THEODOR MAXIMILLIAN BILHARZ (1825-1862): THE DISCOVERER OF SCHISTOSOMIASIS

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Received: June 15, 2011; Accepted: June 24, 2011

Abstract- Theodor Bilharz (1825-1862) is one of the founders of tropical medicine. He is best remembered for his discovery of the *Schistosomiasis* worm. During his short life span, he received his medical degree in Tubingen then specialized in anatomy and microscopy in Freiburg. In 1850, he was sent by his professor von Siebold to Egypt in order to investigate the worms which infest the Egyptian population. By 1853, Bilharz was able to identify the worms and their eggs in the bladder and the liver and to describe the disease which remains his enduring scientific legacy. In 1856, the disease was named Bilharzia as designated by Meckel von Hembach. His discovery of Schistosoma was just a part of his contribution in science. Bilharz worked for over a decade on the study of ethnology, geography and ecology. He also discovered Heterophyes Heterophes and Hymenolepis nana in the human intestine. His death in 1862 during an outbreak of typhoid in Egypt when he was helping people suffering from the disease and thereafter contracted it himself, terminated a life of service to science. Bilharz was buried in the cemetery of Roman Catholics in Old Cairo.

Keywords: Theodor Bilharz, *Schistosomiasis*, Egypt.

Introduction

During our relatively short history on Earth, humans have acquired an amazing number of parasites, about 300 species of helminth worms and over 70 species of protozoa [1]. Many of these are rare and accidental parasites, but we still harbor about 90 relatively common species, of which a small proportion cause some of the most important diseases in the world, inevitably, these are the ones that have received the most attention. Since most of these parasitic diseases occur mainly in the tropics, the field of parasitology has tended to overlap with that of tropical medicine, and thus the histories of these two fields are intertwined [2].

The German scientist Theodor Bilharz (1825-1862) (Figure 1) is one of the founders of tropical Medicine. He played a big role by discovering the *Schistosomiasis* worm while in Europe at that time the focus of research was on the life history of tapeworms. *Schistosomiasis* was a major killer of the Egyptian people. We do not have exact numbers reflecting the incidence of the disease at that time, nevertheless in the period between 1933 and 1945 over 300,000 Egyptian were treated from the disease per year [3]. Bilharz was and is still considered the savior of the Egyptian lives. His name will forever be

pronounced by the thousands of patients who attend daily at Egyptian hospitals to be treated for Bilharzia. In our biography we reviewed the life of this great scientist who made this notable contribution.

The light of the world

On March 23 1825, the small city of Sigmaringen in the Dukedom of Hohenzollern in Germany saw the birth of Theodor Maximillian Bilharz, which was described by Angelika Althoff as "Das Licht der Welt" or the light of the world [4]. He was the first of nine children [4]. His father Joseph Antony Bilharz (1788-1877) was an advisor to the duke [5]. He had a moral modest character, with full loyalty and dependence to his country gentlemen [4]. In 1824, Joseph Bilharz married Elisa Fehr (1800-1889) who came from a well known family "Zollikhofer" in Switzerland [4]. Theodor was closely linked to his younger brother Alfons (1836-1925) who was always in his company. Theodor's love of nature developed early and with Alfons, he collected and examined rocks, plants and butterflies with enthusiasm and care. With great intelligence and excellent language ability, Theodor completed his gymnasium time in 1843 in Sigmaringen with best notes (Figure 2). He also had

great interest in literature and was even talented in writing poems from which "Die Trane des Seraphs" or the travels of the Seraphs [4], but did he know he could be one of those Seraphs?

The beginning of brilliancy

In the winter semester of 1843, Theodor began a two year program in the field of philosophy and natural science in Freiburg. In autumn 1845, he followed the highly valued anatomist Friedrich Arnold (1803-1890) to Tubingen where he switched to actual medical studies. Friedrich Arnold was privy counselor and professor emeritus of anatomy and physiology at Heidelberg. He studied medicine at the University of Heidelberg with his elder brother Johann Wilhelm Arnold (1801-1873). His anatomy-teacher was Friedrich Tiedemann (1781-1861). Arnold was a popular teacher, a man of vivid appearance and a deep concern for the welfare of his students [6]. His lectures and courses, his excellent presentations and his teaching talents were unique and were extremely admired by Bilharz.

"In medicine, everything depends on the teacher – the method, the mental band by which he is able to link scarce and ambiguous facts". Said Bilharz [4].

Theodor's interest in medicine did not mask his other interests, and he used to introduce himself as.....

"My name is Theodor Bilharz. I come from Sigmaringen. I study Medicine, but a lot of other things are interesting for me; Botanik, osteologie, Zoologie, Mineralogie, Geologie and last but not least Meteorologie. Neither the beginning nor in the course of my studies, it is the real medicine, which attracts me. It is the natural science, among them the morphology and physiology of humans and animals that attract." [7].

In addition to the prescribed studies, Bilharz undertook scientific treatises in the English and French languages. Some professors immediately recognized his outstanding talent and passion.

In 1846, the Medical faculty of the University of Tubingen offered a prize for a work on the theme: "The Blood of Invertebrates Animals." Full of zeal, Bilharz edited the problem and received the first award. In April 1849 Bilharz passed the state exams and received the title: "Practice of Medicine, Surgery and Pharmaceutics".

For more intensive studies, he joined Carl Theodor von Siebold (1804-1885) in Freiburg. Von Siebold was a German physiologist and zoologist. He studied medicine and science at the university of Berlin and Gottingen. His best known publication was the "Lehrbuch der Vergleichenden Anatomie" [8]. In this work he was responsible for the introduction of the taxa Arthropoda and Rhizopoda and for defining the taxon Protozoa specifically for single-celled organisms

[8]. Under the guidance of von Siebold, Bilharz specialized in comparative anatomy and microscopy. "I try to get that prepared under Siebold's auspices, that my stay in such prosperous regions might also be beneficial for science. The path to become a professor is maybe shorter via America than via Tubingen." [4]. In 1850 he received an appointment by Georg Ludwig Kobelt (1804-1857) as provisional prosector [4]. Kobelt was a German anatomist from Baden. He learned medicine at the University of Heidelberg, where he studied under Friedrich Tiedemann (1781-1861). Kobelt is credited for providing the first comprehensive and accurate description concerning the anatomy of the clitoris. The eponymous Kobelt's tubules are named after him [9].

The anatomist Arnold and the biologist von Siebold influenced the learning of Bilharz to such an extent that Bilharz followed his teacher Arnold to the University of Tubingen where he became acquainted with the German neurologist and psychiatrist Wilhelm Griesinger (1817-1868). He later returned to Freiburg in order to apply himself to the study of biology and Helminthology under the direction of von Siebold. His acquaintance with Griesinger was one of those chances which bring people together to make history [5]. Thanks to his permanency, existence and certitude, Theodor received his Doctor diploma without passing any exams, a fast unusual achievement [4]. The scientific career of Bilharz started in Germany where von Siebold developed in him the aptitude for research in helminthology and advised him to investigate the worms which infest the population in Egypt. At that time in Europe the burning interest of research workers was focused on the relation between cysticerus and the life history of tapeworms [4]. In May 1850, Bilharz embarked on a journey to Egypt [4].

Egypt in the 19th century

Egypt as described by Bilharz "this land blessed by God for intestinal worms", was a junction of the world's commerce, trade and a gather place for all races with their various modes of life and habits [4]. Kasr El-Aini, The Faculty of Medicine Cairo University is one of the biggest and oldest medical schools in Africa and the Middle East, Established at 1837, the faculty was named after Al-Aini Pasha (1444-1502), whose palace was originally the school's main building [10]. It was out a desire for expansion, that the School of Medicine was moved from Abou Zaabal to Kasr El-Aini at 1837. It later became a hotel, where kings and princes were received during the big official receptions given by the Mamluks. Finally, under the French occupation of Egypt, this palace was transformed into a military hospital. When Abbas Pasha I (1813-1854) ruled Egypt (1848-1854), he tried to pull down all that was French according to the British councilor's advice. As a result, Clot Bey (1793-1868) the head of the medical administration of the country- resigned in 1849, and was succeeded by Dr. Duvigneau, then Peron Bey, and then Shafir Bey, who was the first Egyptian President of the Medical School [11].

The historical trip

In 1850, Griesinger was appointed director of health of Egypt and the head of the school of medicine. Griesinger named Bilharz as assistant to accompany him in Egypt. When he knew about this mission, Siebold sent Theodor Bilharz's father.

"...I can't help it to speak out the wish that the stay of your good Theodor may be a credit to him and to science. As far as I had the pleasure to get to know this young man, I won't believe anything else than that a longer stay in wonderful Egypt would be excellent used by your son. God may save his health." [4].

Bilharz's pleasure at the prospect of receiving an appointment in Egypt excited him to such an extent that he related that he was unable to shut his eyes during that night .He started his journey on May 25, 1850 to Vienna where he joined Dr. and Mrs. Griesinger.

The whole party sailed from Triestby way of Corvozenta, Athens, Syria, Smyrna and finally reached Alexandria on June 18, 1850 [5]. The journey was for Theodor a unique experience. He was enthusiastic about art and nature, Eastern and Western architecture [7]. Once in Cairo, Bilharz and Griesingers lived together in Azbakia in a beautiful house, from where they used to travel every morning to the school of medicine [5].

Shortly after his arrival in Cairo, Bilharz prepared lectures in the old medical school of Kasr-el-Aini. In addition to that, he took care of the clinical department in the military hospital [12]. Biharz was able to create a large number of graphs based on data from the history of sick patients [7].

Bilharz's interest in Anatomy extended his work hours into the evening in order to carry out as many dissections as possible, to the extent that he autopsied four hundred bodies in seventeen months. At that time, post-mortem dissections were not known in Egypt, as these performances were contrary to the tradition of the country. In 1852, however, Griestinger left Egypt, to be replaced by Bilharz as professor of Medicine, but later Bilharz was transferred to work in Surgery. After the death of Abbas the First, Mohamed Said succeeded him as Khedive (1854-1863). As Said Pasha was Francophil to a very great extent, he recalled Claud Bey to Egypt, to head the school of Medicine. As a result of this appointment, the German professors were dismissed from the school. Through the efforts of the German Consul, the Khedive ordered

the return of Bilharz to the school, but Clot Bay accepted him as professor of Anatomy in order to keep him away from medicine and surgery. Bilharz accepted the new appointment willingly, and continued to work as a teacher of Anatomy. Although anatomy was a subject of great interest to Biharz, he was also very attached to Egypt which he considered to be a most beautiful country. He lived of the palace of Souliman Pasha Elfaransawi (Formely Colonel of Seve of Napoleon's army). This palace looks over the Nile near old Cairo, facing the most bewildering landscape; a panorama of palm trees, desert and, in the far distance, the Great Pyramids rising high towards a clear sky and sunshine, representing the history of pharaonic Egypt [5]. His brother Alfons stayed with him in Egypt for seven months, he noted in the chronicles of the family:

"My brother was residing in one of the smaller Arabian houses in old Cairo, not far from Soliman Pascha's palace, where the Reyer and the Lauter family lived in a wing that was explicitly attached for their use...earlier, my brother had lived in a quite similar house until it was split from the top to the bottom by the earthquake of 1853" [4].

History of Schistosomiasis

In 1910, Marc Armand Ruffer found *S. haematobium* eggs in two Egyptian mummies dating from the 20th dynasty, 1250 to 1000 BC [13]. Thus, there is direct evidence that schistosomes were present in ancient Egypt, and there have been numerous attempts to find descriptions of this condition in the medical papyri [14]. The most contentious word is 'aaa', which occurs in over 50 early papyri including the Ebers papyrus. In some medical papyri 'aaa' occurs together with the initial hieroglyph suggesting a penis discharging what has been interpreted as blood [15].

The juxtaposition is the papyri of 'aaa', antimony-based remedies, and possibly worms in the body suggests schistomiasis haematobia, and this interpretation is widely quoted in historical and parasitological textbooks. However, since schistosomiasis was almost certainly common and widespread in ancient Egypt, it is curious that the Egyptians did not have a word for it unless it was so common that it was ignored [2].

The famous Egyptians were famous throughout the ancient world for their medical skills. Papyrus Ebers, at more than 100 pages, is the longest medical papyrus and dates from 1550 BC [16]. It is a mixture of magical spells, appeals to the gods, pharmacologic remedies, and clinical observations. Of the many diseases covered in the papyrus, hematuria is discussed no less than 50 times, indicating that hematuria was a prevalent complaint of ancient Egyptian patients. Hematuria is one of the symptoms

of *schistosomiasis*, and given what is known from the studies of mummies, it is a reasonable diagnosis. In Papyrus Ebers, one remedy often has been quoted as linking the hematuria directly with worms, suggesting that ancient Egyptian physicians understood the cause [17].

The problem of Schistosomiasis in Egypt did not become serious until the development of perennial irrigation after 1821, when there was a rapid increase in agricultural production and rural population [18]. The differences between the schistosoma species are principally related to the different intermediate and definitive hosts that they infect and the location within the human host to which the parasites migrate. Broadly speaking, the main snail hosts of S. haematobium are those of the Bulinus species, and the adult worm develops in the veins of the human bladder. The disease presents with ulcerations in the bladder wall causing dysuria, hematuria, and urinary frequency. Over time, chronic cystitis develops S. mansoni usually develops within Biomphalaria snail species, and the adult worm develops in the mesenteric vessels of the small intestine. The other main parasitic species, S. japonicum, usually develops in the Oncomelania snail, while the adult worm develops in the large intestine and, as in the case of S. mansoni, eggs are transmitted through human feces [19]. Early on, intestinal mucosal ulcerations caused by S. mansoni or S. japonicum may bleed and produce bloody diarrhea. As lesions progress, focal fibrosis, strictures, fistulas, and papillomatous growths may develop.

There is no doubt that the discovery of Bilharzia worm is of great significance, because the disease affects over hundreds of millions of people. Clot Bay and Lautner attempted in vain to discover the cause of the disease by repeated dissections, but all efforts failed until Bilharz discovered the worm, which is known according to our present nomenclature as Schistosomum Weinland in 1858.

The big discovery

The first fruit of research which was reaped by Bilharz in Egypt was related to von Siebold in a letter dated the first of May 1851, in which he revealed his discovery of the Bilharzia worm.

"As helminths in general, and those who attack humans in particular are concerned, I think Egypt is the best country to study them. Nematodes in particular populate the intestines of the indigenous population in unimaginable quantities. It is not unusual to encounter 100 individuals of Strongylus duodenalis, 20-40 Ascaris, 10-20 Trichocephalus and close to 1000 Oxyuris. My attention soon turned to the liver and associated structures; in the blood from v. portae I found a number of long, white worms that with the

naked eye appeared to be nematodes. A look in the microscope revealed a magnificent Distomum with flat body and a twisted tail. These are a few leaves of a saga as wonderful as the best of thousand and one night - if I succeeded in putting it all together." [20]

His correspondence of the subject continued until 1853. Biharz described the disease of the bladder produced by the worm, which he found also in the portal vein and mesentery (Figure 3).

In the beginning he was puzzled as to the nature of the worm, because he found the male at first, and it was not known at that time that the sexes in any member of the class trematoda were separated. He, however, was the first to discover the occurrence of this phenomenon in trematodes, where he found the female lying in the gynecophoric canal of the male Bilharzia. He described it in detail and drew it accurately on the first of December 1852.

He also found the worms and their eggs in sections of the bladder and liver. Later he demonstrated the eggs in the intestinal submucosa. The nature of the terminal-spined ova, present also in his specimens, remained obscure to him. In March 1852, Bilharz described the infiltration, sclerosis and polyposis which appeared in the bladder as the result of Bilharzia; in May of the same year he attributed diseases of the kidney and nephrolithiasis to Bilharzia and was able to find the eggs in the stools and urine. His attention was directed by Giesinger and Lautner to the possibility of Bilharzia as a cause of dysentery; and was followed by the discovery of Bilharzia egg in diarrhea and acute dysentery cases. In addition he indicated calomel as a treatment for Bilharziasis.

There is appoint of doubt however, whether the valid name is Schistosomum or bilharzia, because the latter name was designated by Meckel Von Hembach in 1856. According to the law of priority the latter name ought to be accepted but the international committee of zoological nomenclature has kept the word Schistosomu [5].

Other discoveries

His discovery of Schistosoma was just a part of his contribution to science. In 1857, Bilharz wrote a monograph covering his research on the electrical organ of the Egyptian electric eel or "thunderfish" – a common symbol seen in Egyptian hieroglyphics. This was an effort which Bilharz considered to be of much greater importance than his discovery of Schistosoma. Much of his work for over a decade focused on the study of ethnology, geography and ecology. Compilation of materials and observations on these latter subjects can be found, but Bilharz did not personally publish much of his work, believing them to be of little significance [21]. Bilharz also discovered

Heterophyes Heterophes and Hymenolepis nana in the human intestine [5].

A short trip to Germany

In 1858, Bilharz returned for the first and only time back to his homeland. It was a five months holiday where he travelled to Vienna where he gave a lecture about his Helminthic researches before keping himself by Freiburg, Tubingen and his hometown Sigmaringen. Overall young but already a well known professor, he was welcomed by his old friends and without exception he made the best impression to all of them. The ophthalmologist von Graefe (1828-1870) and the physiologist Du Bois Reymond (1818-1896) and Helmholtz (1821-1894), the pathologist Virchow (1821-1902) and the Egyptologist Brugsch (1827-1894). Alexander von Humboldt (1769-1859) and the geograph Petermann (1822-1878), the physician Carus (1789-1869), the surgeons Billroth (1829-1894) and Trendelenburg (1802-1872) and the zoologists Wagner (1813-1883) and von Baer (1792-1876), the publisher Brockhaus, the historian Mommsen (1817-1903) and the clinician Kussmaul (1822-1902) were the weighty spirits that Bilharz knew during this holiday [12]. In November 1861, he wrote a letter to his brother Alfons from Cairo (Figure 4).

The tragic end

The first journey undertaken by Bilharz was a glorious journey to Egypt accompanying Griesinger, but the second was a fateful one on the red sea cost accompanying Ernst the Second of Koburg-Gotha (1844-1893). Bilharz had to join the restless duke after persuading him and obtaining permission for him from the Khedive of Egypt. There was at that time an outbreak of typhoid in Mesawoa where Bilharz found it his duty to attend patients suffering from the disease, and thereafter contracted it himself. On his return to Egypt he went directly to the house of his friend Lautner. In spite of all the care and efforts of his friends, he died on of May 9, 1862 and he was buried in the cemetery of Roman Catholics in Old Cairo, were his grave was discovered in 1928.

When the grave was opened, he was found dressed in his uniform (in Egypt at that time doctors wore military uniforms). The delegates of the Congress of Tropical Medicine, held in 1928 in Cairo, attended a ceremony of remembrance at his grave which they decorated with wreaths and flowers, in recognition of the discoveries of this great scientist.

Bilharz is one of the founders of tropical Medicine. His name will ever be pronounced in Egypt as he is well known for the entire population [5]. In Sigmaringen a school, a street and a pharmacy are named for him. Bilharz was one of the earliest founders of scientific infectology [20].

While no monuments stands to commemorate his contribution to medicine and science, Egypt erected in his honor the Theodor Bilharz Research Institute, one of the foremost centers for research. Perhaps his impact on Egyptian science is best reflected in the writings of Professor Olav Thulesius during his search for Bilharz' grave: "When I was in Cairo searching for the grave of Bilharz I asked a taxi driver for help. When I mentioned the name of Theodor Bilharz he immediately knew who I was talking about and what disease I meant. For a whole day he helped me to locate the small and forgotten churchyard in the old town where Bilharz was buried" [21].

Conclusion

"I know her well, the sorceress science. Once, I was almost about to sacrifice my life for it, just because of its beautiful eyes. There I learned to serve life and science in equal measure, the sword in one hand, the plough in the other. And that is the best, I believe, for those who are not children of luckiness. Tempora mutantur, it mutamur in illis." [4].

If these facts represented the sum total of Bilharz' work we might be inclined to dismiss his biography as the sad but not unusual story of a man who made one notable contribution and died voung. But Bilharz' scientific activity included another aspect that is well worthy of mention. For more than a decade of his short life he actively pursued the study of ethnology. geography, and ecology. He has assembled considerable collections of material and notes on these subjects. His interests apparently were directed towards the comparative anatomy of the Negro, the diseases of Egypt, the ecology of the Egyptian people, and the Egyptian flora and fauna. It is therefore not surprising that he came to be recognized as the outstanding scientific authority on Egypt. He communicated his knowledge freely for students, colleagues, and friends [22].

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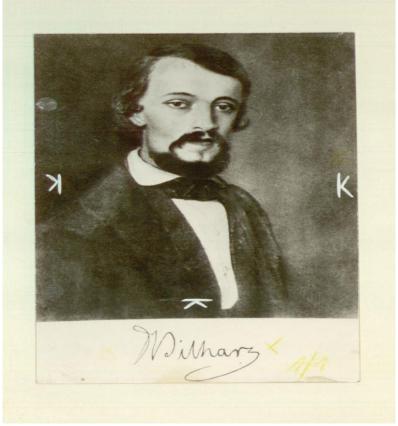


Fig. 1- Picture of Theodor Bilharz. Universitaetsarchiv Duesseldorf 7-39, 14

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Fig. 2- School report for Theodor Bilharz from 1841. Universitaetsarchiv Duesseldorf 7-39, 1.

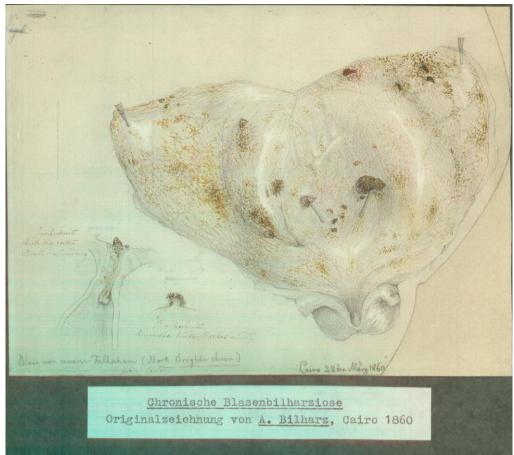


Fig. 3- Chronic bladder Bilharziazis, original drawing by Alfons Bilharz, Universitaetsarchiv Duesseldorf 7-39, 12.

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Fig. 4- Letter to Alfons, Cairo, November 16 1861, first page. Universitaetsarchiv Duesseldorf 7-39, 8.