The Influence of William Osler on the Development of Clinical Laboratory Medicine in North America*

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I. Introduction

When William Osler died in 1919, he was already a legend as one of the greatest physicians in the history of medicine. He had not accomplished any outstanding research such as Pasteur, Koch, or Ehrlich, and there were many contemporary clinicians who were his equal or superior. However, he possessed a unique personality which included natural aptitude for leadership, great self-discipline, capacity for work, vitality and ambition, unusual psychological understanding of himself and other human beings, the best in Victorian concepts of good character, contagious optimism, historical understanding and perspective of the field of medicine, and brilliant ways of communicating clearly his ideas orally and in writing. These characteristics combined with rigorous training, first as a naturalist and then as a pathologist, enabled him to advance clinical medicine in North America as a teacher and organizer probably more than any other individual.

Osler made a few important moves during his career. He attended McGill Medical School from 1870-72 and was a Professor of the Institutes of Medicine there from 1874 until 1884, when he left to become Professor of Clinical Medicine at the University of Pennsylvania. He remained in that position until 1889 when he left to take the appointment of Physician-in-Chief at the new Johns Hopkins Hospital where he organized the medical department and helped develop the new school of medicine which opened in 1893. It was here that he spent secret of his dislike for mathematics or his comparatively poor understanding of chemistry, although he recognized the importance of these areas,—especially the explosive development of immunology and physiological chemistry at the turn of the century. However, during the last quarter of the 19th century, when he was to exert his greatest influence, the ability to correlate the signs and symptoms of patients with gross and microscopic findings were the most important first steps in placing the practice of medicine on a scientific basis. So Osler's abilities, "wedded" to the needs of medicine at that time, produced a harmonious marriage which helped so vastly a backward medical America with its medical diploma mills, inferior hospitals and lack of first class medical centers or research facilities.

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his most important years as one of the famous "Big Four" (which included, in addition to Osier in medicine, Halsted in surgery, Welch in pathology and Kelly in gynecology) during those "heroic" years at the "Hopkins." He made his final move to England in 1905 to become the Oxford Regius Professor of Medicine, a position he held until the end of his life. In retrospect, although every move he made was misunderstood by friends and colleagues who held him in such high esteem and yet were left behind, it was probably the best for the development of medicine in North America since Osler always left behind a legacy of good deeds and accomplishments which served as bases or inspiration for the work of others and in this way made his influences more widespread.

Although much has been written on the contribution of Osier to clinical medicine, medical education, the history of medicine and anatomic pathology, very little has been mentioned about his influence on the development of clinical laboratory medicine. Most likely this was because during Osier's time the development of the laboratory examination of human fluids and tissue necessarily required the contribution of not only different individuals, but also such diverse fields as bacteriology, hematology and physiological chemistry, all of which were in their infancy. In researching the origins of laboratory medicine, this author kept finding Osier's name as one of the major European inspired clinicians who was stressing the importance of the laboratory in aiding the practicing physician. It is the purpose of this paper to document Osier's contributions to this field, which should be of interest not only to individuals in the clinical laboratory field, but also to the many admirers and followers of the writings about Sir William. Direct quotations and their sources will be given when possible in the interest of historical objectivity.

The large clinical laboratory today is a highly complex, automated, computerized organization performing hundreds of various procedures on human fluids and tissues as adjuncts to the clinical health evaluation of individuals in our society. Its present organization is more or less divided into the departments of chemistry, microbiology (including bacteriology, mycology, virology and parasitology), serology and hematology (including immunohematology and blood banking). But in the history of medicine, the clinical laboratory is a comparatively new phenomenon with humble beginnings and slow growth during the last half of the 19th century. It is only since the beginning of the 20th century that the almost exponential growth of the numbers of tests performed has occurred.

Each of these departments has its own particular history with its different pioneers and developers. The fields often developed completely independently of each other with different degrees of importance, depending on the changing pattern of diseases, disease concepts and clinical emphasis over the years. The term "clinical pathology" was first used in 1896 by Julius Dreschfeld, professor of pathology at Manchester University, who wrote, "But even apart from post mortem examinations there is a bedside or clinical pathology." Eventually the term came to be defined as the analysis of body fluids in the living patient to aid the clinician in diagnosis, prognosis and therapy. Then, as all of the branches of the clinical laboratory grew over the years, a medical specialist, the "clinical pathologist," came into being to direct it.

But at the time William Osler entered the field of medicine, there was no such field as clinical pathology. The only area remotely resembling it was "clinical microscopy," which had started about 1835, and was essentially the use of microscope in clinical medicine and encompassed the beginnings of histology,
hematology and parasitology (bacteria were not known to be pathogenic at that time). Prior to 1840, the microscopes were so poor in quality that the most eminent clinicians were justly skeptical of microscopical findings and believed that microscopy was a waste of the physician’s time. John Hunter states in the late 18th century:

“I am led to believe that we may be deceived by the appearances viewed through a magnifying glass”

and Bostock a few years later, at the beginning of the 19th century said:

“an historical detail of the errors into which this instrument has led even those who have been most skillful in its application would have the effect of inducing us to place little confidence in hypothesis and speculations which are derived from objects which can only be detected by the use of high magnifiers.”

In 1851, Bransby Cooper in an article in the Guys Hospital Reports, encouraging the use of the microscope for physicians, wrote apologetically:

“It is but a few years since the microscope was employed for no other purpose than mere amusement, and a man of science, more especially if he were engaged in the study of medicine, scarcely dared to admit that he sought its aid, from the fear of having it said, that he was engaged in investigations quite foreign to his legitimate pursuits, and that he was trifling away his time.”

However, starting with Alfred Donne, perhaps the first clinical microscopist, who gave a course and wrote a book in medical microscopy in Paris in 1837, and later John Hughes Bennett who attended Donne’s classes and then gave a similar but more complete course in Edinburgh in 1841, progress was made using the microscope so that, by 1850, physicians formed the most numerous group of microscopists. Some of the specific advances made by the use of the microscope were the differentiation of pus from amorphous material in urinary sediment, determination of malignant from simple ulcers by examining cells of scrapings, detection of the fungus of favus and the recognition of cases of leukemia from blood examination. In London, L. S. Beale established a private laboratory and gave a series of lectures entitled “The Microscope in Medicine.” He wrote a book by the same name, which was first published in 1854, went through four editions during the next quarter century and was to influence William Osler during his early days of medicine. This acknowledgment was made by Osler in a 1906 obituary on Beale in Lancet:

“The influence of Dr. Beale as a scientific investigator and as a clinical physician was much more widespread than perhaps was recognized. . . .His early histological studies were of great value, while as practical physicians we must always be thankful to him for the stimulating work which he did in medical microscopy. His two well known books “How to Work with the Microscope” and the “Microscope in Medicine” were of greatest service to two generations of medical students. Both in Canada and the United States there are scores of men of my day who will recall with gratitude labors which so often helped to lighten their own.”

II. Osler’s Preparation for Clinical Microscopy

One of the main reasons Osler was to play an important part in the development of clinical pathology was due to the skill he achieved in using the microscope as a schoolboy at Canada’s Weston School during the late 1860’s. It was here that he came under the influence of the Reverend W. Johnson who taught him not only how to use the microscope, but also how to be precise in his observations. He learned never to consider a detail unimportant because it was a detail. Osler took his microscope with him wherever he went and he was encouraged by Johnson to collect and prepare many specimens of diatoms, polyzoa and entozoa. One of his boyhood friends, the Reverend Arthur Jarvis of Toronto stated that on a fossil hunting trip in 1866:

“Osler was the scientist of the expedition. To him was entrusted the delicate work of grinding down and mounting specimens for microscopical slides.”
Osler's first paper was entitled "Christmas and the Microscope" published in Hardewicke's Science Gossip in 1869 in which he describes his collecting and studies of microscopical life in the ponds and streams of the Eastern Canadian woods during winter. A little later, while a student at the University of Toronto Medical School, he wrote a paper, which included a minute and scientific description of the life history of Canadian diatoms with a list of 109 species found near his boyhood home. Osler's interest in natural science was further developed by Dr. James Bovell, who was his teacher and perhaps the greatest influence in his life, since it was during this period with Bovell that he decided to study medicine rather than theology. This relationship is best described by Bovell's granddaughter in a letter as follows:

"He (Osler) was about twenty in those days and literally lived at our house. He adored Grandfather and the latter loved him like a son—and they were both crazy about the microscope."

Other indications of Bovell's influence was most aptly portrayed in Harvey Cushing's comment that:

"The man must have come to exercise an extraordinary influence over the boy, and to his last days, in moments of absentmindedness or when trying a pen, it was the name of James Bovell that came first to the paper, not his own."

It was through these early influences that Osler learned the importance of observations, their accurate documentation and then tabulations and conclusions that were features of his personality throughout his entire life and were also to influence hundreds of students and readers of his books and papers. W. S. Thayer, Osler's chief resident and protege during the early heroic Johns Hopkins years and later head of the department of medicine, reiterated this philosophy by paraphrasing Osler in the beginning of his essay, "Osler, the Teacher:"  

"Observe, record, tabulate, communicate. Use your five senses. The art of the practice of medicine is to be learned only by experience; tis not an inheritance; it cannot be revealed. Learn to see, learn to hear, learn to feel, learn to smell, and know that by practice alone can one become expert. Let not your conceptions of the manifestations of disease come from works heard in the lecture room or read from the book. See, and then reason and compare and control. But see first. No two eyes see the same thing. No two mirrors give forth the same reflection. Let the work be your slave and not your master."

This quotation is given here only to emphasize how the credo of the middle of the nineteenth century naturalists came to the wards of the best hospitals in the 1880's and 1890's as differentiated from the more pseudoscientific, romantic and often falsely theoretical medicine before that time.

Osler was elected a member of Natural History Society in 1874 and Cushing stated:

"It was apparent that at this time he looked upon his medical work more or less from the standpoint of a naturalist, with the microscope always at hand. . . . There can be little doubt that had William Osler at this time (1870) come under the influence of Leidy or Agassiz or possibly Huxley, he would have gone on with his biological studies and abandoned medicine."

III. Osler As an Early Parasitologist

Osler became the first president of the Microscopical Club at Toronto and, as a logical extension of his work as a naturalist, began giving lectures on entozoa of animals at the Veterinary School. He was instrumental in instituting the study of comparative pathology in Canada and published several papers in this field, including such subjects as diphtheria in calves, glanders in horses, verminous aneurysm in a horse and described a rabies, pig typhoid, bronchitis in calves, glanders in horses, verminous aneurysm in a horse and described a pneumonia in dogs due to a previously unknown nematode which was named Filaria osleria.

His first major medical study was also related to his interest in parasitology. It
was a communication entitled “Trichina Spiralis”51 in which he stated:

“When a student with Professor Bovell of Toronto, I had several opportunities of studying these parasites. In the month of February 1870, while dissecting a subject with Dr. Zimmerman in the Toronto School of Medicine, we discovered numerous trichinae throughout the whole muscular system, all of which were densely encysted, many having been calcified.”

He attempted to study the development of the trichinae by feeding the muscle from the cadavers to cats and dogs with negative results, but reported that he succeeded in transmitting the trichinae to the muscles of the thigh and abdomen of a rabbit in 21 days.

Osler also published52 the first survey of cases of echinococcus disease in America, three of which were his own patients. He reviewed the epidemiology of the infestation and emphasized the pathological findings associated with its occurrence.

Thus, very early in his career, Osler exerted a major influence in the development of parasitology in Canada and was even instrumental in securing for McGill Medical School a professorship in parasitology. His later work with malarial parasites and intestinal amoeba will be discussed along with his other studies in clinical pathology during his tenure at the University of Pennsylvania and at Johns Hopkins.

IV. Research on Platelets

Osler’s next work was a major contribution to knowledge about platelets. Following his graduation from McGill in 1872, he worked for 17 months as a post-doctoral student at the laboratory of Professor J. Burton Sanderson at the University College in London, where he undertook studies on the very small corpuscles of the blood (later called platelets). The work was published53 as “An Account of Certain Organisms Occurring in the Liquor Sanguinis.” Although masses of small corpuscles had been observed and commented upon by Donne in 184221 and later by Max Schultze in 1865,76 it was Osler who, using the microscopical skills he learned studying diatoms in Canada, carefully observed the changes that occurred to these tiny corpuscles in a drop of blood on a glass slide.

He wrote:

“... repeated examinations demonstrated the fact that in a drop of blood taken from one of these young animals (rats), the corpuscles were always to be found accumulated together; while on the other hand, in the vessels (whether veins, arteries or capillaries) of the same rat they were always present as separate elements showing no tendency to adhere to one another. The masses, then, are formed at the moment of the withdrawal of the blood from corpuscles previously circulating free of it.”

These observations answered the logical question he had asked himself:

“How is it possible for such masses, some measuring even 1/400 of an inch, to pass through the capillaries, unless supposed to possess a degree of extensibility and elasticity, such as their composition hardly warranted attributing to them?”

Although some investigators at the time believed that these corpuscles were related to bacteria, and Osler in his title refers to them as “organisms,” he objectively writes:

“Finally as there is no evidence that these bodies are in organic continuity with any other recognized animal or vegetable form, or possess the power of reproduction, nothing can at present be said of their nature or of their relation to bacteria.”

It must be kept in mind that at that time the theory of Spontaneous Generation, although already devastatingly disproved by Pasteur, was still championed by Bastian and others in Great Britain.

Later in one of Osler’s more well known articles on infectious endocarditis84 in 1881 when he discussed the masses on the mitral valve he states:

“I was greatly struck with the resemblance which certain of these bodies (cocc) in this instance bore to the individual elements of Schultze’s granule masses” (platelets).
Thus in this paper, although he still entertained the possibility that bacteria could be related to platelets, he also anticipated Bizzozero's findings that platelets are related to thrombus formation.

In March 1886, Osier delivered three lectures for the Cartwright Foundation on (1) the blood platelets, (2) the degeneration and regeneration of the blood corpuscles and (3) the relation of the corpuscles to the processes of coagulation.

In order to appreciate the significance and difficulties of this work of Osier in clinical microscopy, it should be pointed out that at this time there was no staining of blood cells since Paul Ehrlich had not started his classical work with aniline dyes until 1877. Thus, although the microscope resolution was quite good at the time of Osier's studies, it is easy to appreciate how unstained platelets would have been difficult to study, and, with Brownian movements, they could have been thought to have some relationship to microorganisms. In contrast, it is of interest that at this time pathology had scarcely started in North America. William Henry Welch, the father of American pathology, had won a Varick microscope as a student at Bellevue Medical College but had written his father in June 1873:

"I can only admire without understanding how to use its apparently complicated mechanism."

V. Osier as an Observer of Pathology in Europe

Following his work in Sanderson's laboratory, Osier went to Berlin where he visited the best medical institutions and was able to attend lectures and demonstrations by Virchow who greatly impressed him. He wrote in a letter:

"This most remarkable man is yet in his prime (52 years of age) and the small wiry, active figure, looks good for another twenty years of hard work... On Monday, Wednesday and Friday from 8:30 to 11:00 he holds his demonstrative course in Pathology, the other mornings of the week, the course of Pathological Histology while on the fourth day at one o'clock he lectures on general pathology. Virchow himself performs a postmortem on Monday morning making it with such care and minuteness that three or four hours may elapse before it is finished... On Wednesday and Saturday, the demonstrations take place in a large lecture room accommodating about 140 students and with the tables so arranged, that microscopes can circulate continuously on a small tramway let into them. Generally the material of from 10 to 12 postmortems is demonstrated, the lecturer taking up any special group, and enlarging on it with the aid of sketches on the blackboard and microscopical specimens, while the organs are passed around on wooden platters for inspection. A well provided laboratory for physiological and pathological chemistry also exists as well as rooms where men may carry on private investigations."

The content of this letter is presented primarily because it reveals some of the influences of German medicine on Osler that were to help change the course of medical education and training in North America.

Undoubtedly inspired by Virchow, Osler performed almost 800 autopsies on his return to McGill, obtaining 150 carefully dissected and prepared gross specimens which are still preserved in the pathological museum at McGill as are his careful and complete handwritten notes of many of his autopsies, several of which were published in the Montreal General Hospital Pathology Reports, during the years 1877-1878.

VI. Early Emphasis on the Use of the Microscope by Medical Students

In 1874 Osier returned to Montreal where he was appointed Professor of the Institutes of Medicine (then the lectures on the basic sciences). It must be remembered that at that time in Canada and the United States medical education consisted almost completely, even in the best schools, of lectures with little or no laboratory or microscopic work. Osler, obviously stimulated by what he had seen in Germany and England determined to change that system and as part of his "Introductory Remarks" in Oc-
tober 1874 to the students of his class he stated:

“In the spirit (of reforms in medical teaching), the course you are about to begin has been inaugurated. An opportunity will henceforth be afforded to the students attending this school of becoming practically acquainted with the use of the microscope in physiology and pathology; and I may venture to congratulate McGill College as the first in this country to offer such a course. . . . The first essential in a course like this is a proper supply of good microscopes, every student must be furnished with one to enable him to follow out the demonstrations with any degree of satisfaction. These have been obtained from Dr. Hamack of Paris and Potsdam and are the same as are in use in the chief laboratories of Europe.”

What Osier didn’t say was that the 12 microscopes which he ordered were paid for by a small salary of $600 he received for volunteering to work in the smallpox wards, a task which was very dangerous, and ultimately led to his contracting a mild case himself, although he had been repeatedly vaccinated.

Of that course, George Armstrong, who was a student at that time wrote in later years:

“The first class in histology was held Saturday afternoon in the student cloakroom in the basement of the building. We were given bits of tissue which we embedded in little paper boxes of wax, and the sections were cut with razors.”

By 1881, Osler was giving four separate courses at McGill, Practical Physiology, Normal Histology, Morbid Anatomy and his favorite course, Clinical Microscopy, “especially designed to meet the requirements of a practitioner.”

In the introduction to “Students’ Notes, Normal Histology for Laboratory and Class Use” published in 1882, Osler wrote:

“Once in active practice, not a day will pass without an opportunity of using the microscope to assist in the diagnosis of obscure affections. It is of equal importance with the stethoscope, the ophthalmoscope and the laryngoscope, and ignorant of its teachings you cannot practice with due credit to yourself, or with full justice to your patients. To become expert in its use requires time and patience—not more time, however, than with judicious economy, the hard-worked student can well afford, and not more patience than should possess the soul of anyone who aspires to such a profession as medicine.”

In addition to his teaching responsibilities, Osler was actively engaged in research and writing. Related to the study of blood, he published an article on the development of blood cells in the bone-marrow and discussed at great length a case of progressive pernicious anemia with postmortem findings, giving detailed description of the various blood types in the bone marrow, many observations being quite original. Most remarkable was the fact that such detail could have been given considering that blood and bone marrow were examined as wet mounts without any stain whatsoever. His clinical microscopy also led him to a study in 1879 of a case of Bright’s disease in a child in which he noted persistence of erythrocytes and casts after the disappearance of the protein in the urine. At that time the urinalysis was simple with chemical tests for protein and sugar only and an examination of the sediment. Since centrifuges, either driven by water or electricity, were not used until the 1890’s, the solid materials were allowed to settle to the bottom of the tube after which they were usually taken up in a pipet to be put on a slide for examination. Osler had a method of obtaining sediment which according to an early colleague, George Dock, was quite unique:

“When he came from a consultation, he brought with him a bottle of urine he carried with the cork down in his coat pocket. When he arrived at the laboratory, he carefully turned the bottle right side up, and used the cork to spread the sediment on a slide.”

VII. Osler’s work on Phagocytosis

Osler was one of the first individuals to recognize that there were certain cells in the body which possess the ability to ingest foreign material through amoeboid action. In an article entitled “On the Pathology of Miner’s Lung,” he noted that carbon particles that could only have
arisen in the lung were found in the lymphatic chain, in some cases some distance from the alveoli. He states:

“This fixation of the carbon granules in cellular bodies is very remarkable, and must be regarded as an effort of the economy to render harmless what might otherwise be very irritating substances. These (amoeboid class of connective tissue corpuscles) were usually large, twice or three times the size of the colorless blood corpuscles, and very abundant, as if the supply had been equal to the demand.”

He then performed experiments in which he injected India ink into the axilla and through the pleura into the lung of a two-day old kitten. The animal was sacrificed after 20 hours and microscopically he found India ink in numerous leukocytes which had infiltrated the connective tissue of the axilla, as well as the pleura. These experiments were done many years before the elaborate theory of Metschnikoff on phagocytosis (which ultimately earned him the Nobel prize) but Osler in his typical gracious manner stated in an address on Phagocytes before the Alumni Association of Bellevue Hospital in 1889.

“The theory elaborated by Metschnikoff has been hinted at by many previous observers, but to him is undoubtedly due the credit of bringing it into prominence, and of doing in connection with it a very large amount of interesting work.”

Metschnikoff, of course, did the major work showing that not only were inert foreign particles ingested by his amoeboid phagocytes, (including leukocytes) but also microorganisms which made them a prime defender against most infectious diseases, an extrapolation which Osler and several others failed to make earlier. Even in 1889, Osler was still not entirely convinced of the general importance of this cellular defense mechanism since he concluded his lecture by saying:

“While phagocytosis is a widespread and important physiological process throughout the animal kingdom, and while it undoubtedly plays a most important part in many pathological conditions, the question of an active destructive warfare waged by the body cells against microorganisms of disease must still be considered an open one.”

VIII. Osler’s Relationship to the New Field of Bacteriology and Experimental Pathology

Even though Osler’s knowledge of bacteriology was rudimentary, it was not due to his lack of interest. He was one of the first in America to recognize the significance of Koch’s discovery that the tubercle bacillus was the etiological agent in tuberculosis. Only four months after Koch’s announcement in 1882, Osler gave a demonstration of the organism in sputum at the meeting of the AAAS in Montreal. This was at the time when Koch’s ideas were met with strenuous resistance in the United States, particularly by Henry Formad of Philadelphia, a former student of Virchow, who had, for several years postulated that tuberculosis or its predisposition was hereditary and the disease itself was manifested when nonspecific irritations of the lung occurred. Even George Sternberg, who was an early champion of bacteriology in this country, concluded that the tubercle bacillus was not the etiological factor in tuberculosis.

In June 1884, Osler went to Leipzig to work in the laboratory of Julius Cohenheim, the great German pathologist, where he wrote to a friend.

“I go there at 8 A.M. until 10:30 at Bacteria... I have asked Howard (Palmer Howard at McGill) to get a little inner room rigged up for the Koch apparatus which we ought to have so that we could have some cultures under way when the Association is there. I shall try to bring some cultures which will do for stock. The only trouble is that the heat may destroy them.”

But about that time he was offered the professorship of medicine at the University of Pennsylvania, and his “going for the bacteria” came to an end. Cushing wrote regarding this turn of events:

“Osler’s sojourn in Leipzig (was) his debut into bacteriology. But the time, alas, was too short, and he...”
was a little late in getting a start in this field which with his early botanical and microscopical training would have fascinated him. Another year in Montreal, particularly if he could have lived 'under the roof of his laboratory' might have seen him an active worker in the etiology of the infectious diseases."

This is questionable since Osler's work was almost always as an observer of phenomena and experimental work for its own sake had little appeal. A hint about how he might have felt about esoteric laboratory research appears in a rather wistful comment he wrote under a few sketches of leukocytes he drew in his laboratory notes while a student of Burton Sanderson.8

"These figures are all that remain of research which cost several months' work in an attempt to determine in the leukocyte the antagonistic action of atropine and physostigmine."

Perhaps, even then, Osler recognized that life in a laboratory was foreign to his nature and that his love of people and outgoing personality could best be expressed in pursuing clinical medicine. It is even reasonable to think that his acceptance of the professorship of medicine at the University of Pennsylvania rather than to return to McGill as Professor of the Institutes could have been influenced by the 17 months in Sanderson's laboratory.

Along these same lines, William G. MacCallum, a student and later colleague of Osler at Hopkins, stated:37

"Osler's training lay not in chemistry—the growth of bacteriology found him a spectator and experimental methods seem to have had little attraction for him. Nor did he attempt any protracted researches in pathology for its own sake. Instead his interest was and has always been in the observation of rather gross and striking anatomical alterations, usually on account of the symptoms which they produced and not with the aid of investigating their minute details or their ultimate causes."

William Henry Welch in the foreword to an Osler Memorial wrote:83

"In his later years in Baltimore and in Oxford, Osler was well aware of the development of new lines of attack upon the problems of disease as presented by the living patient, by experimental physiological and pathological methods, and especially by application of new physiochemical discoveries. While not at all unsympathetic with these newer directions of clinical study, they were not the lines in which his training and experience lay and which he cultivated and taught."

However, Osler's interest in bacteriology as a tool in the evaluation of patients occurred early in the development of bacteriology and always remained. For example, in April 1885 at the Pathological Society of Philadelphia, Osler showed the organism on a slide of pus from the urine in a case of renal tuberculosis,66 and he was one of the first to advocate the use of Gram's stain as evidenced in a letter9 to his friend, Ogden, in which he asks:

"Have you used the Gram's method for staining bacilli and micrococci? It is especially good" (He goes on to give much detail about this stain.)

**IX. Osler's Move to Philadelphia**

In 1884, Osler left McGill and went to Philadelphia as Professor of Medicine. He was given the responsibility of managing two wards. He quickly improvised a small clinical laboratory under a part of the hospital amphitheatre, where he is said to have "produced an atmosphere so encouraging and helpful that young fellows trooped to his side."10

In the outpatient department at Philadelphia General Hospital, the laboratory was described by George Dock in this way:19

"Some idea of the primitive conditions appear from the fact that the laboratory of the outpatient department consisted of a microscope without a substage or oil immersion lens, so that hyaline casts or tubercle bacillus could not be seen, and a couple of reagent bottles, test tubes, and an alcohol lamp. Osler put his own Zeiss microscope at the service of the staff, the same microscope that began the work of the clinical laboratory at the Hopkins Hospital five years later."

Also, Joseph McFarland, later Professor of Bacteriology at the University of
Pennsylvania, wrote in a memorial to Osler:

"... the time of which I speak (1885), the microscope was scarcely used in medicine except for the examination of urinary sediments; but Osler took his microscope into the hospital wards and searched the blood of all fever patients for malarial parasites... He also busied himself looking for dysenteric amoeba, filarial worms and with the diseases of the blood. He had what I think was the first blood corpuscle counting apparatus in Philadelphia, and his observations and deductions were most scientific, instructive and interesting."

(Actually McFarland was in error regarding the blood counting apparatus, since Frederick Henry and Charles Nancrede of the Hospital of the Protestant Episcopal Church had a Mr. Zentmayer in Philadelphia make a hemocytometer for them which they used in 1878.)

While in Philadelphia, Osler wrote several fine chapters for William Pepper's System of Medicine (1885), particularly the one entitled Diseases of the Blood and Blood Glandular System which was quite modern in its approach, especially the sections on the physiology, composition and morphology of blood. At this time, there was no specialty of hematology and Osler would have to be considered as much an expert in this field as any other physician at that time. His original work with platelets, macrophages and thrombi would justify that opinion, in addition to his role in establishing the Vasquez-Osler syndrome. This condition is characterized by polycythemia, chronic cyanosis, enlargement of the spleen and was a new entity which he described in 1903.

When he left Philadelphia in 1889 to go to Johns Hopkins Hospital, his work at the University of Pennsylvania was summarized by one of his associates, James Wilson, in remarks made at a farewell dinner in his honor:

"What did he do for us? He made himself agreeable to the older men, and demonstrated to the younger men how medicine should be learned and taught. He broadened our conceptions in regard to the inductive method in medicine. Facts, facts, and always the facts. The facts of the ward, of the microscope, of the laboratory and the post-mortem room."

This probably summarized more than anything else about Osler's contribution to medicine—that he stimulated and inspired those he taught, and in this way help bring medicine in America from a subjective, somewhat ritualistic art to a more objective science.

X. Osler and Malaria

Osler was also instrumental in bringing about the use of the microscope in the diagnosis of malaria in the United States. Although the French army surgeon, Laveran, had in 1880 discovered certain pigmented bodies in the blood of cases of malaria, American physicians largely ignored the findings. But William Councilman (who was later to become a colleague of Osler at Hopkins), at a meeting of the Association of American Physicians in June 1886, presented a summary of Laveran's views with which he was inclined to agree, based upon his own researches.

Osler, who was also at the meeting, and whose expertise as a microscopical observer of blood cells was already highly regarded, was extremely skeptical. Part of the discussion following the paper by Councilman was:

Osler:
"I have had the opportunity of examining six cases of acute malaria... There were present within the red corpuscles such bodies as are represented (here). The number of the corpuscles containing them was variable, sometimes four or five in a single field of a one-twelfth immersion, sometimes many more... I am not prepared to give a positive opinion as the nature of these bodies. They look to me more like vacuoles or areas of hyaline transformation than definite organisms. Secondly, there appear in certain of these vascular spaces solid bodies... These possibly may be organisms. That these bodies actually represent organisms, I am skeptical."

Doctor George Sternberg:
"I have seen the body in question, and have observed its amoeboid movements in the blood of a patient... at Rome. I can hardly conceive that I was looking at a vacuole as suggested by Dr. Osler; and moreover, the fact that there is something in the red corpuscles which is differentiated by staining, seems to exclude the idea of vacuoles."
Doctor William Councilman:
"I think that Dr. Osler would have received a more
definite idea of the bodies if he had examined the
stained specimens under the microscope. Fre­
quently one finds in the stained preparations appar­
ently several bodies . . . ."

So Osler went back to Philadelphia
General Hospital, where malaria was
common in those days, and spent the
sweltering summer of 1886 over his mi­
croscope examining the blood of approxi­
mately 70 patients suspected of having
malaria. He confirmed the work of Lave­
ran and Councilman and went on to write
several papers69,70,71 on malaria, but al­
ways referring back to his discussion fol­
lowing Councilman's paper, as "speaking
out in the fullness of my ignorance." As a
clinician, he emphasized the importance
of making the diagnosis of malaria by the
examination of the blood, since at that
time every fever was generally called
"typho-malaria" and treated with
quinine. To the physicians of the 1880's
and those for hundreds of years before,
fever with severe shivering was consid­
ered caused by a mysterious nocturnal
miasm, and it took years to convince
physicians that in malarial regions, the
examination of the blood would prove the
most valuable method of diagnosis of
malaria. A few years later at Hopkins the
regulation was put into effect that no
diagnosis of malaria could be made with­
out a microscopic demonstration of the
parasite.

It is of interest to describe Osler's
technique for examining the blood:69

"The layer of blood . . . should be very thin and
uniform, the corpuscles as far as possible, isolated
and not aggregated in clumps of rouleaux. It is well
to surround the cover with paraffin if the examina­
tion is prolonged. No reagent of any kind should be
added. Cover glass preparations may be made and
stained in methyl blue or fuchsin and mounted in
balsam. Osmic acid preparations may also be
employed. Although these bodies may be seen with
a power of 500 to 600 diameters, it is essential for
the satisfactory study of the changes to use higher
powers."

This description is given only to em­
phasize the difficulties that the early
workers must have had, since today the
improved Wright's stain and Giemsa
stains make the microscopic search for
malaria parasites so simple. It would
scarcely occur to any clinical pathologist
to look for living malaria organisms in un­
stained preparations.

At Johns Hopkins, Osler and his new
students and colleagues continued the
work on malaria. He inspired William
Thayer, who later became professor of
medicine at Hopkins, to perform many
studies on this disease.75,80 Thayer, in
turn, stimulated William MacCallum36
and Eugene L. Opie40 (who were both
students at the time but were later to be­
come distinguished pathologists) to make
fundamental discoveries about the life
cycle of malarial parasites in birds and
later in humans.

XI. Osler at Hopkins

In May 1889, Osler was at work in Bal­
timore organizing the medical clinic at
the new Johns Hopkins Hospital. As
physician-in-chief, he organized his de­
partment patterned after the best hospi­
tals in Germany with a hierarchy of long­
term residents. This was in contrast to the
usual house staff of short term interns
which was the practice in America at that
time. His chief resident, Dr. H. A. Lafleur
described the first days of the opening of
the hospital.34

"There was a feeling of elation—one might even
say of exaltation that the structure which had taken
twenty years to evolve, absorbing the energies and
thought of so many able minds, had at last become a
fait accompli. And to none other than to Dr. Osler
was this a red letter day. To blaze perfectly new
roads, untrammeled by tradition, vested interests,
or medical "deadwood" . . . . The days that followed
were filled with the many details of organization.
There were records, forms and charts of various
sorts to be devised, instruments of precision and
appliances for diagnosis to be purchased, diet lists
to be drawn up, and not least, a clinical laboratory to
be furnished and equipped—the latter a temporary
affair, as those who had planned the magnificent
pile of buildings had omitted to make provision for this essential feature of a medical clinic. . . . Among the many instances in which Dr. Osier did good service to the medical profession of Baltimore, none was more conspicuous than his insistence of the diagnosis of malarial infection by microscopic examination of the blood, and per contra, the rejection of the term "malarial" in pathological conditions where no parasites were found after careful and repeated examinations. He repeatedly drew attention to the futility of quinine in large doses for ailments which had not been proven to be of malarial origin. He was the first in America to report the presence of amoeba in so-called tropical dysentery, confirming the recent discovery of this parasite by Kartulis in the endemic dysentery of Egypt. I will remember the day (in 1890) he brought to the clinical laboratory a specimen of pus from an abscess of the liver and lung, and after a short search detected motile amoeba in large numbers. . . . As sporadic cases of dysentery were by no means uncommon in Baltimore, we all became keenly interested in knowing whether or not amoeba would be found. We soon were able to determine them in a series of cases during the next year. . . . Dr. Osier appreciated very highly the laboratory side of medicine. He was well trained in pathology and clinical microscopy and urged his assistants to study biochemistry in all its relations to medicine. When he visited the laboratories of his department, and he did this quite regularly, he always came as a student asking what we had to show him."

Thus even since the opening of the Johns Hopkins Hospital, the importance of the work of the clinical laboratories was emphasized. Then later when the Medical School opened in 1893, Osler, recognizing the need to teach medical students the techniques used in the clinical laboratory, was instrumental in having built new laboratories near the wards to give every third and fourth year student his own laboratory space and outfit for microscopical, chemical and physical work on materials from patients in the wards. At Osler's request, this clinical laboratory was put under the direction of Dr. William Thayer, one of his resident physicians, who had just returned from Paul Ehrlich's laboratory in Germany with the newest methods of staining blood cells. Later Drs. Futcher, McCrae, Emerson and Boggs, all residents or students of Osler, took over teaching of this course.

Except for the direct staining of bacteria in specimens, bacteriology was kept separate from the clinical laboratory. A clinical bacteriologist (part of the physician resident staff) who also resided in the hospital directed the bacteriological work of the wards and also engaged in research under the direction of William Henry Welch. The techniques of bacteriology had already developed sufficiently since Koch's and Pasteur's early work, to make it a specialty and separate from clinical microscopy. (This was to be the pattern in hospitals affiliated with medical schools up to the present time and only became a part of the clinical laboratory in non-university hospitals where routine bacteriology is carried out and is under the direction of the modern clinical pathologist.)

Osler wrote an article entitled "Clinical Microscopy at Johns Hopkins Medical School" for the British Medical Journal in 189972 in which he gave a synopsis of the course.

In relationship to the clinical laboratory course, Dr. L. F. Barker, who replaced Osler as head of medicine at Hopkins, wrote in later years:22

"The most distinctive advance made in instruction in technique was, however, the establishment of a systematic course in the application of the laboratory methods of chemistry, physics, and biology to the study of patients. . . . By many it is believed that, of the several contributions made by Professor Osler to the organization of the clinic, the development of the clinical laboratory, and of the thorough education of students by competent instructors in clinical laboratory work before entering upon their duties in the medical wards is preponderant."

William Henry Welch, toward the end of his last illness, also wrote:28

"Osler introduced three great reforms: (1) the creation of an upper resident staff, corresponding to assistants in a laboratory; . . . (2) the introduction of the British system of clinical clerks and surgical dressers . . . and (3) the establishment of laboratories as an integral part of the clinic where students were taught laboratory methods of diagnosis, and of examination of excreta, secretions, blood. . . ."
Osler and Welch also had influence on the development of other institutions. This is documented with regard to Harvard Medical School by Frederic A. Washburn who was the Director of Massachusetts General Hospital and wrote in his book about this period.81

"It should be brought out that in 1893 Massachusetts General Hospital had its laboratory work done partly in a little den fitted up under the front steps and was unfit for human occupation, partly in the nurses' room connected with the wards, partly at the Harvard Medical School, a mile away, partly at the pathological room in the department of outpatients... and partly in a small room connected with the Allen Street House, ill adapted for the purpose, and fitted up with some temporary and imperfect facilities for the work which had to be done, and for which there was no other place. Therefore, in the early nineties Massachusetts General and Harvard Medical School began to realize that the new institution in Baltimore, The Johns Hopkins Hospital and Medical School were surpassing them in methods of study and the teaching of pathology and bacteriology. Dr. William Councilman was called from there to take the chair of the new laboratory, which was opened in 1896. Dr. James Homer Wright, a pupil of Welch and Councilman at Hopkins, was appointed Pathologist in March 1896."

Osler also played an important role in the writing of one of the first major textbooks on clinical pathology in the United States and also in the establishment of one of the first private medical laboratories. This came about through his appointment of Dr. Charles Simon as assistant resident physician in the first year of the Johns Hopkins Hospital. As a result of Osler's advice, Simon went to Europe in 1891 to study physiological chemistry under Gautier in Paris and Bunge in Basel. On his return to the Hopkins Hospital in 1892, he continued his laboratory work in a room under one of the wards and started writing a Manual of Clinical Diagnosis which was published in 189677 and went through ten editions in succeeding years. At the time of publication of his text, he suffered a breakdown in his mental health, making it impossible for him to practice medicine. The outlook for his future looked quite bleak but Osler, who was his personal physician, suggested a unique solution. "There is a stable," he said, "in the rear of your house. Get the landlord to fix it up and start a diagnostic laboratory."

Thus with Osler's encouragement, Simon established the first private medical laboratory in Baltimore and very probably one of the first in the United States. Local physicians welcomed such a laboratory and its reputation together with that of his book spread throughout the country. Before long many physicians went to him for training in the new laboratory methods of diagnosis. Osler also sent physicians to his laboratory, and over the course of several years, Simon's establishment became more and more like a school from which many students were to establish similar laboratories in their local communities.21

Osler left Hopkins at the peak of his career to become Regius Professor of Medicine at Oxford, to the chagrin of not only his colleagues and students in Baltimore, but also to the entire medical community on this side of the Atlantic. By this time he was a well-known public figure and considered one of the great heroes of American medicine. His counsel was sought by many individuals, even outside the field of medicine. In light of today's psychology, he was a very strong father figure for the entire rapidly growing medical profession. There was a sense of desertion and anger at his departure to England, but it should not have come as a complete surprise since he had left from McGill and Philadelphia under similar circumstances. To those he left behind, his actions were difficult to understand because most human beings seek to find a permanent niche in life where they are loved, respected and allowed to do the work they desire. But in the case of Osler, he had always emphasized the danger of university people staying too long in one place which he felt resulted in stagnation and cronism.
He expressed this philosophy in his famous valedictory "fixed period" speech which he gave at Hopkins before his departure to England.73

In this address he also elaborated his opinion that the effective vital work of a man is accomplished between the ages of 25 and 40, and that for the most part very little creatively comes from individuals over 60 years. Osier was, of course, giving reasons why he was leaving Johns Hopkins at the age of 55, since in his speech he stated he was looking forward to a life more "private, inactive, calm (and) contemplative."

The demands that were being made upon Osier at Baltimore at that time were overwhelming. In addition to all of his academic duties, professional and public activities, he felt obliged to see approximately five private patients each day, many of whom were physicians or their families who came from all over the world to consult him, many of them with hopeless illnesses. It was difficult for him to refuse to see these patients, in addition to the rich and influential people who were never discouraged by his deliberately high fees. It has been estimated that his private practice income was approximately $31,000 per year during the years 1901-1904 which would be equivalent to approximately $175,000 per year today.29 Thus, his desire for a more "private, inactive, calm contemplative" life was certainly understandable. He, naturally, was not specific regarding his own "fixed period," but to colleagues he made it clear that he felt he was becoming less and less of a pioneer in the progress of medicine. This is substantiated in comments by his professional contemporaries.

Dr. James Herrick of Chicago, the discoverer of sickle cell anemia, in his Memoirs31 related an incident which occurred in 1902:

"At a meeting of the American Medical Association . . . at Saratoga Springs, I sat next to Dr. Osier in the Section of Physiology and Pathology. In those days the sections were small—less than a hundred were present on this occasion—and discussions were more informal and intimate than they are today, when the speaker from the raised platform, through the microphone, reads a carefully prepared "discussion" to an audience of perhaps a thousand. A paper was presented by Dr. Victor C. Vaughan of Ann Arbor on Ehrlich's side chain theory, which was then a front page subject in high grade medical circles. Dr. Vaughan knew his subject. He drew on the blackboard the benzene rings; he took off hydroxyl molecules here or something else there; talked of toxins, haptophores, etc. Dr. Osler listened intently, and then as Dr. Vaughan closed, he turned to me and said seriously, wistfully and pathetically: "Herrick, I wish I were nineteen and had it all to do over again." Soon after this he went to Oxford. I have wondered whether one of the reasons why he left America at the relatively early age of 55 was not his consciousness but that he could no longer keep up with the rapid advances in medicine."

Dr. Rufus Cole, one of Osler's chief residents and later head of the Rockefeller Institute, in an article about Osler in 194914 also gave a similar opinion:

"Although I never heard him speak of the matter (that methods other than observation and enumeration might be required to bring insight into the real nature of the various diseases) he was undoubtedly thinking about it, and I had the feeling that one important reason for his decision to give up his work in investigation and teaching—his removal practically amounted to that—was that he felt the time to be ripe for the introduction of new methods into the study of disease. He was no chemist or physicist or mathematician; he was not even familiar with the techniques of bacteriology."

XII. Osier in England

At Oxford, Osier continued to emphasize the importance of laboratory work in conjunction with the clinical medicine but not with the intensity of prior years.

He wrote introductions to two textbooks on clinical pathology.

In the first, the 1905 American translation of Lucolf Krehl's book The Principles of Clinical Pathology,32 Osler in his introductory notes writes:

"How helpful it would be if clinicians had always at hand skilled physiologists, pathologists, and chemists to apply their most advanced techniques to clinical problems, and not the techniques alone, but the biological and chemical principles upon which medicine as an exact natural science is founded."
In the second book, that written in 1906 by Charles Emerson (one of his former students at Hopkins) entitled Clinical Diagnosis, Osler wrote in the introduction a history of clinical pathology at Hopkins and goes on to say:

"But the aim of a training such as this book implies is to send out into practice men able to give patients the benefit of modern scientific methods in the diagnosis and treatment of disease—men who use the microscope, who examine sputum and who can do the routine urine and blood work with confidence. The men to study a book of this kind are the young practice men who are keeping up the practical knowledge obtained in the medical school and who appreciate a small laboratory as the most valuable stock-in trade."

In June 1914 he was asked to dedicate the new pathological laboratory at the Royal Mineral Water Hospital in Bath. In his address, he made comments on the organization of a clinical laboratory in which he stated that at that time, 1914, clinical pathology was becoming so complex that it was not possible for any one man to control a clinical laboratory thoroughly.

"There must be a man for both departments, the one for the bacteriological and more clinical side and the other for the chemical side. No doubt with the increase in laboratory work there would be increased opportunity for careers for a certain number of men. There should be in a laboratory two groups of men: the men who wished to make laboratory work their career, and the group who intended to become surgeons and physicians."

The work of a laboratory is primarily for services in the interest of the patient, but he emphasized that in the larger hospitals the laboratory would also be a center of research. He also expressed hope that the hospital laboratory services should be made available to local practitioners.

On July 23, 1914 he also delivered an address on the organization of the clinical laboratory in which he deplored the fact that in many of the hospitals of Great Britain, a surgeon still could not get a section of tumor cut for examination, which was still somewhat true in the United States also.

In the course of an address on March 22, 1920, given in Osler's memory at the Johns Hopkins University, William H. Welch, after discussing the qualities that gave Osler his dominant position in medicine, said further that Osler's reputation, though founded on his scientific work, did not rest solely upon that work, but largely upon the inspiring and stimulating character of his clinical teachings.

"I doubt whether the history of medicine records a man who had greater influence upon the students that came under his teaching. He inspired them with a remarkable devotion and loyal affection. He was their example. His life embodied his precepts, and his students cherished his work. Cultivate peace of mind, serenity, the philosophy of Marcus Aurelius. Think not too much of tomorrow, but of the work of today, the work which is immediately before you."

XIII. Conclusion

The significant influence of William Osler on the development of clinical pathology is presented. Even though he did not make any fundamental discoveries in the field, he strongly employed the usefulness of the laboratory in diagnosis of disease. This emphasis combined with his generally great influence on medical education in America during the last quarter of the 19th century and the early 20th century make a strong case to consider Osler "the father of clinical pathology" in North America.

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