Outstanding discoveries made by medical students

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ABSTRACT

Some historical accomplishments and discoveries made by medical students were achieved due to their talents, luck, observation, serendipity and "sudden unexplained understanding" of the fact, and also, due to proper atmosphere and encouragement induced by their mentor/ director/teacher.

Key words: discovery, medical students

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"The luck of having talent is not enough; one must have a talent for luck"
(Hector Berlioz, medical student who became a famous composer).
-"dans les champs de l'observation le hasarol ne favorise que les esprits prepares"
(Louis Pasteur)

INTRODUCTION

Today scientific research focuses more on evidence-based medicine and less on intuition and experience. In medicine, we speak of knowledge, sensitivity, intuition and luck. Logical thinking and intelligence, interest and inquisitiveness, perseverance and steadiness, technical ability, experience and information, are indispensable for a potential success. The Greek Sophists distinguished between *techne* (knowledge, skill) and *tyche* (fate and unattainable power) [1]. During the Renaissance the terms were revived as *virtus* and *fortuna*. Talent may not always be the most important factor. Discovery is often preceded by accurate observation, understanding the background and sudden insight. Can we teach the student such an insight? Hippocrates wrote: "The art of medicine is long; life is short; the right moment fleeting [or occasion slips through our fingers]; experience can be misleading..." the father of medicine neatly summarized the problem and its solution. During relatively a short time we must study a lot, draw conclusions, internalize, grasp the opportunity and help those in need.

"Young Endeavour"
Back in 1958, William Carelton Gibson: (1913-2009) published *Young Endeavour*, a book which looks on the precocious contribution to science done by medical students [2]. The 292 pages of the book are organized in 12 chapters, according to medical fields, such as, anesthesia, cardiovascular system, digestion, infections, nervous system, and in non-medical fields like physics, optics, or bibliography. The book is furnished with illustrations, pictures, citations and a comprehensive literature survey. Gibson surveyed four centuries and did not mention living persons. He admitted that in order to list the contributions of all students along history- many volumes should be dedicated to this impossible mission [3].

Sir Henry Dale , in his introductory notes to Gibson's book, wrote that " it is evident that opportunities to try his hand at research, and thus obtain some practical experience of its methods and of the significance of its results, are much more readily available now to the proper kind of interest and enterprise, than they were in the by-gone days, when there was so relatively little to be learnt , and whom it might , accordingly , have seemed so much easier to spare the time for a diversion from the narrow way of formal education. There were those among us, indeed, who were so fortunate as to receive even then, some of the rare opportunities which were on offer". In his conclusions, Gibson made a plea for greater interest in and increased facilities for undergraduate medical research. His last sentence reads:"If the history summarized in these pages helps up, students and teachers alike, to be more imaginative investigations of Nature, it will have been well worth the writing". Albert Sent-Gyorgy, Nobel Prize laureate, 1937, said that "Research is four things: brains with which to think, eyes with which to see, machines with which to measure, and money."

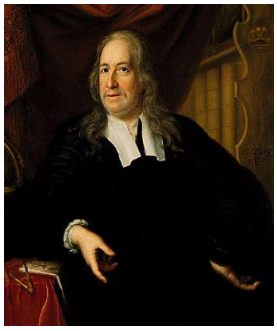
Some discoveries made by students were achieved due to their talents, luck, observation, serendipity and "sudden unexplained understanding" of the facts [4-5], but also, proper atmosphere and encouragement induced by their mentor/ director/teacher.

A few examples of contributions made by medical students, mentioned by Gibson. Niels Stensen (Steno), (1638-1686), Danish anatomist, natural scientist, and theologist, was a medical student when he discovered the parotid duct in sheep in 1661. Stensen acquired a knowledge of German, Dutch, French, Italian, Latin, Greek, Hebrew and Arabic. Among his teachers were

Niels Stensen (Steno)
(1638-1686)

Thomas Bartholin (1616-1680), Bartholin's brother Erasmus (1625-1698), and the anatomist and botanist Simon Paulli (1603-1680). In Amsterdam Stensen studied anatomy under professor Gerhard Bläes (Blasius). Steno described later the "Fallot's tetralogy", a congenital cardiac anomaly, the Stensen's foramina (an incisive foramina of the hard palate, transmitting anterior branches of the descending palatine vessels and more [6-7].

Olof [Olaus] Rudbeck (1630-1702) was one of the pioneers in the study of lymphatic system. As a student at Uppsala University he began dissecting small animals and found the lymphatic connection between the intestines and the circulating blood, leading the prepared nutrients via the thoracic duct to the veins. He also observed the



Olof [Olaus] Rudbeck (1630-1702)

direction of the lymphatic flow and it was along William Harvey's novel theory of blood circulation [8-9].

Probably, parallel to his discovery, the Danish Thomas Bartholin made the same observations, and much dispute arose.

Paul Langerhans (1847-1888)

Paul Langerhans (1847-1888) was a medical student in 1869 when he discovered the islets in the pancreas which bear his name. A year earlier, he had already showed cells in the skin, using gold chloride stain. In 1868 using the technique taught to him by Julius Cohnheim, 1839-1884), he stained a sample of human skin with gold chloride and described the dendritic cells in the skin which now bear his name and which from their morphology he believed to be nerve cells. It was during his studies for the doctorate at the Berlin pathological institute that he made his second important contribution (1869) of the islet cells of the pancreas. These cells are known as Langerhans cells. His numerous other contributions to anatomy, pathology, anthropology, and clinical medicine (particularly leprosy and tuberculosis) are less known. In 1870 he joined the Kieperts, father and son, two noted German geographers, on an expedition to the Middle East. His clinical and anthropological findings from this journey appeared in the journal published by his famous mentor, Rudolf Virchow. Langerhans later contracted tuberculosis and spent his last years on the island of Madeira, where he continued to investigate, practice medicine, and to write [10].

Friedrich Wöhler (1800- 1882)

In 1821, as a young medical student, the future famous physician-chemist Friedrich Wohler, wrote that upon heating, a chemical compound could be seen "winding out from itself worm-like to many times its former bulk." It became a staple of laboratory demonstrations, and they soon became popular throughout Europe and it appeared in America in 1865 [11]. In November 1865, scientists were warning the public of the possible dangers of the popular "toy" [12]. Friedrich Wöhler (1800-1882), during his basic studies had acquired an sincere interest in practical chemistry and mineralogy. He chose to study medicine at Heidelberg University. Among his teachers were Leopold Gmelin and Jöns Jakob Berzelius in Stockholm. Wöhler was a prolific writer of textbooks; his organic and inorganic chemistry texts went through thirteen and fifteen editions, respectively, in his lifetime. Wöhler is best known for his synthesis of urea and the isolation of aluminum. He is also known for his important studies of the elements boron, silicon, beryllium, and titanium [13].

Daniel Alcides Carrión García (1857–1885)

In Lima, Peru, a medical student named Daniel Carrión believed that Oroya fever and verruga peruana were the same disease. To prove this, he inoculated himself with blood from a verruga, developped Oroya fever, and died. He was a medical student after whom Carrion's disease is named. He was inoculated by close friends with blood from a wart Daniel Alcides between the eyes of a 14-year-old boy. His aim actually was to prove a link between the acute blood stage of Oroya fever with that of the later chronic form of the disease Verruga Peruana typified by numerous red wart like dermal nodules. Neither the cause nor mode of transmission of Oroya fever was then known

John Bruce MacCallum (1876-1906)

and furthermore, the relationship between the acute and chronic forms of the disease was not proven. After his death from the disease, his friend was arrested and tried for murder [14].

John Bruce MacCallum (1876-1906) as a student contributed to the anatomical knowledge of the tuberculosis, returned to California (working under arrangement of the muscle fibers of the heart, went on to study in Leipzig, where he contracted Jacques Loeb) where he investigated the role of ionic balance in the absorption of foodstuffs through the intestinal wall. He died prematurely of the consumption [15]. Frederick Augustus Dixey (1855-1935), was one of the 'pioneers of osteogeny', while assisting Sharpey-Schafer, in researches on bone formation in the fingers and toes.' [16]. A histological preparation made by him was used for an illustration still reproduced in Quain's "Anatomy". But it was

Martin William Flack CBE (1882-1931)

as an entomologist that Dixey will be remembered: his first entomological publication was on the phylogenetic significance of wing markings in certain Nymphalid butterflies, and until his death on January 16, in his eightieth year, he was associated with the study of evolutionary entomology at Oxford, so intimately bound up with the name of Poulton" [17]. One medical student's contribution to medicine nearly won him a Nobel Prize. Sir Frederick Banting, (1891-1941) a Canadian orthopaedic surgeon, decided after returning from the battlefields of World War I, to switch to basic scientific research. In 1921, he approached John Macleod (1935-1876), professor of physiology at the University of Toronto, with a project to discover a cure for diabetes mellitus. He asked for assistants and, he choose a second year medical student, Charles Herbert Best (1978-1899) and a technician- James Collip. After one year of hard work, they discovered the" Isletin" (insulin). The Nobel Committee, however, awarded the prize only to Banting and Macleod. Irritated, Banting shared half of his prize money with Best and Macleod shared his with Collip. Best succeeded Macleod as professor of physiology at University of Toronto in 1929. During World War II Best was influential in establishing a Canadian program for securing and using dried human blood serum. In his later years, best was an adviser to the medical research committee of the United Nations' WHO [18]. Group Captain Martin William Flack CBE, (1882-1931) was a British physiologist, made, as a student, anatomo-respiratory cardio-physiological pioneering work (under Sir Leonard Hill and Sir Arthur Keith). During the War, he defined tests which differentiated suitable from unsuitable candidates for flying. Flack's test: endurance test of the heart. A combined but simple test for evaluation of the capacity of military personnel and pilots. The Keith-Flack node's the sino-atrial node of the heart, often called the pacemaker of the heart. Keith and his

John Gregory (1724-1773)

assistant Flack described it in 1906 [19].

Contributions made by medical students, not mentioned by Gibson Sometimes medical students helped to publicize their mentor or teacher's thoughts. Dr. John Gregory's (a Scottish physician, ethicist and philosopher, lectures were later collected and published anonymously, most probably by medical students, and his son John was among them. In A Comparative View of the State and Faculties of Man, with those of the Animal World (1765), Gregory believed in a universal human nature that could be discovered through scientific experiment [20-21]. He was the first to include in his lecture an introduction to medical ethics. Petrus Camper (1722-1789) was a Dutch painter, physician and anatomist. As a student Camper made an important discovery of microscopic anatomy, as he in one of his dissertations established that the lens of the eye is made

Petrus Camper (1722- 1789)

up of fibres, as had already been assumed by the great natural scientist and miscroscopist Antonie van Leeuwenhoek (1632-1723) [22-23].

A few eponyms are named after him: Camper's facial angle, Camper's chiasma, Tendinous chiasm of the digital tendons. Camper's fascia: the fatty part of the superficial fascia of the lower anterior abdominal wall. Camper's instrument Vectis - a lever which is a pre-cursor to the obstetrical forceps. Camper's ligament the layer of fascia extending between the ischio-pubic rami inferior to

the sphincter urethrae and the deep transverse perineal muscle.

John Filson, a medical student, surveyed Cincinnati, Ohio [24]. Filson (1753-1788) was an American author, historian of Kentucky, pioneer, surveyor and one of the founders of Cincinnati, Ohio. John Filson served as an Ensign in Montgomery's Pennsylvania Battalion of the Flying Camp and was taken prisoner at Fort Washington (1776) during the Battle of New York. He worked as a schoolteacher and surveyor in Pennsylvania until 1782 or 1783. While on a surveying expedition near the Great Miami River, he disappeared, (1788), probably killed by hostile Shawnees [25].

John Filson (1753-1788)

Richard Friedrich Johannes Pfeiffer (1858-1945), a student and later assistant of Koch at the Institute of Infectious Diseases in Berlin, Germany, published in 1892, the preliminary results of the experi-ment conducted a year before: Pfeiffer examined 31 cases of influenza, six of which included autopsies. In all cases, he found a bacillus in the bronchial secretion in the peri-

Richard Friedrich Johannes Pfeiffer (1858-1945)

bronchial tissue and on the pleura. He also observed the absence of this bacillus in the bronchial catarrh produced in cases of pneumonia and tuberculosis. He inoculated different animals. The results obtained with these experiments led Pfeiffer to conclude that the pathogen - *Haemophilus influenzae* - was the cause of "flu", although he was unable to reproduce it in other animals. Pfeiffer's eponyms include: the bacillus - Gram negative, non- motile, non-sporing rod of the genus *Haemophilus* in the *Brucellacae* family.

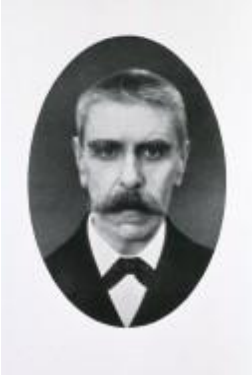
Pfeiffer's meningitis -Meningitis caused by Pfeiffer's bacillus *Haemophilus influenzae*. Pfeiffer's phenomenon -destruction or dissolution of bacteria. Pfeiffer's test-animal test for bacteriolysis. And *Pfeifferella* is an obsolete genus of bactera [26].

Louis Prévost (1838-1927)

Geneva born, Jean Louis Prévost (1838-1927) studied medicine at Zurich, Berlin, Vienna, and Paris. In 1864 he worked and studied in Paris under Alfred Vulpian (1826-1887), and as a student, he published a work on softening of the brain with Jules Cotard (1840-1887), and also on infantile paralysis .Jean His thesis on the conjugated deviation in unilateral brain lesions, is named the Prévost's syndrome. With his mentor, he published the Vulpian-Prévost law: In patient with symptom in the unilateral brain affection, the head is rotated toward the affected hemisphere. In 1868 he finished his medical studies and returned to Geneva. He later collaborated with the English neurologist Augustus Volney Waller (1816-1870). Among his pupils, were Joseph Jules Dejerine (1849-1917), Jean Baptiste André Dumas 1800-84, and Paul Charles Dubois (1848-1918).

After Prévost's death, Moritz Schiff (1823-1896) was appointed professor in the newly created Faculty of Medicine in Geneva [27]. The Prévost's syndrome is, a conjugated deviation of the eyes seen in unilateral brain lesions. Jovan Andrejevitsh [Andrejević] (1833-1964) a Serb who graduated in 1861. Later, he was known as a writer, translator and literary critic. Professor R. Ernest Bricke, appointed him for his assistant. Still a student, he published his work "About the Fine Structure of Liver" (Uber den feineren Ban den Leber) showing that the small channels in liver are a part of the biliary tract, and the biliary capillaries do not touch blood capillaries. His achievement was appreciated by the Viennese Royal Academy of Science [28]. Julius Wagner-Jauregg was an Austrian psychiatrist and neurologist, (1857-1940). As a student, Wagner-Jauregg, who worked and studied under Salomon Stricker (1834-1898) at the Institut für Allgemeine und Experimentelle Pathologie and became very skilled in performing animal experiments, had published two papers, one on the sympathetic supply of the heart which was published under both Stricker's and his name, and a second paper on "Contributions to the knowledge of the Julius Wagner-Jauregg (1857-1940)

respiratory active-ties of the Nervus vagus," published in 1879. It is worth to note that as a child, he contracted typhoid fever, and later, in his student period, and he contracted tuberculosis with haemoptysis.



Julius Wagner-Jauregg (1857-1940)

Nevertheless, he continued his studies and was fully engaged in sports. Recently, it was revealed that Wagner-Jauregg supported the Nazi ideas, although some of his mentors were Jewish, and first wife, Balbine Frumkin, was also Jewish [29].

Ernest Duchesne (1874–1912) was a French physician who had observed that certain moulds kill bacteria. He made this discovery in 1897 thirty-two years before Alexander Fleming discovered the antibiotic properties of penicillin, a substance derived from those moulds, but his research went unnoticed. Duchesne died at an early age in 1912, never seeing the world's acceptance and use of his important discovery [30-32]. The American Benjamin Robinson SCHENCK (1873-1920)

Jay McLean (1890-1957)

and Alejandro POSADAS (Argentine parasitelogist, 1870–1902) were medical students at the time of their discoveries. Schenck's disease is a chronic disease, occurring in two forms, caused by the fungus *Sporothrix schencki*. In one type there is lymphatic spread to in the musculo-skeletaal system, gastrointestinal and nervous systems. The pulmonary type is marked mainly by pneumonia. *Sporothrix schenckii* was renamed *Sporotrichum beurmanni* after more thorough studies were made by de Beurmann in 1903 [33].

Posadas-Wernicke disease is a systemic mycosis caused by of dust particles containing Arthroconidia of *Coccidioides immitis*.

In 1916, McLean, a second-year medical student at Johns Hopkins University, was working under the guidance of Howell investigating procoagulant preparations, when he isolated a fat-soluble phosphatide anti-coagulant. Howell coined the term heparin for this type of fat-soluble anticoagulant in 1918. In the early 1920s, Howell isolated a water-soluble polysaccharide anticoagulant, which was also termed heparin, although it was distinct from the phosphatide preparations previously isolated. It is probable that the work of McLean changed the focus of the Howell group to look for anticoagulants, which eventually led to the polysaccharide disco-very [34].

As an undergraduate at Goa Medical College in 1986, Jayant Vaidya, "realized" while lying on his right side at night, that the left side was sweating profusely although his left side of the body was directly receiving cooler wind from a fan. When he turned, he noticed that the left side quickly dried, and the right side was sweating. He then performed an experiment on 16 people to confirm the findings" [35]. "The mechanism of this effect of posture on autonomic control of sweating, which is controlled by the sympathetic cholinergic outflow, is up for speculation. Perhaps the hypothalamus, from where the sympathetic chains start, has lateralized functions that are dependent on signals from the vestibular apparatus" [35]. Later, his research (at University of Dundee, Surgery and Molecular Oncology) was focused on breast cancer – its natural history, biological and mathematical models, causes and mechanisms of local recurrence, novel treatment approaches, e.g. intra-operative radiotherapy and minimally invasive local treatment.

Manu Liladhdar Kothari

On page 689, in "Hamilton Bailey's Physical Signs in Surgery" [36], one can find a footnote: Manu Liladhdar Kothari, contemporary-house surgeon, The King Edward VII Memorial Hospital, Bombay. Still a student, in December 1955, he wrote to Hamilton Bailey about his own observation that in inflammations of the hip, the fixed adduction deformity can be measured visually without moving the patient's painful limb as was advised. And, the angle between lines joining anterior superior iliac spine and the deformed position with a line drawn bang horizontally from the spine on the normal can be measured visually. Only by inspecting the inguino-scrotal or inguino-labial curve, Kothary noted, male's inguinal hernia and the female can be differentiated from the femoral hernia.

In 1973, McManus wrote his first paper on laterality, a topic on which he is today considered one of the world's experts. Chris McManus of University College, London, received the 2002 Ig Nobel Prize for Medicine for a letter he had published in Naturein 1976. Mc-Manus, a medical student at the time, cited research showing that the right testicle tends

Ian Christopher McManus

to be higher in right-handed men, whereas the converse is true in left-handers. McManus examined 107 antique sculptures. He discovered that in most sculptures, the right testicle was higher, but the left (lower) testicle was larger. McManus did not know why ancient sculptors were dressing to the left, as it were, but speculates that it may be symbolic. The Greeks believed that the right side was associated with the male and the left side with the female — male children were thought to come from the right (higher) testis and female children from the left [37].

Francis Weld Peabody (1881-1927), entered medical school in 1903 and almost at once his talents were recognized. After a varied and exciting indo-ctrination in his profession, including responsibility for children ill with the dreaded poliomyelitis, an extensive medical trip to China and an unintended role in the start of the Bolshevik

Francis Weld Peabody (1881-1927)

Russian Revolution, he became a successful chief of a new Harvard unit at the Boston City Hospital. The expectations for a long productive life were faded away out by cancer six years later when he was only 45. Gifted in many areas, and his especial compassion and wisdom in patient care have made Peabody's short life an inspiring role model. His own credo was given as a talk to the students at the Harvard Medical, BOSTON School on October 21, 1926 [38]. While still a student, he undertook with his teacher J H PRATT the solution of a bacteriological problem relating to typhoid fever, and this was published in JAMA. Only twenty-two years old and still in medical school when Wilhelm Reich (1897 - 1957) was welcomed into Freud's circle, Reich was soon regarded as the most promising psychiatrist [39]. Sir Roger Gilbert Bannister (1929-), is a famous British Neurologist. While still a medical student, his historic opportunity came on May 6, 1954, at Oxford when

Wilhelm Reich (1897 - 1957)

when Bannister competed for the British Amateur Athletic Association. "He had arranged for his friends Chris Chataway and Chris Brasher to set the pace for the first laps, so he completed the first three quarter-mile laps in under three minutes. Finishing the last lap in less than a minute, Bannister broke the tape and collapsed as the announcer delivered his time to the cheering crowd: 3:59.4. The unbreakable record had been broken. At age 25, Roger Bannister made history." Sir Roger was the inaugural recipient of the Sports Illustrated sportsman of the Year award in January 1955 (1954 Sportsman of the Year [40].

Finally, a few anecdotes on notorious or dangerous medical students who did not entered history books due to any discoveries: Johann Georg Wirsung (1589-1643) a German anatomist who was for a long-time Prosector in Padua, was murdered in 1643 by Giacomo Cambier, a Belgian student, perhaps due to the result of an argument

Roger Gilbert Bannister (1929-)

as to who was the real discoverer of the pancreatic duct. Two students were present at the dissection when Wirsung had discovered the duct: Thomas Bartholin (1616-1680) and Moritz Hoffman.

Five years after Wirsung's death, Moritz Hoffman (1622-1698) claimed that it was he, and not Wirsung, who was the actual discoverer of the duct. Herman Webster Mudgett (1861 – 1896), ["Dr. Henry Howard Holmes"] was an American serial killer. Holmes owned a hotel in Chicago during the 1893 World's Fair, which was the location of many of his murders. He had confessed to perform to 27 murders. He graduated from

University of Michigan Medical School in 1884. Still a student, he stole bodies from university, disfiguring the corpses, claiming that the people were killed accidentally, Mudgett collected insurance money from policies he had taken out on each one. After graduating, he moved to Chicago to practice pharmacy. He also began engaging in many shady businesses, real estate, and promotional deals under the name "H.H. Holmes" [41]. Alexander Aleksandrovich Bogdanov [Александр Александрович Богданов] (born Alexander Malinovsky) (1873-1928) was a Russian physician, philosopher, economist, science-fiction writer, and revolutionary whose scientific interest ranged from the "universal systems theory" to the possibility of human "rejuvenation" through blood transfusions. Bogdanov died as a result of one of the experiments, when the blood of a medical student suffering from malaria and tuberculosis was given to him in a transfusion. Some scholars have speculated that his death may have been a suicide while others attribute it to blood type incompatibility, which was poorly understood at the time.

Returning to the main subject, I believe that today medical students should be exposed to medical humanities themes, including history of medicine, bio-ethics[42] rhetorics [43] (the proper ways to approach patients and families) and so forth. A special attention should be given to the historical achievements and contributions of medical students. I feel, that beyond the basic elements of talent, curiosity, dedication, learning from the past, living and exploiting "the right moment" and luck, the contributions made by students, were made possible also because of the good and proper directing /guiding and openness of their mentors and teachers.

Conflicts of interest

I declare that I have no conflict of interest.

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Note: all pictures were taken from the Internet.