

Ralph Pemberton MD (1877–1949), pioneer rheumatologist

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Education and personality

Ralph Pemberton (Figure 1) was born on 14 September 1877 into a distinguished family that had resided in Philadelphia since the seventeenth century. He matriculated at the University of Pennsylvania at the age of 16, earning baccalaureate and master of science degrees before obtaining the MD in 1903. He had a classical education and remained proficient in Greek and Latin throughout his life, as well as speaking French and German fluently. Pemberton was an amateur artist, producing ink and watercolour sketches, played the piano and, on the scientific side, became a palaeontologist who did field work in the Dakota region of the United States during holidays¹.

Early medical career

Following a medical residency at the University of Pennsylvania (Blockley) Hospital, Pemberton in 1905 began a private practice. The evolution of his medical interests can be traced by changes in the focus of his numerous publications. These began during his residency with two paediatric case reports. He became an instructor in the Department of Medicine of his Alma Mater in 1907. At this time he began to collaborate with J E Sweet in physiological experiments which pertained particularly to the influence of other endocrine glands on pancreatic function. This work resulted in six publications between 1908 and 1912². Pemberton's interest in metabolism and nutrition persisted from then on. To further his expertise in metabolic research he resigned his faculty position in 1910 to spend the next two years studying in Berlin and then in Strasbourg with the pioneer biochemist, Franz Hofmeister (1850–1922).

Pemberton was skilled in correlating clinical observations with biochemical findings, many of which were obtained in his laboratory by collaborators. Leading hypotheses regarding the aetiology of rheumatoid arthritis at the beginning of the twentieth century were that the disease is caused either by a bacterial infection which is deposited in joints from the blood³, or that it results from systemic absorption of toxins produced by bacterial fermentation in the intestines⁴. Pemberton's interest

in rheumatic diseases began with an investigation of the latter hypothesis, published in 1912 in a paper entitled optimistically "The metabolism and successful treatment of chronic joint disease: a preliminary report"⁵. This was a quantitative analysis of changes in the bacterial content of faeces in response to dietary changes. He concluded two years later that rheumatoid arthritis "is clearly not due to intestinal putrefaction"⁶. Despite this, he continued to advocate the benefits of temporary low-calorie, low-carbohydrate diets for rheumatoid arthritis, although he eventually concluded that this should be used only in cases of gastrointestinal dysfunction, especially an enlarged colon⁷.

Military experience and physical medicine

During World War One Pemberton became a major in the Army Medical Corps assigned to a military hospital in New Jersey. He took this opportunity to perform clinical and laboratory examinations on 400 soldiers who were hospitalized for arthritic complaints. Several publications in 1920–1 exhaustively described his findings⁸. The importance of these investigations lay mainly in that they established the normality of various measurements in rheumatoid arthritis, such as basal metabolism, and the serum content of creatine, inorganic salts, and lactic acid⁸. This military experience kindled a permanent interest in the rehabilitation of soldiers⁹.

Upon his return to civilian life in 1919 Pemberton resumed his medical practice in Philadelphia and is believed to have become the first American physician to limit his practice to patients with rheumatic disease¹⁰. He also established arthritis clinics at two Philadelphia area hospitals (Presbyterian, and then Abingdon).

Much of Pemberton's physiological and therapeutic research from 1923 on was related to his hypothesis that the underlying abnormality in "arthritis" is impaired oxygenation and supply of metabolites to joints due to inadequate blood flow¹¹. Among other studies, this led in 1926 to some of the earliest biochemical analyses of synovial fluid, and clinical experiments that demonstrated the equilibrium between blood and synovial fluid of glucose and other diffusible substances¹². At about this time



Figure 1. Portrait of Ralph Pemberton, undated. (Courtesy of the National Library of Medicine, Bethesda, MD.)

Pemberton began to study the metabolic effects of heat¹³. This work initiated a major interest in physical medicine, both in its clinical use and in the physiological assessment of its mechanisms of action¹⁴. It resulted in the text *Principles and Practice of Physical Treatment* by H E Mock, Pemberton, and J S Coulter¹⁵.

The large number of patients he had attracted enabled Pemberton in 1927 to compare the findings in the 400 soldiers with 700 civilian cases, the largest rheumatological evaluation to that time. Unfortunately, a specific diagnosis was recorded in only a minority of cases, and the greatest difference between the military and civilian patients was that 77% of the former, but only 24% of the latter, "recovered completely". His final conclusion was that better education of physicians is needed: "A more general familiarity with the subtleties of the disease and with the measures necessary for successful therapy would achieve a great reduction of suffering and economic loss on the part of society"¹⁶.

Later career

In 1928 Pemberton was appointed associate professor and in 1931 professor of medicine at the

University of Pennsylvania. He attended to his belief in the need for graduate education in rheumatic diseases first with his pioneering involvement in the organization of a rheumatic diseases specialty. This began in 1927 when he travelled to Amsterdam to visit Dr Jan van Breemen, a physiotherapist, at whose recommendation the International Committee on Rheumatism had been initiated in 1925. This was the stimulus which led in the next year to the establishment of the American Committee for the Control of Rheumatism, chaired by Pemberton. This group, which initially consisted of five internists and three orthopaedic surgeons, in a decade developed into the American Rheumatism Association, so named in 1937¹⁷. Pemberton was its president in 1938-9.

In connection with the May 1932 meeting of the American Medical Association the Committee had organized the first public scientific meeting on arthritides and prepared an educational brochure for the occasion. This was the forerunner of the *Primer on the Rheumatic Diseases*, now in its tenth edition. The first *Primer* that was widely disseminated, being published in the *Journal of the American Medical Association* in 1942, was the work of 12 physicians, of whom Pemberton was one¹⁸.

Pemberton maintained an interest in the aetiology of rheumatoid arthritis and its differences from osteoarthritis until the end of his career. In the 1940s, before the discovery of anti-inflammatory corticosteroids, he began to consider "imbalances in the neuro-endocrine chain" to be perhaps operative in the aetiology of rheumatoid arthritis¹⁹, and in his last major paper he described attempts to induce arthritis in rats by hormonal manipulation, albeit with little success²⁰. Therapeutically he continued to rely on rest and mental relaxation, nutritional adjustment and physiotherapy, removal of foci of infection and orthopaedic measures²¹. Drug therapy was a last resort and in this he was among the more persistent believers in the benefits of arsenic²².

Pemberton's bibliography included at least 110 medical articles and authorship or co-authorship of four highly regarded medical monographs. He was a member of professional societies in internal medicine, physical medicine, and nutrition, and was honoured internationally by medical and scientific societies. He died on 17 June 1949, aged 71 years.

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