Thomas Hodgkin: medical immortal and uncompromising idealist

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Thomas Hodgkin was born into a devout Quaker family in Pentonville, England, in 1798 *(Table 1)*. His upbringing imbued him from early life with honesty, discipline, and concern for the less fortunate (1, 2). As a Quaker, Thomas wore plain clothes and spoke in a formal manner. At age 21, he wrote an "Essay on the Promotion of Civilization," in which he criticized the imperialistic behavior of colonists that led to the degradation or death of North American Indians and other native peoples. Thomas also developed an interest in science. From 1817 until 1820 he served as apprentice to an apothecary and "walked the wards" at Guy's Hospital in London. While a medical student at Edinburgh, Hodgkin visited European medical centers during 1821–1822 and met René Laennec in Paris. Laennec had recently devised the stethoscope and taught Hodgkin how to use it. He received his medical degree from Edinburgh in 1823, the same year he met Moses Montefiore, a wealthy financier and philanthropist who was to become his lifelong patient and close friend.

In 1826, Hodgkin was appointed first lecturer in morbid anatomy and museum curator at the new Guy's Hospital Medical School in London. During the next 12 years at Guy's, Hodgkin made a number of major contributions *(Figure 1)*. Despite his brilliance Hodgkin was rejected for a clinical staff position in 1837, after which he resigned from Guy's Hospital. 1857 marked the first of five journeys with Moses Montefiore on behalf of Jews, Christians, and Arabs in various countries. In 1865 Samuel Wilks wrote his paper using the term "Hodgkin's disease." In the following year Thomas Hodgkin died of dysentery in Palestine. He is buried in Jaffa.

Table 1. Chronology of the life of Thomas Hodgkin

1798	Born into Quaker family in Pentonville, England
1817–20	Apprenticed to an apothecary; "walked the wards" at Guy's Hospital
1821–22	Visited European medical centers; met René Laennec in Paris; brought stethoscope back to England
1823	Received medical degree at Edinburgh; met Moses Montefiore
1826	Appointed first lecturer in morbid anatomy and museum curator at Guy's Hospital
1832	Published paper on "enlargement of lymph nodes and spleen"
1837	Rejected for clinical staff position at Guy's; resigned
1849	Married Sarah Frances Callow Scaife
1857	Took first of five journeys with Moses Montefiore
1865	Samuel Wilks published paper on "Hodgkin's disease"
1866	Died of dysentery in Palestine; buried in Jaffa

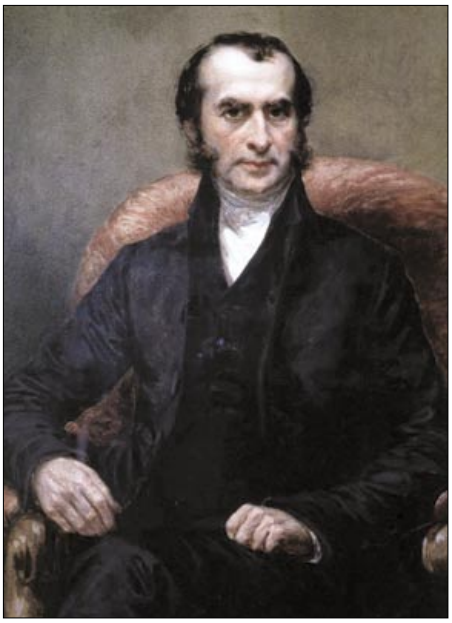

Figure 1. Thomas Hodgkin. Reproduced courtesy of Gordon Museum, Guy's Hospital, GKT, King's College London.

GUY'S HOSPITAL AND HODGKIN'S DISEASE

Hodgkin's years at Guy's Hospital were remarkably productive (1–4). He performed hundreds of autopsies and cataloged over 3000 specimens in the Green Book. Hodgkin presented the first systematic lectures on pathology in England and published a two-volume monograph (5). He described aortic regurgitation 5 years before Corrigan (6). Hodgkin, Richard Bright, and Thomas Addison were contemporaries and became known as "the three great men of Guy's" (7, 8). All three correlated clinical with postmortem findings and all had diseases named for them, but

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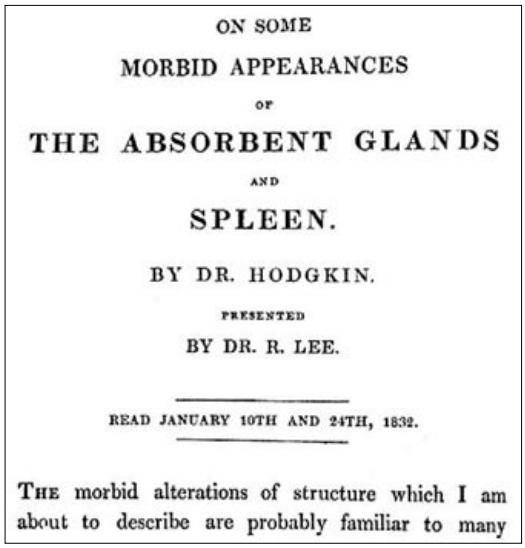
Figure 2. Laennec pattern stethoscope, Gordon Museum, GKT, King's College London. (Photo from author's collection.)



ON SOME

MORBID APPEARANCES

OF

THE ABSORBENT GLANDS

AND

SPLEEN.

BY DR. HODGKIN.

PRESENTED

BY DR. R. LEE.

READ JANUARY 10TH AND 24TH, 1832.

THE morbid alterations of structure which I am about to describe are probably familiar to many

Figure 3. 1832 publication; the first description of lymphoma.

Hodgkin's remains the most familiar. The term "Bright's disease" is no longer used, and Addison's disease is rare.

Hodgkin brought the first stethoscope to Guy's Hospital and delivered a lecture on Laennec's method for its use to the hospital physical society in 1822 *(Figure 2)*. The older physicians at Guy's were unimpressed with this peculiar-looking cylinder and used his stethoscope as a flowerpot, standing it on end. Once they left the room, the students removed the flowers and began examining each other with the instrument. In 1829 Hodgkin published a catalogue of pathologic specimens he had assembled in the museum, which was a landmark contribution (9). The museum helped make Guy's one of the leading teaching institutions in London and all of England. Moreover, the availability of material from his own cases enabled others to later confirm his work.

In 1832 Hodgkin published his article "On Some Morbid Appearances of the Absorbent Glands and Spleen" (10) *(Figure 3)*. In the report he described clinical histories and postmortem findings of seven patients with enlargement of lymph nodes and spleen but without inflammation or other significant pathological findings. Hodgkin recognized that tuberculosis coexisted in some of the patients, but the firmness and size of the nodes made him conclude that these findings were different. Hodgkin thus recognized the disorder grossly (9, 10). He pointed out that the disease spread to contiguous lymph node groups in an orderly manner and that splenic involvement was a late development (11).

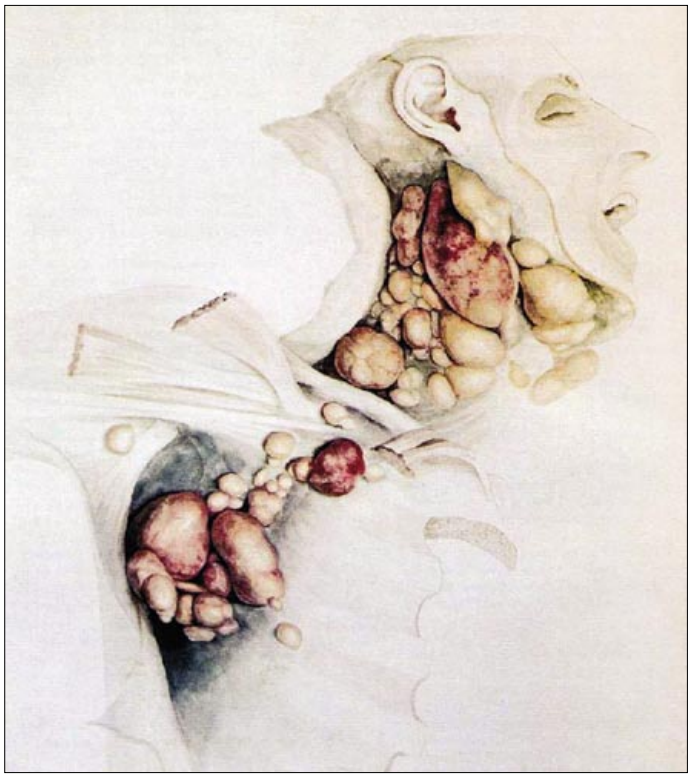


Figure 4. Hodgkin's disease watercolor drawing by Robert Carswell in 1828. This was case 7 in Hodgkin's report.

Figure 5. Abdominal lymph nodes (Hodgkin's original case 2), Gordon Museum, GKT, King's College London.

Hodgkin, who noted that Malpighi had described a similar condition in 1666, apparently did not use the microscope even though he had previously collaborated with Joseph J. Lister in an 1827 paper describing red cells and muscle (12). Using Lister's improved achromatic lenses, they discovered the biconcave shape of human erythrocytes and the striations in skeletal muscle. This paper has been termed the "foundation of modern histology" (13). Why Hodgkin did not look at the microscopic appearance of the lymphoma he described grossly remains unclear, though it may have been due to the primitive status of microtechnique and specimen preparation around 1830.

Three of the cases in the 1832 article were patients of Richard Bright and Thomas Addison, and one was the patient of Robert Carswell (14). The latter physician was Hodgkin's friend who brought him drawings of a similar condition he had seen in France

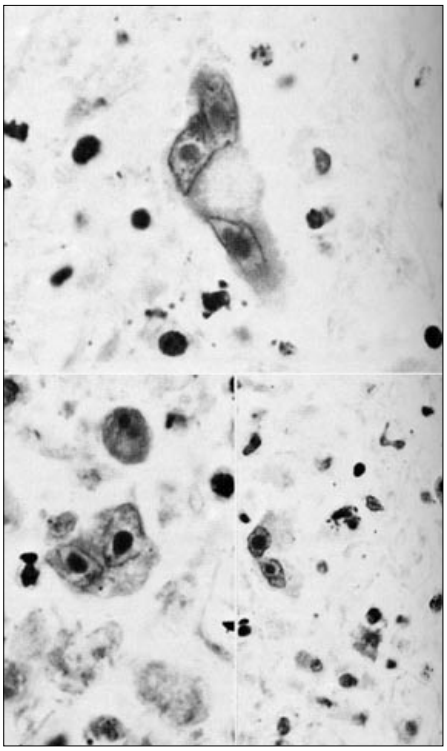


Figure 6. Histopathologic appearance of Hodgkin's original case 2. Gordon Museum, GKT, King's College London.

CASES OF

ENLARGEMENT OF THE LYMPHATIC GLANDS AND SPLEEN,

(OR, HODGKIN'S DISEASE,)

WITH REMARKS.

By SAMUEL WILKS, M.D.

Having spoken of the lardaceous affection, I must now call attention to a form of disease which in my earlier paper, before alluded to, I treated of in connection with it. I refer to a disease where the lymphatic glands are increased in size, and associated with a deposit of a morbid kind in the internal viscera, more especially in the spleen. Although my own observations were at the time original, I had been forestalled by Dr. Hodgkin, who was the first, as far as I am aware, to call attention to this peculiar form of disease. I believe that the publication of my own paper revived the subject, but in consequence of being referred to in connection with lardaceous disease, I have considered myself to have been partly the cause of the two affections being confounded. It is for this reason that I make this personal allusion to myself, and, at the same time, take the opportunity of endeavouring to remove the subject from the false position in which it has been placed. I will not say that the cases described by Hodgkin may not have certain affinities with the lardaceous disease, but there is sufficient peculiarity in them to warrant them standing alone, and without any support from another affection. A perusal of the original cases, or, what is better, an examination of his specimens on our shelves, will show that the disease is not to be confounded

Figure 8. Title page of 1865 publication by Samuel Wilks. Note the term "Hodgkin's disease," the first time the eponym was used.

Figure 7. Thomas Hodgkin exhibit, Gordon Museum, GKT, King's College London. (Photo from author's collection.)

(Figure 4). *Figure 5* shows the abdominal lymph nodes from Hodgkin's original case 2. In 1926 Herbert Fox confirmed microscopically that two of Hodgkin's original three patients included in the first report actually did have Hodgkin's disease (15). One patient was found to have lymphosarcoma, now known as non-Hodgkin's lymphoma. Thus Hodgkin's name is associated with both categories of malignant lymphoma, and his name echoes in the halls of major medical centers throughout the world every day. *Figure 6* shows the histopathologic appearance of Hodgkin's original case 2, which was examined in 1968, nearly 140 years after the original description. *Figure 7* shows the Thomas Hodgkin exhibit in the Gordon Museum at Guy's Hospital.

Another well-known Guy's Hospital physician, Dr. Samuel Wilks, published a paper on "lardaceous disease" (amyloidosis) in 1856 in which he unknowingly redescribed some of Hodgkin's original cases (16). He had been unaware of Hodgkin's work on lymph nodes and spleen until he found an 1838 citation by Richard Bright (17). In 1865 Wilks wrote a more detailed paper on the condition and for the first time used the eponym "Hodgkin's disease," thereby immortalizing his predecessor (18–20). *Figure 8* shows the title page of the 1865 paper by Wilks. There was still no histologic description of the disorder. Soon, however, many investigators used the microscope to examine the tissues of Hodgkin's patients and recognized the characteristic giant cells. These included Ollivier and Ranvier in 1867, Tuckwell in 1870, Bristowe and Pick in 1870, Langhans in 1872, Greenfield (who made the first drawing) in 1878, Gowers in 1879, and Goldman in 1892. The most thorough descriptions of the giant cells in Hodgkin's disease were made by Sternberg in 1898 and then Dorothy Reed in 1902 (14, 21, 22).

Dorothy Reed (1874–1964) was a medical student (class of 1900) and house officer at Johns Hopkins. She performed her study on Hodgkin's disease during a pathology fellowship. In the lengthy article published in 1902, she drew the illustrations herself (21). Reed described eight cases, providing detailed clinical histories and hematologic findings. She clearly distinguished Hodgkin's disease from tuberculosis but thought that Hodgkin's was an inflammatory rather than a neoplastic process. *Figure 9*

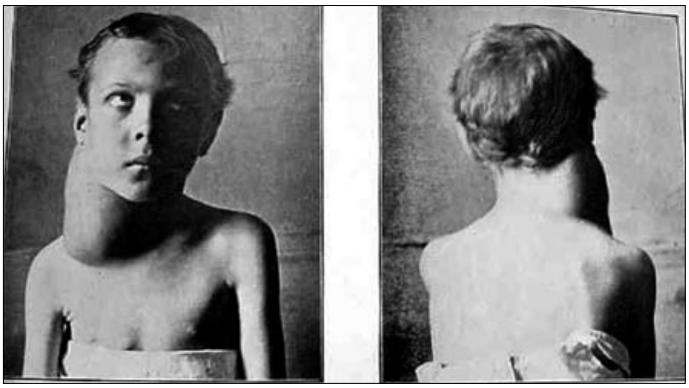


Figure 9. Child with lymphadenopathy of the neck (Dorothy Reed, ref. 21).

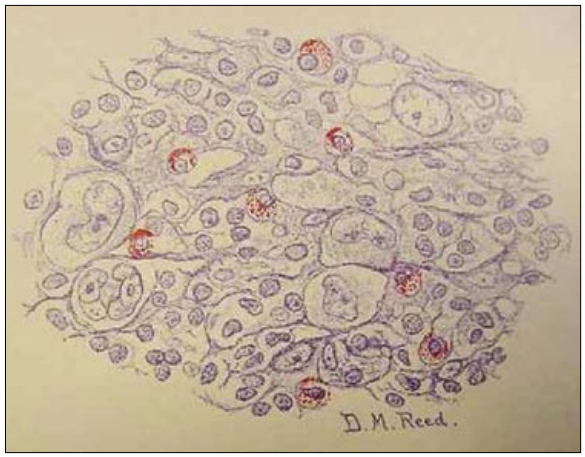


Figure 10. Illustration by Dorothy Reed of the characteristic giant cells in Hodgkin's disease (ref. 21).

shows a child with lymphadenopathy of the neck from Dorothy Reed's 1902 paper, and *Figure 10* shows the microscopic appearance of an involved lymph node drawn in Reed's classic report. The characteristic bilobed or multinucleate giant cells of Hodgkin's disease became known as Reed-Sternberg cells—the eponym that survives to the present. Shortly after completing her treatise on Hodgkin's disease, Dorothy Reed left Hopkins and later had a second distinguished career in public health.

Hodgkin's disease is the only malignancy in which the tumor mass is not due to the number of malignant cells; that is, the Reed-Sternberg cells account for only 1% to 2% of the lymph node infiltrate (14, 21–24). Reed-Sternberg cells are necessary, but not sufficient, for the diagnosis of Hodgkin's disease. In addition, Reed-Sternberg cells have been described in some non-Hodgkin's lymphomas and occasionally in benign disorders. Therefore, for the diagnosis of Hodgkin's one requires 1) Reed-Sternberg cells and 2) the appropriate milieu, that is, a reactive cellular infiltrate usually consisting of lymphocytes, plasma cells, eosinophils, and neutrophils. It is now known that nearly all Reed-Sternberg cells are clonally derived from B lymphocytes. *Figure 11* shows the histologic appearance of a lymph node with Hodgkin's disease showing a Reed-Sternberg cell in the center.

As noted, there was controversy as to whether Hodgkin's disease was an infectious-inflammatory disease or a malignancy. Its relationship to tuberculosis was argued for decades. However, there was no disagreement about the fatal nature of the disorder. The 5-year survival rate for patients with untreated Hodgkin's

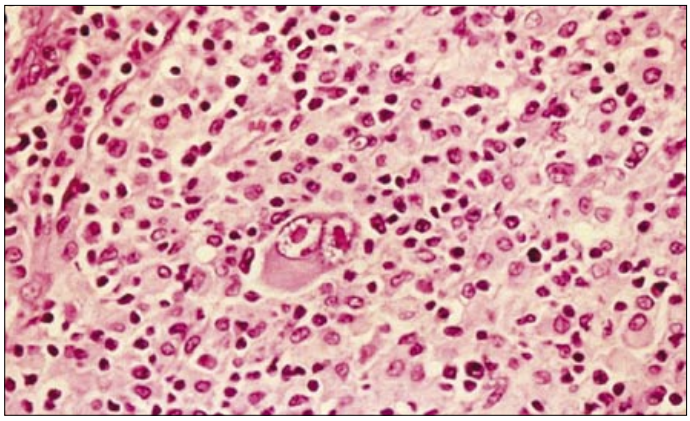


Figure 11. Histologic appearance of a lymph node in Hodgkin's disease.

Figure 12. Patient with bull neck and axillary lymphadenopathy.

disease was <5%, and 90% of patients died within 3 years. *Figure 12* shows a patient with a bull neck and axillary lymphadenopathy. More than 90% of patients with Hodgkin's disease present with peripheral lymphadenopathy, two thirds of them in the cervical region.

Since Hodgkin's original description of the first hematopoietic malignancy in 1832, a number of advances have been made. As noted, the recognition of the characteristic giant cells, only a few of which are present in the tumor mass, is a key histologic feature. The mode of spread—which in 90% of cases is contiguous, spreading predictably from one lymph node group to the next adjacent lymph node group (unlike many other malignancies)—was recognized by Hodgkin and confirmed by many others. During the 1960s a staging system was developed, which served as a prototype for other cancers. The pioneering investigations of Peters and Kaplan demonstrated that radiation therapy could control the disease in a treated field if given in a high enough dose (14). During the late 1960s, DeVita et al showed that combination chemotherapy could cure some patients with advanced Hodgkin's disease (23).

It is now clear that Hodgkin's disease can be cured in most patients. *Figure 13* shows the outcome in over 2000 patients in British Columbia. Note the significant improvement in survival in each successive decade since the 1960s (24). In 2004 approximately 80% of patients in all anatomical stages and all histologic

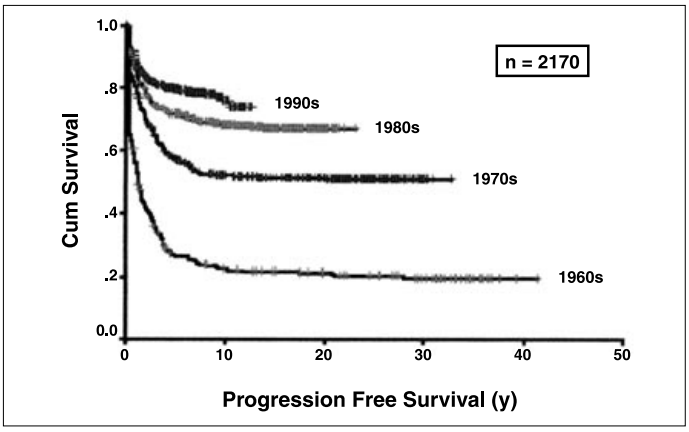


Figure 13. Improved survival of patients with Hodgkin's disease in British Columbia since the 1960s. Cum indicates cumulative. Reprinted from reference 24. Copyright American Society of Hematology; used with permission.

subtypes of Hodgkin's disease could be cured. Despite this great clinical progress, the etiology of this fascinating disorder is still unclear.

PROFESSIONAL AND PERSONAL DISAPPOINTMENT

After Hodgkin resigned from Guy's Hospital in 1837, his academic medical career was over. His efforts on behalf of underprivileged and oppressed peoples throughout the world were lifelong. He remained a social reformer (1, 25). He had played an important role in organizing the new University of London and its medical school, the first nonsectarian institution of its kind in England. Hodgkin declined fellowship in the prestigious Royal College of Physicians in 1836. Two years before, the college had repealed its bylaw that limited the fellowship to graduates of Oxford and Cambridge. However, Hodgkin felt that he would be singled out as an exception and it was unfair that other qualified individuals would not achieve election into fellowship. In addition, Hodgkin was undoubtedly familiar with the experience of John Fothergill, an eminent Quaker physician who also received his medical degree from Edinburgh and had been recommended by the president of the Royal College of Physicians but was rejected by the fellows.

Benjamin Harrison, Jr., was the administrator of Guy's Hospital for over half a century (1797–1848), following in the footsteps of his father (8). He was wealthy, autocratic, and known as "King Harrison," the hospital board being essentially a rubber stamp for his wishes.

Why didn't Hodgkin receive the clinical appointment at Guy's in 1837 (1–3, 8)? There may have been a number of issues leading to Harrison's decision, including Hodgkin's refusal of the fellowship in the Royal College of Physicians, his involvement in the newly organized University of London which was regarded by Harrison as a potential competitor to Guy's, and the fact that Hodgkin had been ill and absent for some time during the year prior to the decision. The other physician who sought the clinical position, Benjamin Babington *(Figure 14)*, was clearly a formidable competitor, although not in the same class as Hodgkin. Babington's father had been a Guy's physician and had cared for Hodgkin's mother. Moreover, Babington was the brother-in-law of famed physician Richard Bright. Babington invented the glottiscope, which Hodgkin renamed the "laryngiscope." The

Figure 14. Dr. Benjamin Guy Babington (ref. 26).

Figure 15. Moses Montefiore (ref. 28).

two men were friends (26). Babington was a fellow of the Royal College, and he received the appointment as assistant physician at Guy's instead of Hodgkin. Another factor probably played a role in Benjamin Harrison's decision. He was a board member of the Hudson's Bay Company and was angered by Hodgkin's outspoken criticism of the company for its exploitation of American Indians. The Hudson's Bay Company gave guns and alcohol to the Indians in exchange for furs, which brought large profits to the company (1). Their divergent views placed Harrison and Hodgkin on a collision course that exploded in 1837. The result of this confrontation was a tragedy for Hodgkin and an irreplaceable loss for Guy's.

Hodgkin endured major disappointment in his personal as well as his professional life prior to age 40. He was not permitted to marry his true love, Sarah Godlee, because of the Quaker rule prohibiting marriage between first cousins. Even though he petitioned the Society of Friends to make an exception on two separate occasions, he was refused. Later, too late for Hodgkin, the Quaker rule was repealed. He finally married Sara Scaife, a widow and not a Quaker, in 1849.

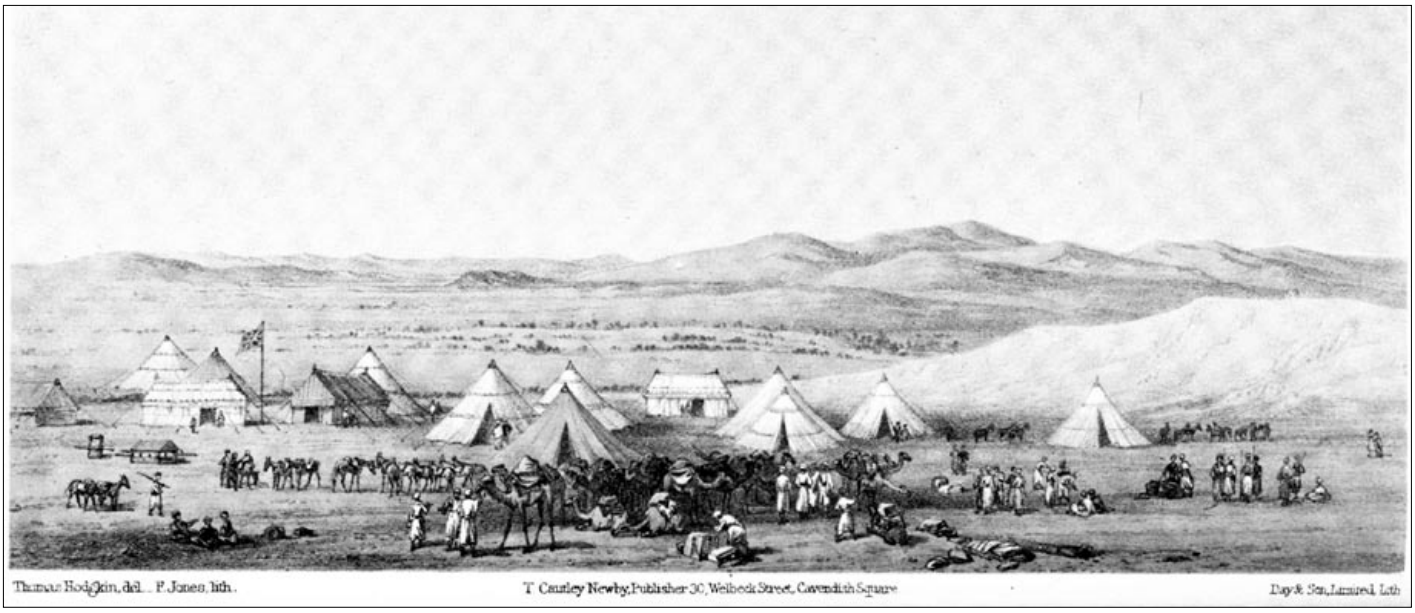


Figure 16. Hodgkin's drawing of The Encampment in Morocco, 1863 (ref. 28).

Figure 17. Hodgkin's grave in Jaffa, Israel.

PUBLIC HEALTH AND SOCIAL REFORM ACTIVITIES

Hodgkin's life was devoted to attempts to help the underprivileged and oppressed peoples throughout the world, in North America, Australia, Africa, Syria, the British West Indies, and Liberia, to name a few sites (1). He lectured on sanitary measures and stressed the importance of protecting child laborers during the early phase of the industrial revolution in England. He cared for the poor, especially Jews in London, and often did not charge fees. He traveled with Moses Montefiore *(Figure 15)* on multiple occasions to help Jews and other oppressed people. He also studied ethnology, geography, and the new science of anthropology. Hodgkin belonged to many organizations with social missions and held leadership positions in some of them. In 1829 he gave four lectures to the public on ways to promote and preserve health. These were published in 1835 (27). He stressed the importance of adequate oxygen, bathing, and proper disposal of sewage. Hodgkin also warned of the dangers of overeating, excessive alcohol use, tobacco use ("smoking encroaches on the freedom and comfort of others"), and occupational dust exposure. He advocated regular exercise and education (including preschools and equal education for girls and boys). These lectures were given while Hodgkin was still at Guy's and were remarkable efforts in educating lay persons about personal, social, and occupational health issues.

Moses Montefiore (1784–1885) was a successful financier and philanthropist. An orthodox Jew, he was a fellow of the Royal Society and had been knighted by Queen Victoria for his good works. He received a baronetcy in 1846 in recognition of his humanitarian efforts on behalf of Jews. Montefiore met Hodgkin in 1823 through his brother, who briefly was Hodgkin's patient but fired him. However, Moses Montefiore and Hodgkin became close friends, and Hodgkin served as personal physician for Moses Montefiore and his wife for many years. *Figure 16* shows Hodgkin's drawing of the encampment during a trip with Montefiore to Morocco in 1863 (28). Their journeys together for philanthropic purposes included a visit to Palestine in 1866, during which Hodgkin became ill with a dysenteric-like disease and died on April 4. He was buried in Jaffa. On his gravestone is the inscription, "Nothing of humanity was foreign to him" *(Figure 17)*. The deaths of two other people who were important to Hodgkin also occurred in April 1866. Four days after Hodgkin's death, Benjamin Babington died, and on April 20, Sarah Godlee Rickman passed away.

HODGKIN AND WILLIAM OSLER

In 1907 William Osler said, "The original description of the simultaneous disease of the lymph glands and spleen by that distinguished old Quaker physician Hodgkin was matched by his equally remarkable contribution on insufficiency of the aortic valves (which antedated by several years Corrigan's account)" (29, 30). Osler had written chapters on Hodgkin's disease in Pepper's *Internal Medicine* and *The Principles and Practice of Medicine*, the first edition of which contained 4½ pages on the

Figure 18. Dr. Paul Farmer and patient. Copyright 2001 © Partners In Health. All rights reserved.

disorder (31). Osler described generalized lymphadenopathy, most often cervical, and Pel-Ebstein fever. In the seventh edition of *The Principles and Practice of Medicine* (the last that Osler revised himself), Osler described the giant cells that had been reported by his former student, Dorothy Reed (32).

Hodgkin and Osler had some interesting parallels. Hodgkin was 51 years older than Osler and lived when scientific medicine was just beginning. During Osler's life, scientific medicine was reaching its golden age, especially in pathology and bacteriology. Both men were experts in morbid anatomy-pathology, both were accomplished teachers of medicine, both had diseases named for them, and the two were indirectly connected via Dorothy Reed. Neither man was said to be a particularly good lecturer.

IS THERE A THOMAS HODGKIN NOW?

Although several physician-scientists might qualify as latter-day examples of a Thomas Hodgkin–type physician, Dr. Paul Farmer seems to be a leading candidate. The book *Mountains Beyond Mountains: The Quest of Dr. Paul Farmer, A Man Who Would Cure the World* by Tracy Kidder, a Pulitzer Prize–winning writer, was published in 2003 (33). *Figure 18* shows Dr. Paul Farmer in Cange, Haiti. There he established a clinic to care for people in the poorest area of one of the poorest countries in the Western Hemisphere. *Table 2* compares Hodgkin and Farmer, both of whom devoted their lives to perfecting the world. The two differed in that Hodgkin was said to have little humor and was unhappy in part for reasons that were clearly related to his professional and personal life. Being a Quaker, he wore simple clothes, used formal language, and was rather stiff in his manner, all of which are very different than Farmer. However, both men had the highest ideals and made a significant impact on world health. Farmer's efforts continue.

HODGKIN IN RETROSPECT

In a letter to William Smith on January 9, 1795, Edmund Burke wrote, "The only thing necessary for the triumph of evil is for good men to do nothing." Interestingly, Burke had purchased one of the calligraphy works of Hodgkin's father. A corollary to Burke's statement is the ancient adage that although one cannot solve all the problems of the world, neither is one free to take no part in the effort. Hodgkin took part in the effort and tried to better the lot of his fellow man. Amalie Kass has commented, "We remember him because he was so good and tried so hard to do good. Not always successfully, sometimes with a limited sense of reality, but always with pure motives. It is inspiring to meet a true idealist, especially in an era when idealism is often either ignored or disparaged. We admire his consistency and his refusal to sacrifice principle for expediency" (34).

Table 2. "Perfecting the world": Thomas Hodgkin and Paul Farmer

	Hodgkin	Farmer
Era	19th century	Present
Strong religious background	Yes	No
MD	Yes	Yes
PhD	No	Yes
Teacher of medicine	Yes	Yes
Medical school faculty	Guy's, 12 years	Harvard
Medical practice	Limited	Part-time
Cared for poor	++++	++++
Anthropology	Yes	Yes
Disease named for him	Yes	No
Humor	+	++++
Gregarious	No	Yes
Outspoken	Yes	Yes
Fees	Minimal	Donated
Had a "financial angel"	Yes	Yes
Ideals	++++	++++
Impact on world health	Modest	Marked

Thomas Hodgkin was an exceptional and compassionate physician who first described the malignant lymphoma that bears his name. During his brief career at Guy's Hospital, he made other major contributions to clinical medicine and pathology. He served as first curator of the museum at Guy's, which became and remains one of the front-ranking medical museums in the world. His adherence to Quaker precepts and strong reformist penchant were constant features of his life. Some of his altruistic efforts were too impractical and unpopular to be successful. Nevertheless, Thomas Hodgkin's life continues to serve as a beacon for social justice and human rights applicable to physicians and lay persons alike.

Acknowledgments

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