# U N Brahmachari: Scientific Achievements and Nomination for the Nobel Prize and the Fellowship of the Royal Society of London

# **Rajinder Singh\* and Syamal Roy\*\***

(Received 30 July 2018)

#### Abstract

Bengal produced a number of high rank scientists, but ignored their history. One such unsung hero is Upendra Nath Brahmachari (1873–1946). Brahmachari discovered pentavalent antimonials, Urea Stibamine for the treatment of kala-azar in 1922 long before the discovery of penicillin. In the history of chemotherapy his contribution stands as major landmark. The drug effectively countered the epidemic of kala-azar during the late twentieth century in the vast track of the Gangetic plain and the Brahmaputra valley. The discovery testifies the monument of labor, knowledge and amply rewarded the clinical success it had attained. He was nominated for the Fellowship of the Royal Society of London, as well as Nobel Prize. The present communication<sup>1</sup> gives a short review about his life and scientific work.

Key words: Dermal leishmanoid, Kala-azar, Leishmania donovani, Urea Stibamine.

### **1.** INTRODUCTION

Even today kala-azar is one of the most dangerous diseases in the world (Fig. 1). Recent studies show that about 60,000 patients die annually (Haldar, 2011). A number of articles deal with the history of the disease (Thakur, 2013; Brahmachari, 1928, pp. 2–5; Gibson, 1983; Shrott, 1945; Murry, 2000; Roy, 2010, pp. 33–66; Dutta, 2003 & 2008).

Lesser known fact is that the Indian scientist Upendra Nath Brahmachari (also written as Upendranath Brahmachari) played an important role to fight against the disease by inventing a medicine. One of his contemporaries H E Shrott recalled: 'It was a dramatic success, overnight, a death rate of 90% was transformed into a cure rate



**Fig. 1.** Kala-azar patient before treatment (left) and after treatment (right) by Brahmachari (Credit: Indian Medical Gazette).

of 90%' (Richards, 1987). Unfortunately, little is known about the man who saved lives of millions of Indians. To fill the gap, the present article focuses on: 1) a short biography of Upendra Nath

<sup>&</sup>lt;sup>1</sup> Part of this work was presented by Syamal Roy in the symposium entitled "Birth of Modern Science in India: Future Challenges" organized by the Indian National Science Academy, Venue: Bose Institute, Kolkata, October 14, 2017. SR is supported by the J C Bose Fellowship, Department of Science & Technology, Govt. of India (SB/S2/JCB-65/2014).

<sup>\*</sup> Research Group - Physics Didactic and History of Science, Physics Institute, University of Oldenburg, Germany. E-mail: rajinder.singh@uni-oldenburg.de

<sup>\*\*</sup>National Institute of Pharmaceutical Education & Research, Kolkata-700054, India. Email: drsymalroy@yahoo.com

Brahmachari<sup>2</sup>, 2) Some of his scientific achievements<sup>3</sup>, and 3) Nomination for the Fellowship of the Royal Society and Medicine Nobel Prize<sup>4</sup>.

## 2. BIOGRAPHICAL SKETCH

Upendra Nath Brahmachari's birth on Dec 19, 1873 in Jamalpur, Bihar (Fig. 2) coincided with a tail end of a deadly epidemic of unknown origin which was later identified as kala-azar. The vivid memories of the epidemic, possibly may have a strong bearing that shaped his future scientific enterprise and led him to look for a cure and to understand pathogenesis of the disease process. Chemistry as well as medicine were very dear subjects to him. Brahmachari graduated from the Hooghly Mohsin College in 1893 with honours in Chemistry and Mathematics and received Thyestes medal and subsequently earned a Masters in Chemistry from the Presidency College in 1894. He studied medicine at the Medical College, Calcutta and received doctorate in Medicine (MD) in 1902. His interest was also beyond the tropical medicine and did extensive work on the haemolysis of the blood which led



**Fig. 2.** Upendra Nath Brahmachari (1873–1946). (Credit: Captain Dhruva Ray and Dr. Kawna Chatterjee, Kolkata).

him to earn his PhD in Physiology from the University of Calcutta in 1904. Thus, he had unique blend of chemistry and medicine which allowed him to see the problem of kala-azar from a different perspective.

In the 1920s, the University of Calcutta provided him research facilities at the newly founded College of Science and Technology. In a meeting C V Raman, Palit Professor of Physics, asked the authorities that the room should be vacated and given to B B Ray<sup>5</sup>, who requires it to establish X-ray spectroscopy at the University of Calcutta. At other occasion he attacked Brahmachari, who had suggested more teaching load for Professors<sup>6</sup>.

In 1927, he retired from the Government service; and joined Carmichael Medical College as Professor of Tropical Diseases. However, before that in 1924–1925, he founded the Brahmachari Research Institute, Calcutta.

Brahmachari belonged to one of the most influential and richest men in Calcutta. There was hardly any institution in Calcutta, which was not supported by him financially. For instance, he supported the journal Science and Culture, which was founded by M N Saha. He was also closely related to the Indian Association for the Cultivation of Science. In 1938 he was the Vice President of the Association (AR-IACS, 1938). In 1943, Sir UN Brahmachari Research Studentship for chemistry research at the IACS of worth Rs. 100 was established (AR-IACS, 1943). On 6th March, 1943, he, in his Presidential address - 'The beginning and the future of the IACS' suggested to sell the place and reconstruct the IACS elsewhere; so that the fields of researches can be extended. He proposed the reintroduction of subjects which were being taught in the beginning

<sup>&</sup>lt;sup>2</sup> Biographical details are taken from Mahanti, 2004; Chattopadhyay, 2002, pp. 234–235; Brahmachari, 1946.

<sup>&</sup>lt;sup>3</sup> This part of our article is largely based on Singh, 2013.

<sup>&</sup>lt;sup>4</sup> Details taken from Singh, 2014; Singh, 2016, pp. 35–44.

<sup>&</sup>lt;sup>5</sup> For Bidhu Bhushan Ray's life and work, see, Singh, 2017.

<sup>&</sup>lt;sup>6</sup> For more detail, see, Singh, 2018, pp. 112–114.

of the 20<sup>th</sup> century. Also, he suggested cooperation with other institutions in Calcutta. His plan did not materialise, as due to World War II construction material become very expensive (AR-IACS, 1942).

He held many important positions during his life time and was conferred with many awards (see below):

Elected Member of Asiatic Society of Bengal (1908).

Rai Bahadur Fellow - Royal Society of Medicine; Member of Central Malaria Committee, Bombay (1915) (Fig. 3)

Griffith Memorial Prize, University of Calcutta; Minto Medal, Calcutta School of Tropical Medicine and Hygiene (1921)

Elected Member of Council & Fellow Asiatic Society of Bengal; Secretary, Medical Section Asiatic Society of Bengal (1921).

Vice President, Asiatic Society of Bengal (1922)

Awarded Kaisar-i-Hind Gold Medal (1924)

President, Asiatic Society of Bengal (1928–1929, 1931)

Nomination for the Medicine and Physiology Nobel Prize (1929, 1942)

President of Society of Biological Chemists, India (1932, 1934–35)

Founder Fellow of the National Institute of Sciences of India (1935) (Now INSA)

President, Indian Science Congress Association;

President, Indian Chemical Society (1936)

Dean, Faculty of Science, University of Calcutta; Professor and Head, Department of Biochemistry, University College of Science, Calcutta (1939–1940)

Nomination for the Fellowship of the Royal Society London (1941–42)

President, Indian Association for the Cultivation of Science (1942)

He died on Feb. 6, 1946.

# 3. BRAHMACHARI'S SCIENTIFIC ACHIEVEMENTS

### 3.1 PhD thesis and further studies

For PhD thesis, Brahmachari submitted 'Studies in Haemolysis' at the University of Calcutta. The thesis was published in 1909. The second version was published in 1913 (Brahmachari, 1913a). Fig. 4 shows that he had high regard for his father and had good contact with the renowned Bengali Jurist and Educationist Sir A Mookerjee.

From the preface of his book, we find that in the context of studying of the haemoglobin-value of the resistant erythrocytes, he discovered a new method of testing blood. He hoped that it may be of useful in haematology (Brahmachari, 1913a). The preface also mentions that Brahmachari started this field of research under the guidance of a British scientist:

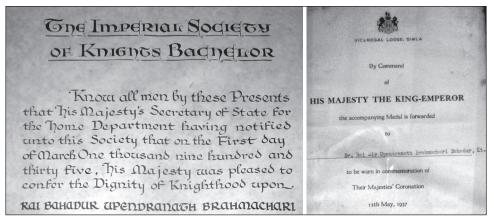


Fig. 3. Honoured as Rai Bahadur, 1915 and Knighted ,1937. (Credit: Captain Dhruva Ray and Dr. Kawna Chatterjee, Kolkata).

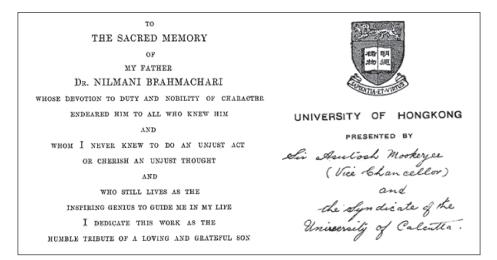


Fig. 4. Left: father-son relation. Right: Support by A Mookerjee. (Credit: University of Calcutta)

my grateful thanks are due to Major [David] McCay, I.M.S., Professor of Physiology, Medical College, Calcutta, at whose suggestion I first took up the study of the subject of haemolysis for the Ph.D. degree from Calcutta University (Brahmachari, 1913a).

Later, independently he extended this field of research, as his publications indicate (Brahmachari, 1909a; 1909b; 1911; 1912; 1913b; 1914; Brahmachari & Ghosh, 1919).

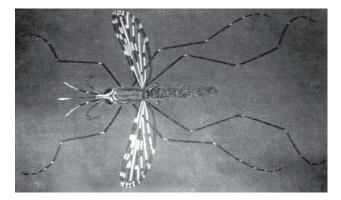
### 3.2 Studies of Anopheles

Mosquitos and flies are/were part of Indian life. From medicine point of view, the 'devilish' character of mosquitoes became clear, after the discovery by R Ross that malaria parasite is transferred by this insect. Brahmachari spent a lot of time to find out that for breeding they prefer shaded water and narrow drains (Campbell, 1902). He even discovered a new type (Fig. 5) (Brahmachari, 1912).

### 3.3. Researches in Kala-azar

# **3.3.1** The background - The spread of unknown disease and identification of the enemy

The first report of the unknown incurable epidemic came from Jessore district (now in Bangladesh) in 1824 and then the incidences



**Fig. 5.** A new anophelines species allied to Myzomyia Listoni discovered by Brahmachari. (Courtesy: Indian Medical Gazette).

started to wane and resurfaced again in Burdwan district in the Lower Bengal which is about 30 miles to east of Jessore in 1860. The mortality was devastating. The cultivation and government revenue generation were also affected. The disease was named as 'Burdwan fever'. In 1870, the Sanitary Commissioner of Bengal, Surgeon-major Charles J Jackson reported that the incidences were heaviest around the town of the Burdwan. About a decade later, in 1858, when the British Rāj formally assumed power reports of virulent form of fever started to come to the British India capital, Calcutta from Garo Hills in Assam. Sir Leonard Rogers, Director, the Calcutta School of Tropical Medicine later declared the disease as kala-azar. Kala-azar continued to spread along the Gangetic plain and the Brahmaputra valley resulting a decrease in population by 31.5% between 1891 and 1901 (Gibson, 1983). In 1898 Ronald Ross was asked to investigate kala-azar. He travelled through Assam to investigate the nature of the disease. Having examined the cases he came to a conclusion that the disease was a form of degenerated malaria. He failed to show that new disease is transmitted by the mosquito. Ross submitted his report, but doubt still persisted about the nature of the kala-azar (Ross, 1899). In medical journalism kala-azar or visceral leishmaniasis, continues to be referred as 'the Assam Fever'.

In the British Rāj, soldiers were usually treated at the Royal Victoria Hospital at Netley where William Leishman was on the staff of army Medical School. A British soldier stationed near Calcutta at Dum Dum afflicted with the unknown disease was taken to Royal Victoria Hospital at Nutley. After a few days the patient died in a state of gross emaciation and enlargement of spleen. The reports mentioned the presence of unknown parasites in the splenic smear during post-mortem. He tentatively suggested that kala- azar was a form of trypanosomiasis (Leishman, 1903). In July 1903, Charles Donovan, Professor of Physiology, Madras Medical College wrote to Ronald Ross enclosing a water sketch of unknown parasites that he had discovered in the splenic pulp and the results of autopsy from cases of remittent fever with enlarged spleen (Donovan, 1903). He asked Ross if he could recognize the parasites. Ross had sent the sketch to Leishman, who returned it stating that it appeared similar to the bodies that he had described. The new parasite is still a taxonomic orphan. In 1903, Ross jointly accrediting Leishman and Donovan for their discovery of the parasite, named it as Leishman-Donovan bodies and taxonomically designated it as Leishmania donovani (Ross, 1903).

## 3.3.2 Antimonials for the treatment of kala-azar

The first clue that heavy metal compounds could be used successfully came when Alphonse Laveran demonstrated the ability of fowlers solution (dilute arsenic trioxide) to kill trypanosomes in experimental infection (Gibaud & Jaouen, 2010, pp. 1-20). In 1912 a Brazilian doctor Gasper de Oliviera Vianna successfully used tartar emetic to cure infection of patients with a skin lesion known as Espaundia. The infection was later reported to be caused by Leishmania braziliensis (Sengupta, 1966). Backed by similar success in Sicily, it did not take long time for doctors in India to put two together and introduce tartar emetic for the treatment of kala-azar. By 1915, Leonard Rogers confirmed the efficacy; only thing left to be reckoned was with its serious toxicity (Rogers, 1915). Patients from rural areas shied away from antimony treatment and many of them neglected to go through the full course of treatment. At the suggestion of Leonard Rogers and J Dodds Price, tartar emetic was replaced by the equally effective but less toxic sodium salt which had recently been synthesized by U N Brahmachari in Calcutta. Although, it proved to be better drug in certain respects, the sodium salt had its own defects like prolong course of treatment which was difficult to reinforce and thus, success was greatly hampered by a large number of patients discontinuing the treatment (Brahmachari, 1937, pp. 53-57).

# **3.3.3** Paul Ehrlich's magic bullet and idea of chemotherapy

At the beginning of 20<sup>th</sup> century, a number of investigators had initiated extensive experiments with organo-arsenic drug, Atoxyl (amino-phenylarsenic acid or arsanilic acid) in the treatment of various diseases. HW Thomas showed that Atoxyl is effective against sleeping sickness but highly toxic for optic nerve and its further use came to a halt (Riethmiller, 1999). The Bible does not go into details about what great wedding crowd thought of Jesus when he turned water into wine. There is no record of Prometheus bringing precious fire to mankind. But Paul Ehrlich, changed a poison into saver of lives of men. One day sitting in his office peering through chemical journals like *Rosicrucian* in search of the formula for the Philosopher's stone, he came across Atoxyl which means: Not poisonous.

Paul Ehrlich, German physician and chemist came up with the opinion that Atoxyl was in reality, the sodium salt of para amino arsenic acid and is amenable for chemical modification. In 1905, Paul Ehrlich and Antoine Bechamp started to prepare many derivatives of Atoxyl and tested many of them in experimental infection of syphilis. They observed that compound 606 (Salvarsan) was the most effective to cure syphilis in infected rabbits. That was Ehrlich's day of the days and in 1910 Salvarsan was introduced for clinical use for treatment of Syphilis and soon became widely used drug for treatment. It was designated as 'Magic Bullet'- a term Paul Ehrlich had coined, meaning a compound that kills pathogen but leaves the host cell unaffected (Riethmiller, 2005). His thoughts inspired many of them worldwide including young U N Brahmachari of Calcutta.

# 3.3.4 Brahmachari and a new method for the diagnosis of kala-azar

In 1909, Brahmachari developed a method to estimate the amount of haemoglobin in the resistant corpuscles. He noted:

... while in health the relative haemoglobin-value of the erythrocytes varies within small limit; in anaemia it varies within much wider limits. ... In kala-azar it is generally below the normal, while in ankylostomiasis it is above the normal (Brahmachari, 1909b).

In Sept. 1917, while giving a preliminary report on some blood reactions in kala-azar, he wrote:

'It is frequently observed that when the blood of a kala-azar patient is mixed with excess of distilled water, a white flocculent precipitate forms. While this reaction is present in a large majority of cases of kala-azar, it has also some-times been observed in other diseases' (Brahmachari, 1917).

Three months later, he stated:

if instead of using an excess of distilled water (...) one uses two or three volumes of distilled water then the precipitate appears almost exclusively in kalaazar (Brahmachari, 1917b).

He tested the method in the case of other diseases like phthisis, malaria, dengue, and pneumonia. The results were negative. With this new data, he was able to find a new method for the diagnosis of kala-azar. He suggested the name as 'Globulin Precipitation Test.'

### 3.3.5 Discovery of Urea Stibamine

The difficulties and disadvantage of employing antimony treatment of kala-azar encouraged Brahmachari to turn his attention to study organic antimonials. The great success of the organic arsenic complex Atoxyl gave him the idea that an antimony compound obtained by replacing arsenic would be specific for kala-azar. Naturally his attempt was governed by the need to synthesize a salt which would not produce any painful effect and in fact, were led by the knowledge that the presence of urea in certain salts like urea salt. Brahmachari gave a new drug for the treatment of kala-azar after about 10 years of draughts of new development since the anti-leishmanial properties of tartar emetic had been discovered in 1913.

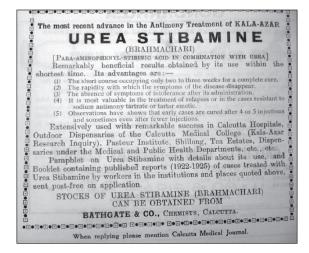
Brahmachari's publication from the year 1906 shows that from the very beginning he was interested in the study of kala-azar (Brahmachari, 1940, pp. 261–264). In 1908, he wrote on the treatment of kala-azar with Atoxyl (Brahmachari, 1908). Probably due to his work for the PhD thesis his attention was diverted. Only from 1915 onwards he intensified efforts to find out a medicine for the treatment of kala-azar. He wrote a sequence of papers on the 'Chemotherapy of antimonial compounds in kala-azar infection' (Brahmachari, 1940, pp. 11–249). In 1916, he reported to the British journal *Lancet* about his success in preparing a stable colloid and its testing for medical purposes (Brahmachari, 1916). In 1917, he summarized the researches on kala-azar and published the monograph '*Kala-azar: Its treatment*' (Brahmachari, 1925), which was republished in 1920 (Anonymous, 1920).

Preliminary observation on the preparation and therapeutic properties of such a compound, viz sodium salt of p-stibanilic acid, was communicated in 1919 to the Indian Research Fund Association and received financial assistance to carry out large number of experiments with various salts. Most of the salts were introduced intramuscularly and were found to be effective against kala-azar. Ultimately, led by the knowledge that the presence of urea in certain salts produces anaesthetic effects, he synthesized the urea salt in 1920 and named it as Urea Stibamine (the urea salt of p-stibanilic acid).

In order to sell it on mass-level Brahmachari made advertisement in local newspapers and journals (Fig. 6).

# 3.3.6 Success of Urea Stibamine

Drug trials were less comprehensive, as the drug was needed to be introduced to the public as soon as possible. In the field, the Urea Stibamine has a raging success with a cure rate of 90% and markedly less toxic than its trivalent predecessors,



**Fig. 6.** Advertisement of the Urea Stibamine in a journal. (Credit: Indian Medical Gazette).

tartar emetic. The Indian Kala-azar Commission gave a glowing testimonial to this new drug. The Director of Public Health, Assam in its annual report in 1933 states:

Urea Stibamine was our main stay in the kala-azar treatment..... since 1923, when the reliable figures for the diseases first became available to the end of year under report, no less than 328,591 persons have been brought under treatment. It is no exaggeration to say that approximately 3.25 lacs of valuable lives have been saved to the province.

Further, timely discovery of drug prevented the spread of the disease to other parts of Assam and Bengal and thus saved other parts from horrors of epidemic witnessed earlier in Assam during the period 1890–1925 (Brahmachari, 1941a). Certainly, Brahmachari had discovered what in those times amounted to the Holy Grail of kala-azar treatment.

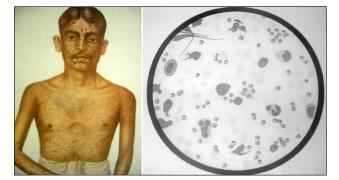
In so far as the therapy of kala-azar is concerned, the discovery of Urea Stibamine is a landmark discovery and amply rewarded by the clinical success it had attained. Brahmachari had extraordinary clinical interest coupled with cognitive skill which led him to discover 'Dermal Leishmanoid' – a skin lesion which developed in certain cases after clinical cure of kala-azar. Apart from kala-azar research Brahmachari had worked in other areas of medical importance such as malaria, filariasis, diabetes, leprosy, meningitis and haematological disorders. But his international recognition and remembrance in posterity is based on his lifelong studies on kala-azar.

H E Shrott once recalled about the success of the medicine as follows: 'It was a dramatic success, overnight, a death rate of 90% was transformed into a cure rate of 90%' (Richards, 1987). There were many more western medicines on the market. In 1932, Government of India appointed a kala-azar Commission. Its chairman was Shortt. According to the report urea stibamine and neostibosan were tested on patients in France, China, Greece and Anglo-Egyptian Sudan. It was observed that urea stibamine is superior to neostibason (Chaudhuri, 1992, pp. 198–199).

# 4. DISCOVERY OF 'DERMAL LEISHMANOID (BRAHMACHARI)'

Brahmachari's medicine saved the lives; but it had side effect. In 1922, in 'A new form of cutaneous Leishmaniasis' (Fig. 7), he stated that he observed eruptions in patients which were cured of kala-azar by him with intravenous injection of antimony. This led him 'to examine the scrapings from the cutaneous nodules of these cases... The examination of the scrapings led to the remarkable discovery that the eruptions were due to cutaneous infection by the parasites of kala-azar' (Brahmachari, 1922).

JWD Megaw, Indian Medical Services, congratulated Brahmachari for the important discovery. He even proposed the term 'Post-Antimonial Dermal Leishmaniasis' (Brahmachari) or 'Brahmachari's Dermal Leishmaniasis' (Megaw, 1922). Brahmachari's discovery was confirmed by Megaw, HW Acton and others (Acton, 1926). Brahmachari was also the first to observe that the disease can appear even during the treatment of kala-azar (Brahmachari & Dutt, 1940, pp. 207–209). Different aspects of the new disease were studied by Brahmachari and his workers (Brahmachari, Das Gupta *et al.* 1930;



**Fig. 7.** Left: Dermal Leishmanoid in a cured case of kalaazar. Right: *Leishmania Donovani* in a smear from the scrapings of the papillomatous nodules. Credit: Indian Medical Gazette.

Brahmachari & Sen *et al.*, 1930a & 1930b). For its treatment Brahmachari *et al.* tried Urea Stibamine in combination with neo-stibosan, berberine (rasaut) (Brahmachari & Banerjee, 1931).

# 5. Researches in Malaria, chemotherapy of quinoline and acridine compound

In the last part of research-life, Brahmachari worked on malaria, black fever and the studies of quinoline compounds. The latter were meant to find out proper medicines (Brahmachari, 1941b), pp. 523–556 & 571–624)). This work did not bring him fame.

# 6. Nomination for the Medicine and Physiology Nobel Prize

Detail study of Indian Nobel Prize nominators and nominees is given in 'India's Nobel Prize nominators and nominees - The praxis of nomination and geographical distribution' (Singh, 2016a & 2016b). The following information is mainly taken from it. Therein it was reported that medicine is one of the fields where Indians never received a Nobel Prize, though the nominations in medicine began much early, that is, 1907. All in all, 18 proposals were sent from India. Out of these 7 were for foreigners. Most of the Calcutta based scientists nominated their own man, U N Brahmachari; whereas other Indians preferred to propose candidates from other countries (Singh, 2016b, p. 39).

In Table 1, we see the number of persons, who were nominated as 'Indian candidates' for the Medicine Nobel Prize. In fact the only 'real Indian' was U N Brahmachari. He never received international support and even within India, his nominators were only from Calcutta.

The fact is – Brahmachari was never a serious candidate to win the Nobel Prize, because he never came in the short-list, that is, list of candidates, who are considered as the 'potential candidates',

**Table 1.** Indian nominees and the country of the nominators. The numbers in parenthesis are the number of proposals for the respective year. Year without number means that the candidate got only one nomination for that year.

Year	Nominees	Nominators' Country
1907 (2), 1917, 1929, 1930, 1931, 1934, 1935, 1940	L. Rogers	India, U.K., Switzerland, Germany, U.S.A.
1920 (2), 1937	R. McCarrison	U.K.
1929, 1942 (5)	U.N. Brahmachari	India
1937	W. Burridge	India

on whose work the Nobel Committee asks its expert to write a report.

Brahmachari was a rich man with contacts with the Calcutta elite – Bengali and British. A visit to his villa gives an impression that in good old days, it must had looked like a small palace. Records like the official honours such as Rai Bahadur etc. are well preserved by his family members. He was even knighted by the British Empire. As we shall see below, it was not the British but the Bengali physicist M N Saha, the discoverer of the Sahaionisation equation, who nominated Brahmachari for the Fellowship of the Royal Society London.

# 7. Nomination for the Fellowship of the Royal Society London

According to the rules and regulations of the Royal Society London only a Fellow of the Royal Society is allowed to nominate other scientists. The nomination certificate must be signed by the Fellows 'From Personal Knowledge' and 'From General Knowledge' (Chaudhuri & Singh, 2018). In the first half of the twentieth century only 10 Indians were elected as FRS (Kocchar, 2001). None of them was from the field of medicine. Brahmachari's work belonged to medicine as well as chemistry. S S Bhatnagar FRS (elected in 1943) could have nominated him.

On August 27, 1940, Saha wrote a letter to Birbal Sahni FRS, a paleo-botanist. In the letter it was disclosed that he (Saha) sent a statement of Brahmachari's work to different British medical men and chemists. To find a scientist from London as 'Proposer' was difficult as Brahmachari never went abroad. He asked J L Simonsen, a British chemist who had worked in India. In 1914, he was one of the founders of the Indian Science Congress (today known as Indian Science Congress Association). He agreed to be 'Proposer'. Saha got the document signed from the physicist K S Krishnan (who was proposed by the Nobel Laureate CV Raman, and elected in 1940)<sup>7</sup> and Sahni. It was a period of World War II. Post was an uncertain matter. The nomination certificate sent by Saha never reached London.

Saha's letter to Sahni of April 9, 1941, indicates that in the beginning of 1941 Simonsen signed and sent a new form to Saha for further processing; that is, to get signed from different Fellows and post it to London.

According to the bye laws of the Society, the candidate can be supported either 'From Personal Knowledge' or 'From General Knowledge'. Here the former means that the nominator is able to judge the scientific work of the nominee. K S Krishnan was hesitant to sign the certificate 'From Personal Knowledge'. Sahni seemed to be in the same dilemma; as Saha's letter to Sahni indicated. For instance, he asked Sahni to read the issues of *Science and Culture* (March 1940, April 1940 and March 1941) in which Brahmachari's work on kala-azar was published. Saha wrote that if he (Sahni) has pangs of conscience for putting his signature under the heading 'Personal Know-

<sup>7</sup>For K S Krishnan's nomination and election, see, (Singh 2004, pp. 172-173).

Sahs showed me the letter he wrote to you about Brahmachari and I endorse every word of it. His work has a high value on the scientific side but its effect on the stamping out of a fell disease has been immense. I shall be glad to talk to Sir Henry Dale about it when I come to London. I sincerely hope that the Council will see its way in nominating him this year. With heat ngan to for hot for hot ? " Yours sincerely. I. P. Bulug

Fig. 8. A part of S S Bhatnagar's letter to A V Hill (Credit: Archive Royal Society London).

ledge', he can sign the certificate 'From General Knowledge'.

According to the record of the Royal Society of London, Brahmachari's nomination certificate was delivered to the society on June 23<sup>rd</sup>, 1941. His nomination certificate in part reads:

Distinguished for his investigation in chemotherapy and the treatment of tropical diseases. Introduced the use of Urea Stibamine in the treatment of kala-azar. He is the author of 'Studies in Haemolysis', 'Treatise on Kala-azar', and some 144 publications.

His affiliation given in the certificate was Professor of Biochemistry, University of Calcutta and Professor of Tropical Medicine Carmichael Medical College.

Brahmachari's 'Proposer' was the chemist J L Simonsen and 'Seconder' – M N Saha. Other Fellows who supported 'From Personal Knowledge' were: K S Krishnan, B Sahni, J W W Stephens, L L Fermor and R B S Sewell. Three other Fellows who supported the case 'From General Knowledge' were: C S Gibson, F G Donnan and J C G Ledingham.

Bhatnagar's letter to A V Hill, dated June 10, 1944 (Fig. 8) shows that he was asked by Saha to support the nomination. From the letter it is evident that Bhatnagar was not interested in signing the nomination certificate. As we have seen above, indeed, he did not support Brahma-chari's case. While Saha was finding support from British man of science, nearly at the same time, that is, 1939, Leonard Rogers started propaganda against Brahmachari. It cannot be seen as per-chance. Since Rogers was in the Indian Medical Services, he played major role in establishing the Calcutta School of Tropical Medicine (Dasgupta, 2011, pp. 591–622). He was well-known in India and England. His attitude towards Indians was that of a paternalist (Power, 1996). Rogers' protégé J W D Megaw, Director, Kolkata School of Tropical Medicine favoured Neostibosan and opposed investigation with Urea Stibamine (Chaudhuri, 1992, pp. 198–199). Not surprisingly, Brahmachari and Rogers were not in good terms with each other.

Shortly before Brahmachari's nomination, Rogers wrote some notorious letter about Brahmachari. He stated that: (i) the exact content of the product was not made public. (ii) It was patented by Brahmachari in 1921. (iii) Compared to other medicine stibosan it was 160 times expensive. Thus, not in the reach of poor people of India (Rogers, 1939). Brahmachari refuted these claims in two letters to *Nature* (Brahmachari, 1940a & 1940b). Rogers' letter influenced the British scientific community, whereas Brahmachari's letters remained unnoticed as the following incidence shows.

As discussed elsewhere, about Brahmachari's nomination for the Fellowship of Royal Society,

Memorandum to Sir Henry Dale on Brahmachari's work. 93 HO 5.3.92 Brahmachari's published work includes chemical papers describing a number of substances, many new, prepared for use in the chemotherapy of kala-azar and malaria<sup>(1)</sup>. The majority of these are joint publications with Indian chemists, but the kala-azar remedy "urea stibamine" with which his name is chiefly associated, since it has been used on a large scale and generally accepted as a useful drug, seems to have been made by Brahmachari himself.

Fig. 9. A part of Memorandum on Brahmachari's work written by Saha and sent to the President of the Royal Society London. (Credit: Royal Society London).

Saha talked to A V Hill, Secretary of the Royal Society, who visited India in the beginning of the 1940s. On April 14<sup>th</sup> 1944, Hill wrote to H H Dale, President of the Royal Society:

Here are the papers which Saha wanted you to see about Brahmachari (Fig. 9). I told him that I did not feel qualified myself to judge the merits of the controversy. I should have to ask the "expert" if call onto do so. <u>You</u> could scarcely get away on that excuse! (underlined in original). And further, "I must say that Leonard Rogers was a bit spiteful to say urea stibamine was patented if it wasn't: that must be a question of fact. But some of Rogers' statements <u>are a</u> bit wild" (underlined in original).

After the facts of the Rogers-Brahmachari controversy were clear, the Royal Society decided to ask for the opinions of the experts on Brahmachari's work. J L Simonsen knew the Indian scenario well, as for a long time he lived in India. In 1943, he was appointed as the Director of the Colonial Products Research Council, London. From 1942 to 1944 he served on the Council of the Royal Society (Robinson, 1960). In a letter of May 25, 1944 to Hill, he evaluated Brahmachari's discovery of the Urea Stibamine 'probably more by luck than by good management'. Still he saw it as a fine achievement. He defended Brahmachari made his findings public; and there is nothing to object

if Brahmachari made money with his private practices and by selling antimony compound under his direction. In the same letter he added: "I feel that Rogers is somewhat unfair; he himself is and was a wealthy man as the result of his large consulting practice, due of course, to the brilliant research work which he did whilst in Calcutta". In spite of these facts, he was not of the opinion that Brahmachari deserves to be an FRS. In the letter, he opined:

As a chemist I do not think that Brahmachari has any claim to election. His later work on anti-malarial which he directed and carried was carried out by assistants is mediocre and is no contribution to science.

He practically withdrew his support by stating that:

His nomination was based solely on his (Brahmachari's) contribution to the kala-azar problem. As you are aware I have not pressed his claims during the past two years because I felt it desirable that these be put forward by others more competent to judge his merits. He is of course now an old man practically 69, so he is not likely to make any further contribution to science.

In spite of this negative report by Simonsen, Dale and Hill thought it worth to ask other expert, that is, W H Gray who had studied Urea Stibamine and other chemical products. On November 9,

1944, he wrote a report. Referring to Brahmachari's books 'Gleanings from my Researches', Vols. I & II, Gray wrote that Brahmachari's work on the chemotherapy of the kala-azar and malaria, is written with other chemists, but the remedy of kala-azar by 'Urea Stibamine' is mainly associated with his name. Gray, further observed that in a paper in the Indian Journal of Medical Researches (10, 508, 1922) Brahmachari's conclusions about the nature of the product were open to criticism from a chemist's point of view. Also in the second paper in Indian J. Med. Res. (12, 423, 1924), Brahmachari gave quite a different composition of the drug 'namely that of the carbamide of ammonium p-aminophenyl-stibonate, again without adequate evidence'. Gray's criticism was limited to the composition of the product. He concluded.

This criticism does not detract from the credit due to Brahmachari for the discovery of this useful drug. It does rather appear that the discovery was a very fortunate one for him. So far, his painstaking work on the chemotherapy has not met with a like success.

As the nomination form shows, in 1945 Brahmachari's case was suspended (which means that the certificate was displayed in the building of the Royal Society). This also suggested that his case was discussed in the meeting. Unfortunately such a record is not kept or made public by the society. The facts are that according to the 'Directions for filling up of the Certificate' – A certificate terminates if, either candidates 'Proposer' or 'Seconder' withdraw the name or a limit period of 5 years has lapsed. This was not in the case of Brahmachari. Unfortunately he died in February 1946. It is a matter of speculation that Brahmachari would have become the first Indian medical academic to become an FRS.

## **8.** CONCLUSION

The Brahmachari's case revealed that as no Indian from the field of medicine was elected as FRS, nobody could nominate him. Physicist Saha tried to solve the problem by nominating him for achievements in chemistry. Three Indian FRS who signed the certificate 'From Personal Knowledge' were not from this field, thus not trustworthy to judge the scientific work of their candidate.

The chemists, that is, the experts of the Royal Society in their reports wrote more about the constituents of the Urea Stibamine than the saving of millions of lives by the use of medicine, which was discovered by Brahmachari.

Rogers' letter in the renowned journal *Nature* left wrong impressions on the minds of the Royal Society authorities. It was rectified only after private communication between A V Hill and M N Saha. There is no doubt that without these contacts, the authorities would never had taken trouble to check the truth of Rogers' statement; and ask experts to write report on Brahmachari's work.

Brahmachari never went abroad. Without Saha's influence it would have been impossible to find Fellows of the Royal Society to support Brahmachari's certificate.

This also shows that a country like India, where the number of Fellows of the Royal Society is not high enough, the Proposer and Seconder have difficulty to find support for the nomination of a candidate.

#### **ACKNOWLEDGEMENTS**

Since 2016 we are in contact with family members of Sir U N Brahmachari. We are thankful to Captain Dhruva Ray and his mother-in-law Dr. Kawna Chatterjee, who welcomed us and allowed to photograph various objects.

We are thankful to Mrs. Joanna Cordes and Joanna Hopkins of Archive Royal Society London for sending the documents referred to in the paper. Thanks are due to Subhra Kumar Mukhopadhyay (Hooghly Mohsin College, Chinsurah), Mihir Kumar Chakrabarti, Paresh Pal (Asiatic Society of Bengal) and Martina-Christine Koschwitz, (Bernhard Nocht Institute for Tropical Medicine, Hamburg) for sending documents. We are grateful for the support from Michael Komorek (Head of the Research Group: Physics Education and History of Science, University of Oldenburg).

#### **BIBLIOGRAPHY**

- Acton, H W and Napier, L E. Post-kala-azar dermal leishmaniasis, *Ind. J. Med. Res.*, 15(1926): 15–97.
- Annual Report Indian Association for the Cultivation of Science (Abb. AR-IACS), 1938, 1942 and 1943.
- Anonymous, Kala-azar and its treatment, by Upendranath Brahmachari, *Br. Med. J.*, 2 (1920): 324.
- Brahmachari, P N. Sir Upendranath Brahmachari, Biog. Mem. Fellow of INSA, 4(1946): 8–42.
- Brahmachari, U. Sporadic kala-azar in Calcutta, with notes of a case treated with atoxyl, *Br. Med. J.*, 1(1908): 1286–1288.
- Brahmachari, U. Some observations on the haemolysis of blood by hyposmotic and hyperosmotic solutions of sodium chloride, *Biochem. J.*, 4(1909a): 59–65.
- Brahmachari, U. On the relative haemoglobin-value of the resistance erythrocytes during the haemolysis of blood with hyposmotic sodium chloride solution, and on the permeability of the erythrocytes of water as a factor in the production of haemolysis, *Biochem. J.*, 4(1909b): 280–285.
- Brahmachari, U. The law regulating haemolysis of erythrocytes in hyposmotic saline solution or distilled water, *Biochem. J.*, 5(1911): 291–293.
- Brahmachari, U. On some new anophelines of Calcutta and on the seasonal prevalence and variations of anopheles fuliginous of Calcutta, *Ind. Med. Gaz.*, 47(1912): 186– 187.
- Brahmachari, U. On the freezing point of the unhaemolysed corpuscles during haemolysis of blood and on the effects of evaporation on the resistance of erythrocytes to haemolysis, *Biochem. J.*, 6(1912): 76–78.
- Brahmachari, U. *Studies in haemolysis*, University of Calcutta, Calcutta, 1913a.
- Brahmachari, U. An investigation into the physicochemical mechanism of haemolysis by specific haemolysins (Preliminary communication), *Biochem. J.*, 7(1913b): 562–567.

- Brahmachari, U. An investigation into the physicochemical mechanism of haemolysis by specific haemolysins, No. II, The corpuscles and the action of inorganic ferments or metal-sols upon them, *Biochem. J.*, 8(1914): 227–229.
- Brahmachari, U. Preparation of stable colloidal antimony, *Lancet*, 188(1916): 728.
- Brahmachari, U. Fourth report on the treatment of kala-azar and some blood reactions in this disease, *Ind. Med. Gaz.*, 52(1917a): 319–322.
- Brahmachari, U. On the presence of an easily precipitable anti-complementary globulin-like substance in human serum and its importance in the diagnosis of kala-azar, *Ind. Med. Gaz.*, 53(1917b): 429–431.
- Brahmachari, U and Ghosh, S N. The bacteriology of the blood and the treatment of influenza occurring epidemically in Calcutta, *Ind. Med. Gaz.*, 54(1919): 90–92.
- Brahmachari, U. A new form of cutaneous Leishmaniosis -Dermal Leishmanoid, *Ind. Med. Gaz.*, 57(1922): 125– 127.
- Brahmachari, U. *Kala-azar: Its treatment*, Butterworth & Co. Ltd., Calcutta, 1925.
- Brahmachari, U. A treatise on kala-azar, John Bale, Sons & Danielsson, Ltd., London, 1928.
- Brahmachari, U. Campaign against kala-azar in India, Jubilee publications, on 80<sup>th</sup> Birthday of Dr. Prof. Bernhard Nocht, Hamburg, 1937.
- Brahmachari, U. Antimony treatment of kala-azar, *Nature*, 145(1940a): 546.
- Brahmachari, U. Chemistry of urea stibamine, *Nature*, 145(1940b): 1021–1022.
- Brahmachari, U. *Gleanings from my researches*, Vol. I, Kalaazar, its chemotherapy, University of Calcutta, Calcutta, 1940.
- Brahmachari, U. Note on the history of treatment of kalaazar with urea Stibamine, *J. Trop Med & Hyg.*, 44(1941a): 67–72.
- Brahmachari, U. *Gleanings from my researches*, Vol. II, Malaria, haemolysis and other subjects, University of Calcutta, Calcutta, 1941b.
- Brahmachari, U and Banerjee, R. Studies in kala-azar and chemotherapy of antimony, Part V, The treatment of resistant cases of Dermal leishmanoid, *Trans. R. Soc. Trop. Med. & Hyg.*, 24(1931): 565–567.

- Brahmachari, U; Das Gupta, J M; Banerjea, R and Basu, B. Studies in Kala-azar and chemotherapy of antimony, Part II, Treatment of kala-azar with intramuscular injection of sodium N-phenyglycineamide-4-stibinate, *Trans. R. Soc. Trop. Med. & Hyg.*, 23(1930): 617– 622.
- Brahmachari, U and Dutt, A M. Chemotherapy of antimonial compounds in kala-azar infection, Part 3 (New series.), Dermal leishmanoid with positive flagellate culture from the peripheral blood, *Ind J. Med.*, Feb. 1927 In *Gleanings from my researches*, Vol. I, Brahmachari, U (Ed.), University of Calcutta, Calcutta, 1940, pp 207–209.
- Brahmachari, U and Ghosh, S N. The bacteriology of the blood and the treatment of influenza occurring epidemically in Calcutta, *Ind. Med. Gaz.*, 54(1919): 90–92.
- Brahmachari, U; Sen, P B and Banerjea, R. Studies in Kalaazar and chemotherapy of antimony, Part IV, Further observations on the antimony-laden cells of spleen after intravenous injection of metallic antimony in a state of fine suspension in experimental animals, *Trans. R. Soc. Trop. Med. & Hyg.*, 24(1930a): 351–352.
- Brahmachari, U; Sen, P B and Banerjea, R. Studies in Kalaazar and chemotherapy of antimony, Part III, Observations of antimony in the spleen cells of animals infected with *Leishmania donovani*, *Trans. R. Soc. Trop. Med.* & *Hyg.*, 23(1930b): 623–626.
- Campbell, R N and Brahmachari, U. A preliminary report on observations of the habits of anopheles, *Ind. Med. Gaz.*, 37(1902): 12–15.
- Chattopadhyay, A. *Biographical dictionary of Indian* scientists - From ancient to contemporary, Rupa Co., New Delhi, 2002.
- Chaudhuri, A R and Singh, R. The FRS nomination for Sir Prafulla C. Ray and correspondence of N R Dhar, *Notes and Records, Royal Soc. London*, 72(2018): 57– 73.
- Chaudhuri, J C. Indian Fellows of the Royal Society and others, Academic publishers Calcutta, Calcutta, 1992.
- Dasgupta, U (Ed.). Science and modern India: An institutional history, c. 1784-1947, History of science, philosophy and culture in Indian civilization, Vol. XV, Part 4, Center for studies in Civilization, Delhi, 2011.
- Donovan, C. Memoranda, on the possibility of occurrence of Trypanosomoasis in India, *British Medical Journal*, 2 (1903): 79.

- Dutta, A K. Pursuits of medical knowledge: Charles Donovan (1863-1951) on kala-azar in India, *J Med Biography*, 16 (2008): 72–76.
- Dutta, A K. A social history of an epidemic: Kala-azar in colonial Northeastern India, 1875–1947, *Wellcome History*, 23(2003): 4–5.
- Gibaud, S and Jaouen, G. Arsenic-Based Drugs: From Fowler's Solution to Modern Anticancer Chemotherapy. In Jaouen G., Metzler-Nolte N. (eds) *Medicinal Organometallic Chemistry - Topics in Organometallic Chemistry*, Vol 32, Springer, Berlin, Heidelberg, 2010.
- Gibson, M E. The identification of kala-azar and the discovery of Leishmania donovani, *Medical History*, 27 (1983): 203–213.
- Haldar, A K; Sen, P and Roy S. Use of antimony in the treatment of Leishmaniasis: Current status and future directions, *Molecular Biology International*, (2011): 1–23. (http://dx.doi.org/10.4061/2011/571242).
- Kar, B. The Assam Fever, *Wellcome History*, 23(2003): 2–3.
- Kocchar, R. Indian Fellows of the Royal Society, London (1841–2000), *Curr. Sci.*, 80(2001): 721–722.
- Leishman, W. On the possibility of the occurrence of Trypanosomiasis in India, *British Medical Journal*, 1(1903): 1252–1254.
- Mahanti, S. Upendra Nath Brahmachari A pioneer of modern medicine in India, *Dream*, 2047(2004): 31–34.
- Megaw, J W D. A note on a new disease "Dermal Leishmaniasis" (Brahmachari), *Ind. Med. Gaz.*, 57(1922): 128.
- Murray, H W. Treatment of visceral Leishmaniasis (Kalaazar): A decade of progress and future approaches, *Int. J. Infectious Diseases*, 4(2000): 158–177.
- Power, H. The Calcutta School of Tropical Medicine: Institutionalizing medical research in the periphery, *Med. Hist.*, 40(1996): 197–214.
- Richards, T. Doctor, soldier, scientist and shikari, *Br. Med. J.*, 294 (1987): 1669–1670.
- Riethmiller, S. Ehrlich, Bertheim, and Atoxyl: The origin of modern chemotherapy, *Bull. Hist. Chem.*, 23(1999): 28–33.
- Riethmiller, S. From atoxyl to salvarson: searching for magic bullet, *Chemotherapy*, 51(2005): 234–242.

- Robinson, R. John Lionel Simonsen (1884–1957), *Biogr. Mem. Fell. R. Soc. Lond.*, 5(1960): 237–252.
- Rogers, L. Tartar emetic in kala-azar, *British Med. J.*, 2(1915): 197.
- Rogers, L. The antimony treatment of kala-azar, *Nature*, 144(1939): 1003–1004.
- Ross, R. Further notes on Leishman's bodies, *British* Medical Journal, 2(1903): 1401.
- Ross, R. *Report on the nature of kala-azar*, Office of the Superintendent of Government Printing, Calcutta, India, 1899.
- Roy, S. Research in Tropical Diseases in India with special reference to leishmaniasis and filaria. In Burma, D P& Chakraborty, M. (eds), *History of Science*, *philosophy and culture in Indian Civilization*, Pearson Longman, New Delhi, 2010.
- Sengupta, P C. Presidential address, Section of Medical and Veterinary Sciences, 53rd Indian Science Congress, Chandigarh, (1966): 1–12.
- Shortt, H E. Recent research on kala-azar in India, *Trans. R. Soc. Trop. Med. Hyg.*, 39(1945): 13–31.

- Singh, R. Nobel Laureate C.V. Raman's work on light scattering - Historical contributions to a scientific biography, Logos Verlag Berlin, Berlin, 2004.
- Singh, R. Upendranath Brahmachari A pioneer of tropical diseases: A summary of his discoveries and scientific work, Shaker Verlag, Aachen, 2013.
- Singh, R. Sir Upendranath Brahmachari and the Fellowship of the Royal Society of London, *Sci. Cult.*, 80(2014): 29–37.
- Singh, R. *Die Nobelpreise und die indische Elite*, Shaker Verlag, Aachen, 2016a.
- Singh, R. India's Nobel Prize nominators and nominees -The praxis of nomination and geographical distribution, Shaker Verlag, Aachen, 2016b.
- Singh, R. Bidhu Bhushan Ray A pioneer of x-ray spectroscopy, Shaker Publisher, Aachen, 2017.
- Singh, R. C.V. Raman's laboratory and discovery of the Raman effect, Shaker Publisher Aachen, 2018.
- Thakur, C P. History of kala-azar,http://www.who.int/ global\_health\_histories/seminars/presentation35a.pdf, May 1, 2013.