

A Note from History: The First Biochemical Test for Detection of Cancer

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The story of this epoch-making discovery as it unfolded in the 1840s has some similarity to a modern day clinical pathology conference. The place is the St. George's Hospital in London and the participants are Dr. William MacIntyre (dates unknown), Dr. Henry Bence Jones (1814-1873), and Dr. John Dalrymple (1804-1852). A gravely ill patient of Dr. MacIntyre's was admitted to the hospital with vague but uninterrupted pain in the chest, back, and pelvis. The patient could not stand or lift his arms without pain. He was afebrile and his pulse was regular. Dr. MacIntyre had no clue as to the nature of the disease, so he called Dr. Henry Bence Jones, a young physician on the hospital staff who had a reputation as a chemist, and asked him to test the patient's urine.

Bence Jones found a substance in the urine that was precipitated by addition of nitric acid. He noted that the precipitate was soluble in boiling water but reprecipitated after the urine was cooled. He informed Dr. MacIntyre about these peculiar findings and stated that the patient had "albumosuria." Soon after the urine was tested, the patient died. Dr. Dalrymple, the pathologist, performed an autopsy and observed multiple hemorrhagic cavities in bones throughout the body.

Reviewing the case, the three physicians realized its unique nature. Soon thereafter, in 1846, Dalrymple summarized the pertinent gross and microscopic postmortem findings [1]. After the

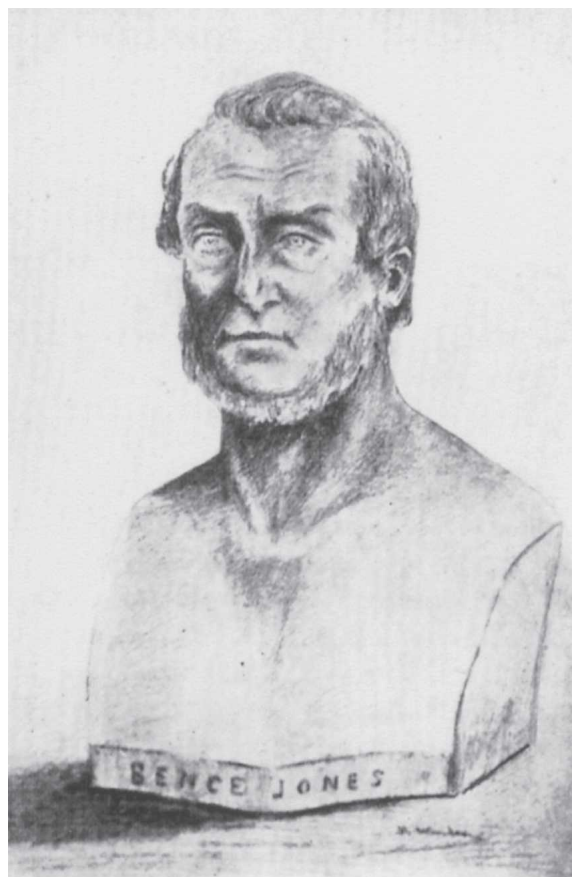


Fig. 1. The bust of Henry Bence Jones that stands in St. George's Hospital, London.

publication of the pathologist's paper, Bence Jones (Fig. 1) reported in 1847 his premortem findings in a short note in the *Lancet*. A year later, he published a definitive paper on his laboratory findings with a detailed description of the technique he had used to analyze the urine [2]. Following these publications, in 1850, Dr. MacIntyre decided to

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summarize and publish the case from the clinician's point of view [3]. As an aside, it is unknown what prevented the three physicians, who were all on the same hospital staff, from summarizing the case in one co-authored report. Offhand, I do not know of any other case in the history of medicine that was written up by three different people (a pathologist, a chemist, and a clinician) and published in three different medical journals in a period of four years [1,2,3].

What is certain is that the discovery of a special "proteid" (albumose) in the urine of a patient with softening of the bones ("myelopathic albumosuria") made Bence Jones famous [2]. He developed a lucrative practice. Bence Jones became the physician of the rich and famous, including the ethnologist Thomas Huxley (1825-1895) and Charles Darwin (1809-1882). Fame did not prevent Bence Jones from continuing his clinical laboratory work. He authored over 30 articles and 5 books, including the first monograph on "The Chemistry of Urine" (1857) and the first book on clinical biochemistry, "Application of Chemistry to Pathology and Therapeutics" (1867).

By the 1860s, the name of Bence Jones was eponimically linked to the protein that he had discovered in the 1840s and reported in 1848 [2]. Search for the source of Bence Jones protein continued for the next one hundred years. Rustizky in 1873 coined the term "myeloma" and in 1889, Kahler (1849-1893) and Huppert (1832-1904) independently introduced the term "multiple myeloma" [4,5]. In 1900, Homer Wright (1871-1928) identified plasma cells as the pathognomonic cells of myeloma and proposed the term "plasmoma" for all myelomas [6].

In the 1940s the origin of albumosuria still remained obscure. The working hypothesis was

that the albumose was derived from the destroyed bone tissue and that the hyperproteinemia of myeloma patients was due to an excess of globulin. During the past two decades, Bence Jones proteinuria and its link to multiple myeloma was definitively established. It was proved that multiple myeloma is a B-cell malignancy associated with elevated levels of certain serum and urine immunoglobulins and with plasma cell infiltrations of bones and occasionally soft tissues. Plasma cell myeloma (multiple myeloma) is the most common primary malignant neoplasm of bone. More than 15,000 new cases are diagnosed per year in the United States. But despite recent advances in combination chemotherapy and stem cell transplantation, the median survival remains between 2 to 4 years.

Bence Jones was a pioneer in chemistry and one of the first physicians to recognize the value of chemistry in the diagnosis of diseases. His discovery of proteinuria in multiple myeloma [2] remained the only biochemical test for cancer until the discovery, in the 1970s, of carcinoembryonic antigen and alpha-fetoprotein.

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