, encompassing nearly two decades. He made his groundbreaking discovery of urea stibamine here. In 1923, he joined the Calcutta Medical College as Additional Physician and worked there till 1927. After formally retiring from government service, he joined the Carmichael Medical College as Professor of Tropical Diseases. Radha Gobinda Kar founded this college, and that's why it is now known as R.G. Kar Medical College & Hospital.

During his career in Calcutta, he was associated with many other institutes, including the National Medical Institute, which, after being clubbed with the Calcutta Medical Institute, became what we now know as the Calcutta National Medical College & Hospital. Notably, he was also a Council Member of the prestigious Calcutta School of Tropical Medicine. He saw many kala-azar patients in the hospital wing – the Carmichael Hospital for Tropical Diseases and developed a keen interest in this deadly tropical disease.

Regarding his research career, he worked on many diseases, the majority being infectious. He discovered a rare fever pattern in malaria, namely, quartan fever, which recurs every four days. Other diseases include influenza, filariasis, leprosy, blackwater fever, cerebrospinal meningitis, and syphilis. These depict his vast experience with a wide variety of pathogens, encompassing viruses, parasites, helminths, and bacteria. He also studied the so-called '*Burdwan fever*' (also known as '*epidemic fever of lower Bengal*'), first reported in Burdwan in the 19<sup>th</sup> century. He deciphered the cause of '*Burdwan fever*' and reported for the first time that it was due to a double infection of malaria and kala-azar. Again, while researching blackwater fever, he observed that in the acute phase of the disease, there was profuse hemolysis in the liver. Here, he used his knowledge of chemistry to develop an anti-hemolytic agent that became the mainstay of treatment for blackwater fever in those days. His research interests were not

just limited to communicable diseases. He even contributed to non-communicable diseases like diabetes.

### Kala-Azar and its Etiologic Agent

Kala-azar is so-called because it is characterized by black ('kala' in Bengali) patches on the skin, accompanied by irregular fever ('azar' from the Bengali 'jor'). The disease is technically termed visceral leishmaniasis as it affects the visceral organs, primarily the liver and spleen, that become enlarged, which is medically termed as hepatosplenomegaly. Kala-azar is caused by the protozoon *Leishmania donovani* and transmitted by the bite of sandflies (*Phlebotomus argentipes*). William Leishman and Charles Donovan jointly discovered the pathogen. That's why both their names have been incorporated into the scientific name of the parasite. The disease is prevalent primarily in the tropical zone and, to a lesser extent, in temperate regions of the world. The disease is prevalent in India, Brazil, Sudan, Ethiopia, Kenya, Uganda, Eritrea, and Djibouti. However, India has the highest prevalence of all countries as there is a double burden of both the parasite and the vector, providing a ripe condition for kala-azar outbreaks. Nowadays, however, explosive outbreaks of kala-azar are few and far between, and the disease is mainly confined to the low socioeconomic classes living in poor housing conditions.

The parasite's life cycle revolves around the vector (sandfly) and the human host. There are two stages in the life cycle of *L. donovani* – the promastigotes that multiply in the gut of sandflies and the amastigotes that multiply within the macrophages of the human host. A brief outline of the life cycle is presented in Figure 5.

### His Research on Kala-Azar

Despite his enormous contribution to various infectious tropical diseases, his passion lay with kala-azar. Here also, he had contributed immensely. His discovery of dermal leishmanoid – a type of cutaneous leishmaniasis – is still remembered to this day and is now known as post-kala-azar dermal leishmaniasis (PKDL). He is also credited for having discovered the first diagnostic test for kala-azar, which is termed the Globulin Precipitation Test, as it solely depended on the flocculation of proteins. It was a very simple

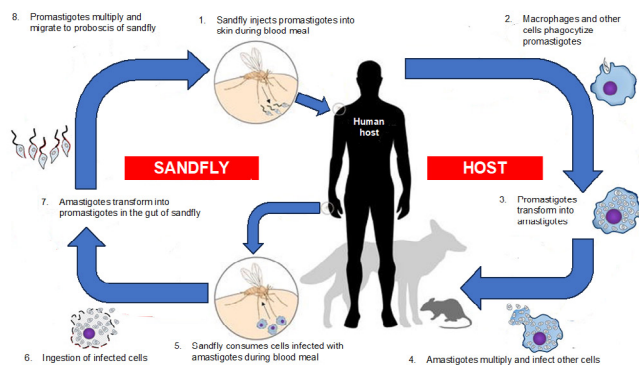


Figure 5: Life cycle of *L. donovani*

and inexpensive technique requiring only test tubes, blood from infected patients, and distilled water. This may sound impossible today, given the high-tech equipment used nowadays. His knowledge and expertise in chemistry were instrumental in developing this test. This was the first test specific for kala-azar and could differentiate it from other infectious diseases like malaria, TB, and dengue.

### Discovery of Urea Stibamine

His knowledge of chemistry paid off during his discovery of urea stibamine, which was his Life's work and claim to fame. The idea for this discovery came from Paul Ehrlich's magic bullet, salvarsan, which was also known as atoxyl and arsanic acid. This was dubbed as a 'magic bullet,' as it miraculously cured syphilis, a dreaded bacterial disease in those days. This drug had an amino group at the para position of a phenyl ring and at the other end, arsenic along with side chains were attached. However, when this drug was tested in kala-azar patients, it failed miserably due to its high toxicity in these patients.

In those days, the mainstay of kala-azar treatment was tartar emetic, chemically known as antimony potassium tartrate. This drug was administered intravenously to kala-azar patients. However, compliance was very low as it caused excruciating pain, as a result of which kala-azar patients were reluctant to take it. To circumvent this problem, Brahmachari replaced the arsenic in Ehrlich's salvarsan with antimony (Sb) and added a urea molecule as a side-chain (hence the name 'urea stibamine'). The reason for using urea is that it possesses anesthetic properties and would help alleviate the pain caused by tartar emetic. This drug worked miraculously to cure kala-azar patients and could well be termed as 'Brahmachari's Magic Bullet' akin to that of Paul Ehrlich (Figure 6).

U.N. Brahmachari worked tirelessly to develop urea stibamine, which he eventually synthesized in 1920. Notably, this was discovered eight years before penicillin, the world's first antibiotic. He also standardized the dose of urea stibamine at 1.5 g. Remarkably, this drug reduced the mortality rate

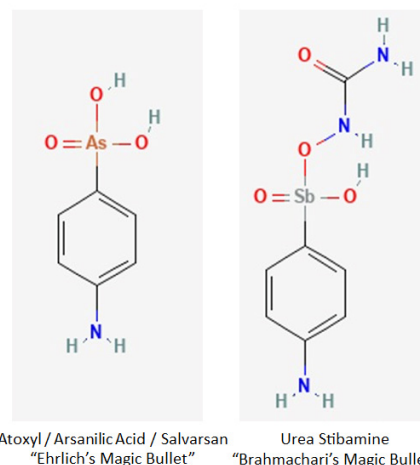


Figure 6: Chemical structure of salvarsan and urea stibamine



miraculously. In 1923, the mortality rate was a staggering 95%. However, by 1936 the mortality rate was reduced to just 7%! The drug was so successful at the time that besides India, it was also widely used in France, Greece, and China. However, U.N. Brahmachari's journey wasn't smooth sailing. It was painstaking, arduous, and labor-intensive. His path was ridden with thorns and thistles, which he had to overcome to succeed. He described the meager resources he had at his disposal. He didn't have running water, electric lighting, or even a proper gas point. Despite all these limitations, he still considered the room at Campbell Medical School, where the idea of this wonder drug dawned upon him, as a place of pilgrimage, a sacred place of worship. This room finds mention in his celebrated book '*A Treatise on Kala-azar*', published by John Bale, Son's & Danielsson Ltd., London in 1928. His dedication and devotion to his research work are encapsulated in the age-old adage '*work is worship!*'

### Recognition, Honors, Awards, and Distinctions

He received much praise and accolades from all quarters for his seminal discovery. Influential people like Dr. Henry Edward Shortt, the then Chairman of the Kala-azar Commission, and Sir John Henry Kerr, then Governor of Assam, praised him profusely, especially due to the huge numbers of lives saved by the drug.

He received many honors and awards, including the Minto Medal (1921) from the Calcutta School of Tropical Medicine, the Kaiser-I-Hind Medal (1924), as well as fellowships from the Royal Society of Medicine, London (1915), the Asiatic Society of Bengal (1921), and the National Institute of Sciences of India (1935), which is now known as the Indian National Science Academy (INSA), located in New Delhi.

He also held many distinguished positions, including President of several reputed societies, including the Asiatic Society of Bengal (1928), the Society of Biological Chemists (1932), the Indian Chemical Society (1936), and the Indian Association for the Cultivation of Science (1942). He was elected Chairman of the Indian Red Cross Society (1935), mainly for establishing India's first blood bank at the Calcutta School of Tropical Medicine. He was also elected as the General President of the 23<sup>rd</sup> Session of the Indian Science Congress (1936) held in Indore. However, the icing on the cake was being conferred two of the most prestigious titles awarded by the British Emperor in the days of the Raj, namely, *Rai Bahadur* (1924) and *Knighthood* (1935). Since then, U.N. Brahmachari has been using the prefix '*Sir*' with his name, without which his name would be incomplete, so to speak!

### The FRS and Nobel Controversies

Despite all the recognition and adulation he received, there were a couple of missed opportunities in his career. The first was not being awarded the Fellowship of the Royal Society (FRS). This is one of the oldest and most prestigious learned societies in science in the entire world. It was founded way back in 1660, and legendary scientists like Sir Isaac Newton, Sir Charles Sherrington, Sir Humphry Davy, and Sir Ernest

Rutherford, among others, were Presidents of the Royal Society at various points in its history.

In the days of the British Raj, renowned Indian scientists like Satyendra Nath Bose and Meghnad Saha became Fellows of the Royal Society (FRS). Meghnad Saha tried his level best to secure nominations from leading scientists in India for Sir U.N. Brahmachari's FRS application. However, World War II was raging at that time, and as a result, the nomination papers didn't reach London. When the war ended in September 1945, Saha, with renewed enthusiasm, started the application process again. However, within five months, on 6<sup>th</sup> February 1946, Sir U.N. Brahmachari breathed his last when his nomination papers were undergoing evaluation. Thus, due to sheer bad luck, he missed becoming an FRS, given the fact that this fellowship is not awarded posthumously.

In the case of the Nobel Prize too, which would have been India's first in the category of Physiology or Medicine, he missed the bus. He received a total of six nominations, one in 1929 and five in 1942, but still didn't get the award. One explanation could be that the nominations were quite weak, as the nominators were little-known outside Bengal, let alone across India or, for that matter, globally. Moreover, Sir U.N. Brahmachari never ventured outside India and had no research exposure abroad. Hence, he was unknown outside India. This was a big barrier in his application for the Nobel Prize. He also didn't have a so-called Godfather to provide that extra boost required to win such a coveted prize. To put things into perspective, if we look at Sir C.V. Raman, who won the 1930 Nobel Prize in Physics, he received a tremendous boost by being nominated by none other than the legendary Sir Ernest Rutherford, who was himself a Nobel Laureate. If Sir U.N. Brahmachari had received such a strong nomination, who knows, we could have got our first Nobel Laureate in medical research. Hence, much like the FRS tragedy, the Nobel Prize debacle was equally tragic.

## In Conclusion - The Unsung Hero of Indian Medical Research

It has been just over 150 years since the birth of Sir U.N. Brahmachari and close to 80 years since his death. At this juncture, one could well ask what legacy he has left behind, what impact he has had on medical research, and whether his achievements and contributions still resonate among the masses because his discovery, by and large, benefitted the deprived and downtrodden masses. While the first two questions can be summed up in a single word, '*immense*,' as for the third, one is not so sure. Experience tells us that public memory is very fickle, vacillatory, and impermanent. Therefore, it is likely that Sir U.N. Brahmachari has faded from public memory. Nevertheless, there is still much to learn from his Life, summarized in the *4 D's - Discipline, Devotion, Dedication, and Diligence*. The present article has tried to touch upon these facets of his character by blending his *Life* with his *Science*. The budding scientists of today and the scientific leaders of tomorrow stand to gain enormously from

his life story. Therefore, among a small group of people, at least, Sir U.N. Brahmachari's legacy will live on, and his name will forever be etched in their hearts.

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