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# Historical Review

## HENRY BENCE JONES – PHYSICIAN, CHEMIST, SCIENTIST AND BIOGRAPHER: A MAN FOR ALL SEASONS

The name Bence Jones is recognized today as the name of a protein excreted by patients with multiple myeloma. It is ironic that Bence Jones was not the first to describe the characteristics of the protein, but he recognized its place in the diagnosis of myeloma when he wrote, 'I need hardly remark on the importance of seeking for this oxide of albumen in other cases of mollities ossium' (Bence Jones, 1847). J. F. Heller (1846) had described a protein in the urine that precipitated when warmed a little above 50°C, and then disappeared on further heating. Although Heller did not recognize the precipitation of the protein when the urine was cooled, it is almost certain that this was Bence Jones protein. He differentiated this new protein from albumin and casein. It should be noted that the term 'albumen' had been introduced less than a decade earlier.

Both Thomas Watson, a well-known physician in London, and William Macintyre had sent a urine sample from a patient, Thomas Alexander McBean, to Henry Bence Jones. Dr Macintyre had examined the patient's urine on 30 October 1845 because the patient had had oedema 4 months earlier. Macintyre's examination revealed no sugar, but the urine was opaque, acid and of high density, and its specific gravity was 1·035. The urine, when heated, was found to 'abound in animal matter.' A precipitate developed after the addition of nitric acid. The precipitate 'underwent complete solution on the application of heat, but again consolidated on cooling' (Macintyre, 1850).

The next day, Dr Watson sent a urine sample and the following note to Henry Bence Jones, a 31-year-old physician at St. George's Hospital, who had already established a reputation as a clinical chemist.

Saturday, Nov. 1st 1845 Dear Dr Jones, The tube contains urine of very high specific gravity. When boiled it becomes slightly opaque. On the addition of nitric acid, it effervesces, assumes a reddish hue, and becomes quite clear; but as it cools, assumes the consistence and appearance which you see. Heat reliquifies it. What is it? Dr Macintyre, a 53-year-old Harley Street consultant and physician to the Metropolitan Convalescent Institution and to the Western General Dispensary, St. Marylebone, had cared for the patient, Thomas Alexander McBean, intermittently for over a year. In September 1844, McBean jumped out of an underground cavern on his country holiday and 'instantly felt as if something had snapped or given way within the chest, and for some minutes he lay in intense agony unable to stir' (Macintyre, 1850). Macintyre applied a strengthening plaster to his chest. This was of only temporary benefit. He was subsequently treated with the removal of a pound of blood and application of leeches, and his pain resolved. He had a relapse during the spring of 1845 and responded well to a course of steel and quinine. He again had a relapse and was cared for by Macintyre and Watson, but his disease progressed and he died on 1 January 1846 (Kyle, 2000). An autopsy revealed soft and brittle bones that were filled with a 'gelatiniform substance' (Macintyre, 1850). Microscopic examination of the bone marrow revealed cells with the features of plasma cells (Dalrymple, 1846).

Bence Jones noted that the addition of nitric acid produced a precipitate that was redissolved by heat and formed again on cooling, an observation which confirmed the findings of Watson and Macintyre. Jones concluded that the protein was an 'oxide of albumen' and from the ultimate analysis was the 'hydrated deutoxide of albumen' (Bence Jones, 1847, 1848). He believed that chlorine was responsible for the formation of this protein. He calculated that there were 66·97 parts of hydrated deutoxide of albumin per 1000 parts of urine, and this amount was equivalent to the protein of albumin in normal blood. Thus, every ounce of urine contained the same amount of protein as an equal quantity of blood (Bence Jones, 1847, 1848).

Some have suggested that the term 'multiple myeloma' should be designated as McBean's disease with Macintyre's proteinuria. Although Bence Jones was not the first to recognize the heat properties of the urine, he recognized its importance in patients with skeletal disease.

### EARLY LIFE

Henry Bence Jones was born on 31 December 1813 at Thorington Hall in Yoxford, Suffolk, England, to Matilda Bence and Lieutenant Colonel William Jones. The home was lent to the family by Jones' maternal grandfather, Reverend Mr Bence Sparrow, Rector of Beccles. Mr Sparrow adopted the surname Bence in May 1804 and was thus known as Rev. Bence Bence (Bence Jones, 1929). The Bence family was related to the Winthrops of colonial America, including John Winthrop, the first governor of Connecticut, and also to the Bowdoins, including James Bowdoin, the first president of the American Academy of Arts and Sciences. Henry Bence Jones' father, William, originated from Cork, Ireland, and served in the Fifth Dragoon Guards and fought in the Peninsular War at Salamanca.

When young, Henry fell and fractured his left arm at the

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elbow at the age of 6 or 7; it required a year for recovery. At age 8, he went to school at Hingham, Norfolk, and he then went to private school in Putney in preparation for Harrow. He said that he learned little at Putney but enjoyed walking in Wimbledon Park. He entered Harrow in 1827, when it had fewer than 150 boys enrolled. In his words, he became a good 'cricketer, football and racquet player, and in all games took an immense delight' (Bence Jones, 1929). He became the best player in the school. He took a tutor, Rev. Hartwell Horne, for the study of Euclid and algebra. He did well with Euclid but not with algebra. He entered Trinity College, Cambridge. He joined the Second Trinity Crew and rowed number 5. He worked hard but was placed only in the third class and took no first-class honours. He hired a tutor for Hebrew but made little progress. He attended the Divinity Lectures and obtained a certificate for ordination but did not pursue a career in the church.

## MEDICAL SCHOOL

Obtaining his degree in January 1836, Jones joined his father who was living in London. Henry considered emigrating to New Zealand, and actually proceeded with the papers but did not go further. His father suggested that he study for a year with a general practitioner, Mr Worthington, but a surgeon at St. George's Hospital (Mr George Babington) introduced Jones to Mr John Hammerton, an apothecary. Jones prepared medicines in the apothecary shop under Mr Hammerton for 6 months. He later said that this 'was of the utmost use to me all my life' (Bence Jones, 1929). He became a pupil in the medical school at St. George's Hospital on 1 October 1838, and began attending lectures in the dissecting room. He worked as a dresser in the surgeon's ward but later returned to the physician's ward. He did his utmost to learn about the stethoscope from Dr James Hope, an assistant physician at St. George's. Jones commented that 'the glorious discoveries of Dr Bright were not valued by any of our medical men' (Bence Jones, 1929). Jones also attended the lectures of Michael Faraday on electricity at the Royal Institution.

St. George's Hospital was established in 1733 in the village of Knightsbridge, which was noted for its clean air. The Medical School was founded in 1831, with a faculty including John Hunter, Edward Jenner, Thomas Young and Henry Gray (anatomist). During World War II a 1000-pound bomb fell on the lecture theatre of the Medical School but it did not explode. The hospital moved to Tooting in 1980.

Jones developed rheumatic fever in the spring of 1839 and went home for 6 weeks and 'recovered without complications of disease of the heart' (Bence Jones, 1929). He returned to London but still felt very weak. He enrolled as a private pupil to Professor Thomas Graham, the father of colloid chemistry, at University College, but most of the teaching was done by his assistant, George Fownes (1815–49). Fownes had studied with Justus von Liebig in Giessen, Germany. The cost of the year's 'pupilage' was £50, which Jones had obtained as a small legacy. Fownes taught Jones the principles of organic analysis, which led to his analysis of the sulphur in a cystine oxide calculus. This resulted in his first medical paper, which was awarded a 'place' in the Philosophical Transactions.

He passed the examinations of the College of Physicians, which was competing with the new London University. He was admitted in the spring of 1841 as a licentiate of the college, but had no university degree. He left London on Easter Sunday 1841 for Giessen, Germany, where he studied in Liebig's laboratory for 6 months. There, he learned advanced analytical methods and analysed the proteins in the brain and egg yolk, which led to a paper in Liebig's *Annalen* (Putnam, 1993). This experience resulted in a lifelong desire to apply chemistry to medicine. Jones was influenced by Liebig's teachings and remained in contact with him throughout his life. Interestingly, Liebig and Jones died 2 days apart, in April 1873, and their obituaries were in the same issue of *Lancet*.

Returning to London, Jones studied in the physicians' wards at St. George's Hospital and then went home to Lowestoft. He proposed to his second cousin, Lady Millicent, daughter of the Earl of Gosford. After difficulties, which were overcome with the aid of Lady Byron (widow of the poet), they were married in May 1842. He and his bride spent some months with Lady Olivia Sparrow at Brampton and, while there, he went to Cambridge and took his M.A. degree. He returned to London on 1 October and began his work at St. George's. He was asked to analyse and catalogue the calculi in the Museum of University College Hospital. Working in a small laboratory in his home, he analysed the calculi and published his second paper. Fownes had been asked to teach a course at Middlesex Hospital but was too busy. He therefore asked Jones to give the 100 lectures to the 'six attentive pupils' (Bence Jones, 1929) beginning in Autumn 1843. Jones said that 'in preparation for these lectures, I acquired more practical knowledge of chemistry than I could possibly have done in any other way' (Bence Jones, 1929). In 1843, he began a systematic study of the chemical composition of the urine in health and disease. He became a member of the Council of the College of Chemistry, founded in 1845 by Sir James Clarke.

In December 1845, he obtained an assistant physicianship at St. George's. The following year, another vacancy occurred, and he became a full physician at the hospital. He was elected a Fellow of the College of Physicians in 1845, and delivered the Gouldstonian Lectures in 1846. He was elected a Fellow of the Royal Society in 1846 with the help of Professors Fownes and Graham. He went to Cambridge and took his degree in medicine in 1846.

'Each year my practice gradually increased and I endeavoured to let no year pass without doing something original in natural science as applied to medicine' (Bence Jones, 1929) (Fig 1). He purchased a home near Folkestone, where he stayed in the summers, but he went frequently to the Continent for 3–4 weeks, visiting baths and spas, including Evian, France. He took his wife and two older children to Chamonix, France, in 1854, but his wife was tired and barely got back to Paris. Consequently, in the future, he travelled alone or with his eldest son. He and his wife had seven children but only one grandchild.

## MEDICAL CONTRIBUTIONS

In early 19th-century England, there was considerable interest in chemistry, and many believed that a knowledge of animal chemistry could be translated to humans and result in improved medical practice. Despite this, most medical schools neglected the physical sciences, and students continued to be instructed in the classics. In fact, Jones believed that medicine would be better served if students spent more time acquiring knowledge of chemistry and physics than Latin and Greek. Michael Faraday, the London bookbinder who became one of the world's greatest scientists, gave lectures on electricity for the medical students.

Jones published a series of journal articles on the sediment, uric acid, calcium oxalate and the alkaline and earthy phosphates of urine. He gave a series of lectures at the conclusion of the course on chemistry at St. George's Hospital in 1849, where the lectures were published the next year as a book *Of Animal Chemistry*. In 1851–52, the *Medical Times and Gazette* printed 18 lectures on digestion, respiration and secretion which Jones had given at St. George's Hospital. Many of his lectures were printed in medical journals, and some of his papers were published in duplicate in several British journals. In addition, some of his articles were translated into German or French, and published in European journals. Jones also translated and edited several books from German. His extensive obituary in the *Medical Times and Gazette* listed 34 papers and six additional articles. However, no accurate, complete bibliography exists.

**Fig. 1.** Portrait of Henry Bence Jones. [From Snapper, I. & Kahn, A. (1971) *Myelomatosis: Fundamentals and Clinical Features*. University Park Press, Baltimore. By permission of S. Karger.]

Jones emphasized the frequency of diabetes in an older population. Eleven of his 29 patients with diabetes were older than 60 years (Bence Jones, 1853). He noted that diabetes in the elderly occurred frequently without marked symptoms. He also noted that diabetes may be detected far more frequently in the elderly than at any other time of life. He advocated small meals free of sugar and acid as the best diet (Bence Jones, 1853). He also noted that sugar was still found in the urine despite withholding sugar-containing foods (Rosenfeld, 1987). He observed that ammonium salts given as medication produced increased acidity of the urine (Coley, 1973). He was the first to describe xanthine crystals in the urine, and differentiated them from uric acid crystals (Bence Jones, 1862).

Jones believed that medication must diffuse throughout tissue before it could produce an effect. He thought that it would be valuable to know the rates of diffusion and the amount of time that the medication was present in the body. Jones and August Dupré gave guinea pigs small doses of lithium carbonate, orally or subcutaneously, and sacrificed them at intervals of a few minutes to several days. Spectrum analysis detected lithium in vascular tissues, the cartilage of the hip joint and the humours of the eye within 15 min. In one-half hour, it appeared in the lens of the eye. Jones and Dupré extended their studies to quinine and noted that quinine had 'passed into all of the vascular, and most probably into the extravascular textures' (Bence Jones & Dupré, 1866) of guinea pigs within 15 min of ingestion of the drug. They extended their studies to humans, and found that quinine was detectable in the urine 10–20 min after ingestion, and had attained a maximal level in tissues at 3 h. Thus, Jones introduced the use of biochemical tracers in medicine.

## PERSONAL HABITS

Jones began his laboratory work each day at 6:00 am. and arrived at the hospital at about 1:00 pm. for ward rounds (Obituary, 1873a). According to Sir Clifford Allbutt, in a lecture to medical students at St. George's in 1922, few students sought a clerkship with Dr Jones because of his 'scandalous unpunctuality.' As Allbutt, the medical student, was waiting at the stair head, he saw Jones 'bounding up the steps two or three at a time, an hour or an hour and a half too late...first appeared the silvery head, then the handsome presence, the sanguine and vivid countenance, the blue eyes; then came the bound towards the beds, and the sharp question – "Which are the worst cases, let me see?"' He frequently chided students with the phrase 'Oh! Medical facts! Medical facts!' He was a sceptic with regard to therapeutics and, as a biochemist, believed in nothing that he could not separate, test and measure. He scorned empirical experience, tradition and authority. He concentrated on 'medical facts.' He would frequently bring foreign professors to the hospital, where lively discussions would occur (Allbutt, 1922).

Another of Jones' students, E. L. Fox, was impressed with Jones' rapidity of diagnosis. However, he said it was difficult for Jones to change his mind. He always taught students to 'Be as long as you like in forming your opinion on a case, but when you have thoroughly formed it, stick to it' (Obituary, 1873a). Fox stated that scientific truth, accuracy and a dislike of empiricism were among Jones' chief characteristics as a hospital physician. His clinical lectures were clear and full of 'matter', and his 'hearty, genial kindliness won for him much affection from his pupils' (Obituary, 1873a). It was not enough for him to be a worthy and successful worker himself, but he sought to make others the same. No one could be more ready to encourage and aid every young aspirant than he. His chief aim in the wards was to make therapeutics scientific. His efforts to utilize scientific treatments made him unwilling to mix several remedies together. His prescriptions were said to be simple and precise. Benjamin Disraeli is said to have used one of his prescriptions for his voice. In his autobiography, Herbert Spencer wrote 'speaking of drugs, Bence Jones said that there is scarcely one which may not under different circumstances produce opposite effects' (Rosenbloom, 1919).

He was described as energetic, enthusiastic, warm and generous. He was sensitive, irritable, and, at times, impetuous and intolerant of opposition and of the trammels of authority. However, he was most willing to acknowledge any error that he made. He was quick to show his resentment at anything that appeared to be spurious or artificial. His appreciation of studies other than his own was somewhat limited and led to hostile criticism on occasion. He mingled little in society, and most of his personal friends were scientists and a few physicians. He was frugal in his habits (Obituary, 1873a).

## ACCOMPLISHMENTS AS A PHYSICIAN

Jones' medical practice became large and lucrative after his appointment as full physician at St. Georges and his recognition as a 'chemical' doctor. In one year (5 April 1864–5 April 1865), his profits were £7400 (Obituary, 1873a). His patients included Charles Darwin, the naturalist. Darwin's son later wrote that towards the end of 1865, his father began to recover under the care of Dr Bence Jones, who dieted his father severely and, as he expressed it, 'half-starved him to death' (Rosenbloom, 1919). Michael Faraday was a patient, and also was subjected to a strenuous diet. Other patients included the German chemist August W. Hofmann and the English biologist Thomas Huxley.

## HEALTH CARE

Jones knew Florence Nightingale because he was a consulting physician at the Institution for Invalid Ladies, which she ran in Harley Street until she left for the Crimean War. After her return, he asked her to found a school for the training of nurses at St. George's Hospital, but she refused. He was an original member of the Nightingale Fund, and served on several boards with her. She was not an easy person to get along with and had a number of disagreements with Dr Jones. Nonetheless, she stated that Bence Jones was 'the best chemical doctor in London' (Putnam, 1993). She noted that he was a staunch supporter of nursing education and improvements of sanitation in the city. Nightingale did not believe in infection or contagion, and thought that typhoid fever and smallpox arose spontaneously in filth. Consequently, she demanded a high standard of sanitation.

Jones played a role in the establishment of the Hospital for Sick Children on Great Ormond Street. The first meeting to discuss the hospital took place in January 1850 in Jones' London home. Bence Jones wrote, 'At that time I had many influential friends, and with their help I was able to form a provisional committee which had considerable influence' (Putnam, 1993).

## THE ROYAL INSTITUTION

Jones became secretary of the Royal Institution of Great Britain (1860–73), which promoted research and teaching of science and informed the public of scientific and technological advances. It also provided research laboratories for Thomas Young, Humphrey Davy, John Tyndall, James Dewar, and the Braggs.

## FINAL ILLNESS

In 1861, Jones wrote that frequent palpitations of his heart led him to examine himself carefully with a flexible stethoscope. He found that chronic rheumatism had 'done permanent damage to one of the valves' (Bence Jones, 1929). Allbutt said that Jones had a mitral systolic murmur. Jones resigned as physician at St. George's in early 1862. He also gave up attending at the Institution for Invalid Ladies in Harley Street. He ceased having trouble with his heart, and his practice grew. The last piece of extra work was his service on the Royal Commission regarding the cattle plague in 1865. In early 1866 his health began to fail, and he again examined himself and stated 'I fancied that one side was half-full of fluid' (Bence Jones, 1929). Despite his findings, he went to Nottingham as the chairman of the Chemical Section of the British Association for the Advancement of Science. Jones was the first physician to hold this prestigious position. He returned to his home in Folkestone on 1 September and was taken 'dangerously ill.' He returned to London at the beginning of winter. His illness exacerbated and he almost died in January, but improved slowly and was able to leave the house by May 1867. He recovered enough to deliver the Croonian Lectures on 'Matter and Force' at the College of Physicians in 1868. From that time on, his energy decreased. In 1870, he travelled to Oxford to receive an honorary degree of Doctor of Civil Letters. In a letter to John Tyndall, written at Folkstone in August 1870, he stated, 'I am very lazy and feel unfit for any work and as neither eating, drinking nor sleeping come pleasantly to me, I am a useless mortal and had better be helping the worms and the grass to grow faster than they otherwise would do' (Putnam, 1993). In

**Fig. 2.** Henry Bence Jones' home at 84 Brook Street in London. [From Kyle, R.A. (1996) History of multiple myeloma. In: *Neoplastic Diseases of the Blood* (ed. by P.W. Wiernik, G.P. Canellos, J.P. Dutcher & R.A. Kyle), 3rd edn, pp. 411–422. Churchill Livingstone, New York. By permission of the publisher.]

early 1873, Jones gave up his practice because of congestive hepatomegaly, ascites and anasarca. Jones submitted a letter of resignation of office of secretary of the Royal Institution on 3 March 1873. He wrote, 'I cannot end this letter without expressing to you again my report that I must cease to be your secretary, but my health forbids me to hope that I can no longer continue to be your most earnest servant. Signed – Henry Bence Jones' (Bence Jones, 1873).

Jones died at his home at 84 Brook Street (Fig 2) in London as a result of congestive heart failure on 20 April 1873, at the age of 59 years. He was buried at Kensall Green Cemetery in grave 4327/59. He had requested only a simple stone and, unfortunately, it has succumbed to the elements. He was survived by his wife and five of his seven children. The Bence Jones Ward exists at St. George's Hospital in Tooting, but it is devoted to gynaecology patients.

Interestingly, although Bence Jones' obituary described his work on renal stones, diabetes mellitus and malignant and tuberculous involvement of the kidney, and emphasis on the value of microscopic examination of the urine, no mention was made of his papers on the unique urinary protein that bears his name (Obituary, 1873b). In the more extensive obituary in the *Medical Gazette*, there was no mention of the protein, except as a listing of the paper 'On a New Substance Occurring in the Urine of a Patient With "Mollities Ossium,"' among his 40 publications (Obituary, 1873a).

A hyphen does not appear in Jones' name in his publications in which he used H. Bence Jones. Apparently he did not like 'Henry'. His descendents added a hyphen about a half century after his death (Rosenfeld 1987). Reference books published during his lifetime enter him under Jones, as does the Royal College of Physicians and the Dictionary of National Biography.

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