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Sydney Ringer: The pipe water of New River Water Company and the discovery of the elixir of life.

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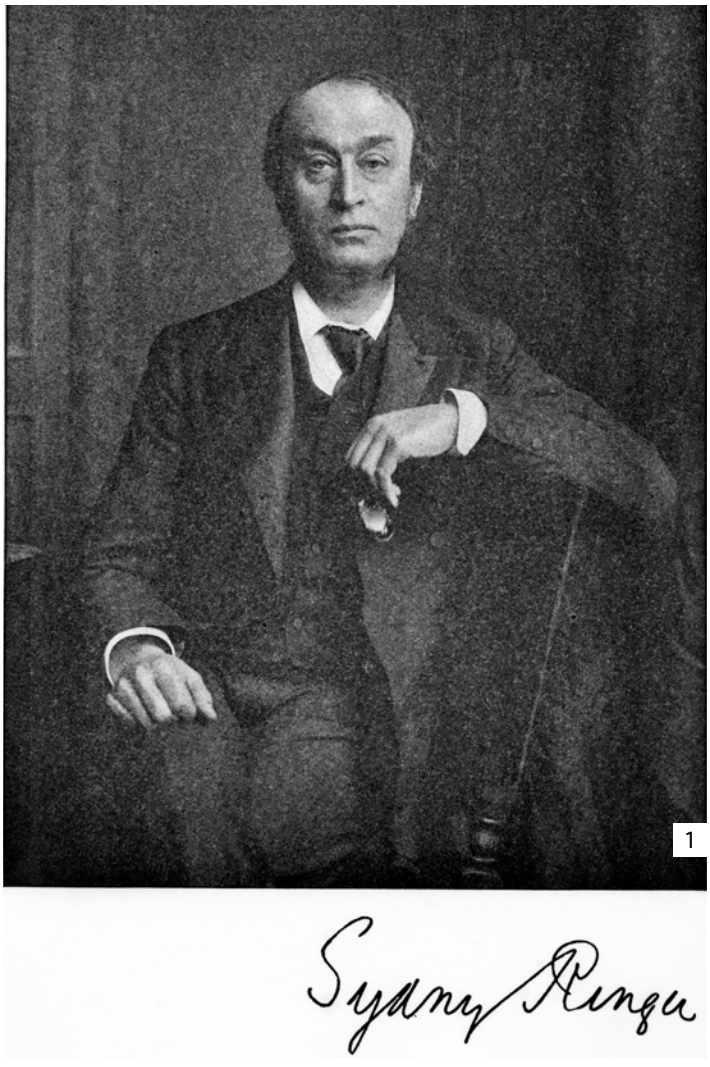
Sydney Ringer published 4 papers between 1880 and 1883 that demonstrated the role of calcium in the contraction of the heart. His research led to the discovery of the role of sodium, potassium and calcium ions in myocyte action potential, cardiac myocyte contraction, and their essential presence in all physiologic solutions. The importance of inorganic ions came about when one of his technicians used ordinary tap water instead of distilled water. Isolation of key inorganic constituents in pipe water led to the creation of the first physiologic saline solution. Modifications in Ringer's original formulations would be used in physiological research on resuscitation from hemorrhagic shock and pathophysiologic states that are basic to modern surgical practice.



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Early life and education

Sydney Ringer (Figure) was born in 1835 in Norwich, England to a family of non-Anglican Protestants, known at the time as nonconformists or dissenters.[1-4] In 1853, he spent a year under surgeon Mr. Benjamin Henry Norgate at Norfolk & Norwich Hospital before entering medical school at University College London (UCL) the following year, the normal sequence in medical education at the time.[4] He chose UCL was because it was one of the few medical colleges that admitted nonconformists, unlike Oxford or Cambridge, where admission was offered only to practicing Anglicans.[4] With a faculty that boasted T. Wharton Jones, William Jenner, Edmund A. Parkes, and J. Russel Reynolds, UCL maintained a tradition of original research and rigorous scientific education.[5-8]

Ringer graduated M.B. in 1860, and served as resident medical officer at the University Medical Hospital from 1861 to 1862.[4] After he earned his medical degree in 1863 he was appointed as assistant physician to the hospital, becoming a full physician in 1866.[9] For four years (1865-1869) he also served as assistant physician at the Children's Hospital, Great Ormond Street.[4]

Professional career

In 1859 Ringer published his first paper while still a medical student, the first of three on the urinary excretion of urea, sugar, and electrolytes.[10] His mentor was E.A. Parkes, who was appointed during that time as the professor of clinical medicine at UCL. Under Parkes Ringer learned to balance the commitments to the practice of medicine, teaching, and original research.[11] Ringer developed into an excellent bedside teacher who maintained the twin standards of clinical instruction and scientific investigation. For most of his career he maintained a small laboratory in the department of physiology.

His text, *Ringer's Handbook of Therapeutics*, was a classic of its day and underwent thirteen editions from 1869 to 1897. The book was originally commissioned as a revision of Jonathan Pereira's (1804-1853) massive *Elements of Materia Medica* (first edition, 1839). Ringer improved the work by offering a concise summary of the actions and indications of drugs that made the book practical for clinical use. Ringer held the chair of *materia medica*, pharmacology, and therapeutics, and the principles and practice of medicine at UCL. In 1887, he was named Holme Professor of Clinical Medicine, a chair he held until his retirement. He was a fellow of the Royal College of Physicians (1870) and Fellow of the Royal Society (1885), and held honorary memberships with the New York Medical Society and the Paris Academy of Medicine.

Ringer's solution

Ringer is most remembered for his invention of Ringer's solution. In four sentinel papers between 1880 and 1883 in the *Journal of Physiology* he described the mixture, the predecessor for future physiological saline solutions.[12-15] His work played a key role in the understanding of the role of calcium in muscle contraction, particularly the contraction of the heart.

Ringer studied isolated heart tissues from the common frog (*Rana temporaria*) to find a substitute solution for blood that was could sustain normal heart function.[14-16] The frog suited his experiments because it had no coronary vascular supply, the extracellular myocytic space communicating with the contents of the ventricular lumen.[16] He examined the effects of various levels of electrolytes, hoping to replicate cardiac function in blood. At first his focus was on potassium and sodium.[13]

One day, Ringer's technician revealed that he had inadvertently used regular tap water from the New River Water Company to prepare the saline solution for the day's experiments rather than the distilled water that Ringer requested.[16] Informed of the error Ringer tried to repeat his results using the distilled water for which he had planned.[12] Something in the New River Water Company water sustained a normal heart beat.[12] Ringer eventually arrived at a mixture of 0.75% sodium bicarbonate, 0.1% calcium chloride, and 1% potassium chloride. Using the concoction, Ringer reported, "the heart will continue beating perfectly."[14] And thus Ringer's solution was born.

Appropriate levels of potassium were also necessary. With progressively lower potassium concentrations the beats would "broaden," in his words, until "fusion of the beats would occur and the ventricle would be thrown into a state of tetanus."[17] The effect, unknown to Ringer, was the effect of low potassium on shortening the refractory period. Despite also being a cation like potassium and "two elements apparently so nearly akin,"[14] sodium had no effect. Ringer also researched fish, finding that they would die in distilled water and depended on sodium and calcium salts for survival.[18]

Ringer's achievements are remarkable given that he did his experiments without a pH meter, digital balance, modern pipette, or ready access to reagents. With his colleagues, including E. G. A. Morshead, William Murrell, Harrington Sainsbury, and Dudley Buxton, he published more than thirty papers from 1875 to 1895 on the actions of inorganic salts on living tissues.

His papers may seem odd to a reader familiar with the modern structure of methods, results, and discussion. He presents his findings in the form of an experimental diary with commentaries of his observations. He seldom presented his data in tables. Publishing in an era before modern statistics, Ringer did not use any form of statistical analysis.[16] The word "frog" surprisingly is not found in the primary calcium papers at all, although the species is clearly mentioned in his first paper.[16] The scientific name *Rana temporaria* first appears in a later paper by Ringer and Salisbury.[17]

Clinical use

Alexis Hartmann, a pediatrician and biochemist, worked with M.J.C. Senn in 1932 to treat acidosis with sodium lactate in his patients.[19] Worried by a too-rapid correction and development of alkalosis, Hartmann combined sodium lactate and Ringer's solution. He felt that "the conversion of sodium lactate into sodium bicarbonate would be sufficiently slow to lessen the danger of alkalosis."[3] The mixture is known today as lactated Ringer's or Hartmann's solution.

Conclusion

Ringer was a natural polymath, drawn to other fields and curiosities. He was an early enthusiast of acupuncture in England. He had family contacts in the Far East, and may have heard of the practice "needling" from a stay in Paris, where it was already known.

Ringer was a brilliant clinician, an avid teacher and a pioneer scientist in biomedical research, an early model of clinician-scientist that would become the model was for medical faculty in UK and the US.

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Legend

Figure. Sydney Ringer's only known portrait (Courtesy Wellcome Library, London).