MEDICAL PHILATELY

George Minot and Pernicious Anemia

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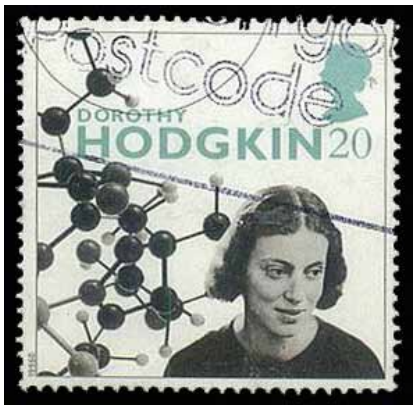
George Minot-Nobel Prize, 1934
Guyana, GB 2000

350 years of Royal Society. GB 20****



Hodgkin GB, 1996
Hodgkin and Crystallography of Vitamin B12

George Minot (1885-1950) was born in Boston, Massachusetts. He was great grandson of James Jackson, co-founder of Massachusetts General Hospital in 1821. Graduating from Harvard College he enrolled at Harvard Medical School and obtained his MD in 1912. As a house pupil (intern) at the hospital he became interested in diseases of the blood and began taking meticulous histories of dietary habits of patients with anemia.

Later as resident at John Hopkins University he worked in laboratory of William Howell, who was interested in blood coagulation and had identified heparin. Minot studied bleeding tendencies in patients with jaundice and determined that it was due to decreased level of a specific substance synthesized by liver (prothrombin). Minot returned to Massachusetts Hospital to study pernicious anemia. He demonstrated that increased reticulocyte count was indicative of increased bone marrow activity and heralded increased RBC count. He reported that x-ray treatment of the spleen in patients with chronic myeloid leukemia extended the period of good health but did not prolong survival.

Minot was diagnosed with diabetes mellitus in 1921. He continued medical practice as a member of a small group of physicians. He asked William Murphy, a member of the group, to participate in his anemia studies. George Whipple had established interest in liver diseases and role of liver in hematopoiesis. At the University of Rochester School of Medicine, Whipple began assessing effects of variety of treatment in exsanguinated dogs. Iron pills, bread and other foods, even arsenic and germanium oxide- among which only raw liver showed real promise. Whipple was feeding cooked liver to the dogs. If he had not noticed a lazy laboratory technician who had given the dogs raw liver instead of prescribed cooked liver-which resulted in much more dramatic response, he might not have discovered the active liver principle. This is thus one more instance of serendipity in medical discovery, like so many others. It closely resembles discovery of thiamine by Christiaan Ejeckman while studying Beriberi in Java.

Minot and Murphy learned of Whipple's discovery and visited him. They decided to try raw liver as treatment. Their daily diet contained 120-240 grams of liver and 120 grams of meat. This caused rapid symptomatic improvement and coincident elevation of red cell count. The reticulocyte count had increased from 1% to average of 8% and bilirubin had lessened. They published their result in JAMA in 1926, reviewing the previous literature and the work of Whipple.[1] The discovery was soon confirmed by many physicians throughout

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the world. Minot, Murphy and Whipple were awarded a Nobel Prize in 1934, becoming the first American recipients of Nobel Prize for Physiology and Medicine.

Because a diet of raw liver is not easy to stomach, extracts of liver were developed for IM injections, and became part of standard management of pernicious anemia until the 1950s. In 1948, anti-pernicious anemia factor was isolated from liver and kidney by Smith and Rickets et al, who named the factor Vitamin B12.[2] They showed that little administration of few micrograms could prevent relapse in the disease. Dorothy Hodgkin and her coworkers went on to use X-ray crystallography to elucidate the structure of Vitamin B12 (Cobalamin) - work for which she too was awarded a Nobel Prize in 1956.

Understanding of the pathogenesis of pernicious anemia increased over subsequent decades. Patients suffered from chronic gastritis and lack of acid secretions. Indeed, at one time, dilute hydrochloric acid was used in the management of pernicious anemia. It is now known that the transport of physiological amounts of Vitamin B12 depends on the combined action of gastric, ileal and pancreatic components. The gastric moiety was discovered and named 'Intrinsic factor' by William Castle in 1930. A further important advance was made in the early 1960s with the recognition that pernicious anemia was an autoimmune disease by Doniach et al in 1963.[3]

Development of effective treatment for pernicious anemia illustrates the complementary roles of clinical and autopsy observations, physiological and clinical research and.... Serendipity!

References

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