Harvard University Gazette

Red-Blooded Doctors Cure Anemia

Researchers persisted with strange methods despite skepticism

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Special to the Gazette

There was no cure for what was known as the "blood thinning" disease. People who developed pernicious anemia -- characterized by dangerously low counts of red blood cells -- were left exhausted, hospitalized, and without the hope of being cured.

In the early 1920s, most doctors believed that pernicious anemia was caused by a toxic substance in the body, and they prescribed doses of arsenic, transfusions, or removal of the spleen as treatments. But after these remedies were administered, patients had relapses. Death was inevitable. Across the world, 6,000 lives a year were lost to the scourge of pernicious anemia.

The idea that would eventually lead to a cure occurred to George R. Minot in 1912. Minot had received an A.B. from Harvard College in 1908, and an M.D. from Harvard Medical School in 1912. As a house officer at Massachusetts General Hospital, Minot saw many patients with pernicious anemia, and "the idea that something in food might be of advantage to patients" occurred to him then.

One of Minot's teachers was Homer Wright, a physician who developed staining techniques for the microscopic study of blood, and Minot had developed what would become a lifelong interest in the study of blood diseases. He pursued such work at Johns Hopkins Hospital in 1913-15, and came back to Harvard Medical School and Massachusetts General Hospital as a staff member in 1915, where he continued his investigations.

In 1923, Minot met and joined forces with William P. Murphy, a young physician who had graduated from Harvard Medical School in 1922, and was to become an assistant instructor at Harvard Medical School in 1924.

In their investigations to find a cure for pernicious anemia, Minot believed that research by George Whipple, a researcher whom he had known while both were at Johns Hopkins Hospital, was particularly significant. Whipple had completed experiments in which he bled dogs to make them anemic. Then he determined which foods restored their red blood cells. His results showed that red meat and certain vegetables were effective treatments, but liver was the best treatment.

Minot wondered if Whipple's findings with dogs could be duplicated in humans. He and Murphy were determined to try it, and proceeded to do so with their private patients. Observing an increase in the patients' red blood cell counts, they thought they were on the right track, and decided to try the experiment with hospitalized patients.

Other physicians were openly skeptical -- how could a disease like pernicious anemia be caused by something as simple as a dietary deficiency? And the disapproval of other researchers was a powerful force -- the skepticism of colleagues had convinced one of Whipple's collaborators, Charles Hooper, to give up on promising results he had achieved in 1918 by feeding liver to three human patients with pernicious anemia. Hooper's abandonment of his experiment ultimately was a tragedy -- if he had persevered, thousands of lives might have been saved.

In trying the treatment, Murphy and Minot were also hampered by a matter of taste -- some patients, even though gravely ill, were reluctant to eat a half-pound of liver a day.

But the treatment worked. And in 1926, the results of the researchers' program were presented at a medical meeting in Atlantic City. By that time, Minot and Murphy had successfully treated 45 patients, in which "clinical improvement had been obvious, usually within two weeks."

As Murphy later put it, the two men had shared the "thrill of watching the patient through a few days of depression following the institution of liver therapy until remission occurs, with its often sudden and almost unbelievable sense of well-being, simultaneously with the maximum increase of the reticulocytes, or new red blood cells."

For their research, Minot, Murphy, and Whipple shared the Nobel Prize for Physiology or Medicine in 1934.

The work didn't end with the announcement of Minot and Murphy's discovery in 1926, of course. Critically ill patients couldn't eat, thus the liver was forced into them through stomach tubes. In 1928, Edwin Cohn, a Harvard physical chemist, condensed and purified a liver extract that could be eaten or injected into a muscle. This extract was between 50 and 100 times as potent as liver, and it was less expensive.

But there was still a big question: what was the active ingredient in liver?

A series of experiments by William Castle, another Harvard physician, found that something in the stomach was related to the disease. Castle had noted that people who had their stomachs removed because of cancer often died because of pernicious anemia, and that red meat other than liver didn't work.

In what can only be described as a disgusting experiment, Castle ate red meat, made himself vomit, and then had patients eat it. But it worked -- his regurgitated stomach contents were as effective as liver. The stomach, he decided, normally contains an "intrinsic factor" that together with an "extrinsic factor" in meat is necessary for red blood cell formation.

Later it was determined that this "intrinsic factor" allowed the absorption of what was, in 1948, isolated and named vitamin B12 -- found abundantly in liver. Since then, the cure for pernicious anemia has involved injections of vitamin B12.

Taken all together, the work by these researchers showed the power of pursuing novel treatment methods, even if they involved unpopular ideas that were laughed at by the medical establishment. In presenting the Nobel Prize in 1934 to Minot, Murphy, and Whipple, Israel Holmgren of the Karolinska Institute paid them the ultimate compliment that can be bestowed upon a physician: "This new method . . . has already saved thousands of lives, and will in the future save innumerable human beings from death."