A CONTRIBUTION TO THE STUDY OF THE NATURE AND ORIGIN OF THE BENCE JONES PROTEIN, DISSERTATION. PP. 7-63

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JACOB ROSENBLOOM

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Trieste

A Contribution to the Study of the Nature and Origin of the Bence Jones Protein

DISSERTATION

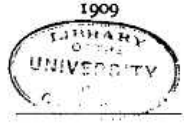
SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY, IN THE FACULTY OF PURE SCIENCE OF COLUMBIA UNIVERSITY.

BY

JACOB ROSENBLOOM, B.S.

NEW YORK CITY

1909



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It gives me great pleasure to thank Prof. William J. Gies for suggesting this problem and for his constant supervision of the work.

Throughout the four years I have been in his laboratory he has been ever ready to give me the benefit of his time and wide knowledge, notwithstanding the pressure under which he has to work.

Through his influence I am enabled to continue along research lines, and to his teaching and example I owe whatever I may be able to produce as a contribution to Experimental Medicine.

JACOB ROSENBLOOM.

LABORATORY OF BIOLOGICAL CHEMISTRY OF COLUMBIA UNIVERSITY, AT THE COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK, May, 1909.

DEDICATION.

Inscribed to my first Professor of Chemistry
FRANCIS CLIFFORD PHILLIPS
as a slight token of my esteem.

I. INTRODUCTION.

This study is a continuation of the preliminary work by Ottenberg and Gies who found in this laboratory that crude elastose, after its subcutaneous or intraperitoneal injection, can readily be detected in the urine by the heat precipitation test. Since the Bence Jones protein has various properties in common with elastoses, Ottenberg and Gies suggested that osseoalbumoid (bone elastin?) might be the forerunner of the Bence Jones protein, which appears in the urine of people with multiple myeloma of the bones.

It was thought that perhaps the osseoalbumoid of the bone might be so acted upon by the enzymes present in the cells of the myelomatous growth, as to give rise to a body having the properties of the Bence Jones protein.

II. HISTORICAL.

It was the writer's intention before beginning his study of the literature of the Bence Jones protein and multiple myeloma, to make a list of all the known cases of myeloma and Bence Jones albuminuria, with the characteristics of each, but this was found to have been done by Anders and Boston, who record cases up to 1903 and give a report of three new cases; by Weber, who records 28 cases up to 1904 and gives the history of ten more cases; by Moffat, who records 39 cases up to 1905; and by Permin, who records 40 cases up to 1907. Decastello in a recent paper gives a description of two more cases and an analysis of the previously recorded cases.

In 1847 Bence Jones presented before the Royal Society of London, a paper "On a New Substance Occurring in the Urine of a Patient with 'Mollities Ossium,' ". in which he described, for the first time, the substance since known as the Bence Jones protein. In the *Philosophical Transactions of the Royal Society* (1848, i, p. 55) he described several properties of this body, and gave his results of a study of it in his case of Mollities Ossium. The Bence Jones protein was rediscovered

and described by Kühne in 1869. It has since been the subject of many investigations, especially by Matthes, Ellinger, Magnus-Levy, Jochman and Schumm, Bradshaw, Park, Moffat, Simon, and others.

Ellinger succeeded in obtaining the Bence Jones protein in small amounts from diseased bone marrow and ascitic fluid. Virchow found it in the bone marrow in cases of osteomalacia, so called. Barr could not find in the bone marrow or bone tumor substance, any trace of the Bence Jones protein or of enzymes. Wood claims to have separated the Bence Jones protein from a portion of bone affected by multiple myeloma, but could not obtain it from the bone marrow in any other portion of the body of the patient. Askanazy was able to demonstrate its presence in the bone marrow of a case of multiple myeloma but was unable to find it in the blood from this patient. Löwy could not detect a trace of the Bence Jones protein in the marrow of the affected ribs and humerus of Kalischer's case. Weber, however, was able to prove the presence of a substance giving reactions similar to those of the Bence Jones protein, in the vertebrae and ends of the femur in a case of multiple myeloma, but he could not detect this substance in any organ or tissue. Bruce, Lund, and Whitcomb found, in a case of multiple myeloma, that the fluid obtained from an affected bone, after sawing through it, gave the reactions of the Bence Jones protein. Ribbinik could not find the Bence Jones protein in the bone marrow substance of the case studied by him. Fleischer, however, has found a substance giving the reactions of the Bence Jones protein in normal bone marrow.

Bradshaw and Warrington, in an analysis of a rib affected with multiple myeloma, found the relation of organic and inorganic substances to be practically normal. Magnus-Levy and also Grutternick and deGraaf have succeeded in obtaining the Bence Jones protein in crystalline form.

Moitessier on subjecting the Bence Jones protein to gastric digestion obtained acidalbumin, primary proteoses (except heteroproteose), secondary proteoses and peptone. After peptic digestion of the Bence Jones protein, Simon could not