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The Strange Story of Jay McLean, the Discoverer of Heparin

Conrad R. Lam, MD*

Most articles that deal with the history of heparin begin with the statement, “Heparin was discovered by Jay McLean in Howell’s laboratory at Johns Hopkins in 1916.” This assertion is based on McLean’s 1916 paper “The Thromboplastic Action of Cephalin” (1) in which he describes his original experiment with the substance. However, the word “heparin” is neither in the title nor in the body of the paper. It was 25 years before McLean’s name appeared as the coauthor of a brief clinical paper reporting the failure of heparin and sul- fapyridine to cure two cases of subacute bacterial endocarditis (2). What was McLean doing during those 25 years after his important discovery?

My early interest in heparin and a personal acquaintanceship with McLean in the 1940s has prompted me to probe into his life story. The story, as it has unfolded, paints the pathetic picture of an insecure individual who had many disappointments in life. His biography has been difficult to piece together, but the version I have assembled, although fragmentary, is the most complete I have seen. The most cohesive account available is an article by A. McGehee Harvey, “Fountainhead of American Physiology: H. Newell Martin and His Pupil, William Henry Howell” (3). Since Howell’s main interest after 1909 was in the coagulation of blood, an account of his work in this field would necessarily include something about McLean.

McLean was born in San Francisco in 1890, had a year of medical schooling there, came to Baltimore in 1914, and was admitted to Johns Hopkins Medical School in 1915, from which he received the MD degree in 1919. McLean was a second-year medical student at Johns Hopkins when Howell assigned him the problem of identifying the active principle in a number of substances known or suspected of being thromboplastic. In McLean’s words, “At the suggestion of Dr Howell I have undertaken a re-examination of this subject to determine if possible whether the thromboplastic effect may be attributed to an impurity, or is a property of cephalin itself, and also to determine in how far a similar property is exhibited by other related phosphatids . . . cephalin, lecithin, sphingomyelin, cuorin, and heparphosphatid” (1). And on pages 255-6: (words in parentheses are mine) “The cuorin (from heart) on the contrary when purified by repeated precipitation in alcohol at 60°, has no thromboplastic effect—indeed it possesses an anticoagulating power as may be illustrated by the following experiment . . . . The heparphosphatid on the other hand when purified by many precipitations in alcohol at 60° has no thromboplastic action and in fact shows a marked power to inhibit coagulation. The anticoagulating action of this phosphatid is being studied and will be reported upon later.”

The subsequent studies and report were not made by McLean, who presumably finished his rotation to Howell’s laboratory and went ahead with his medical school studies. But Howell lost no time in pursuing the promising lead opened up by McLean and, with the help of Emmett Holt (a retired, eminent pediatrician), made an extensive study of the heparphosphatid. In their paper published in 1918 (4), the anticoagulant was named “heparin” because it came from a dog’s liver. In a later paper, Howell (5) described further purification of heparin, which resulted in a marked increase in potency. But the agent was still not ready for clinical use until the late 1930s when a highly purified product was made independently in Toronto (6), Denmark (7), and Sweden (8).

During this time where was the discoverer of heparin, Jay McLean? Harvey’s account states that after his graduation in 1919, he was a member of the surgical house staff as an instructor in experimental surgery and a surgeon of general practice in 1905. The word “instructor” is a warm letter, rather fast in man, later the Reinhoff, Deryl Hart, and surgery of the Duke University, something must have happened to become a Deryl Hart. The text does not contain the word “heparin,” and not until 25 years later did McLean publish a short paper about heparin. Some personal letters and other research have indicated a checkered career. He was trained as a surgeon in the Halsted school but was practicing therapeutic radiology when he died in Savannah in 1957.
Jay McLean, Discoverer of Heparin

house staff (intern?) at Johns Hopkins Hospital and was an instructor in surgery from 1921-1924. In 1920, he had his rotation to the Hunterian Laboratory (surgical experimental laboratory) and while there, he received a warm letter from Harvey Cushing, the famed neurosurgeon of Boston who had established the laboratory in 1905. The letter gave the history of the laboratory and as printed in John Fulton’s biography of Cushing, it occupied five printed pages (9). A picture of the resident surgical staff at Hopkins about 1921 shows McLean in rather fast company, judging from the later careers of many of his colleagues. Among these were Emile Holman, later Professor of Surgery at Stanford; William Reinhoff, later a prominent thoracic surgeon; Warfield Firor, who for a time was Chief of Surgery at Hopkins; Deryl Hart, the first head of the Department of Surgery at Duke University; and Max Zinninger, a prominent surgeon of Cincinnati (Fig 1). Harvey presented a curious quotation from McLean: “Concerning the discovery of heparin, he stated: ‘The discovery of heparin came as a result of my determination to accomplish something by my own ability. It was this determination to become a physiologically-based surgeon, rather than an anatomy-based surgeon that led to the discovery of heparin.’” If that was really his ambition, he could have made a better choice of a service for postgraduate experience. The Halsted School of Surgery, and especially the Hunterian Laboratory, trained surgeons who were expected to be expert with the scalpel (10). One wonders if he did not make that statement after it was evident that he would not make his mark in the operating room. It is curious that in my extensive file on him, there is no evidence that he ever performed an operation, although he must have been on the surgical staff at Hopkins for five years.

After 1924, McLean became instructor in surgery at the University of California, and from 1943 to 1947 he was Associate Professor of Experimental Surgery at Ohio State University. Obviously, there is a gap of 19 years between the time he went to California and the time he came to Columbus.

By 1945, I had become acquainted with Jay through considerable correspondence and during his two visits to Detroit. In a letter dated June 29, 1945, he stated that he had worked with James Ewing, the pathologist, for the 12 years between 1927 and 1939. A biography of Ewing indicates that he was Professor of Pathology at Cornell 1899-1932, and Professor of Oncology until his death in 1943. In the latter capacity, he might have had some clinical practice, but it is hard to see why a man with five years of surgical training would spend that much time with a pathologist, even a great one like Ewing.

Fig 1
Resident surgical staff at the Johns Hopkins Hospital c 1921. Front row: left, Reinhoff; center, Holman; extreme right, McLean. Back row: center, Firor; next to right, Hart; extreme right, Zinninger. Courtesy of Johns Hopkins University Press (10).
A possible clue to McLean’s whereabouts before he worked with Ewing may be found in an obituary that appeared in a Buenos Aires medical news publication in 1937 (11): (translation) “A native of California, Dr McLean was graduated from the famous Johns Hopkins Hospital of Baltimore. He studied in France at the Salpetrière and in the Hospital of St Jacob in Leipzig, Germany . . .” I have no further documentation of this foreign study, but the fact that the rest of the article agrees with known facts lends credibility to the statement.

Some time between 1939 and 1941, McLean moved to Columbus. A letter from him to me, dated Oct 31, 1941 has turned up in my file on heparin. The stationery has the letterthead “Drs Edward Reinert and Jay McLean, 245 East State Street, Columbus, Ohio.” It was typed and signed by a secretary over McLean’s name. “Dear Dr Lam: I am preparing a monograph on Heparin. I would be greatly pleased if you would send me a reprint of your article: ‘Heparin administration: methods and results in thirty cases,’ appearing in Annals of Surgery, Aug, 1941 (114:205).” There is a notation on the letter by my secretary “mailed reprint, 11-11-41.” I received a cordial reply on a penny postcard dated Nov 18: “I thank you for the reprint of your article. . . . I heard much favorable about your exhibit at the last AMA Convention and I am sorry I could not see it. Sincerely, Jay McLean.”

If he had come by my exhibit on “Heparin Administration” at the annual meeting of the American Medical Association in Cleveland, he might have encountered two other visitors whose names are indelibly associated with the history of heparin, his former chief Professor Howell and Charles H. Best, codiscoverer of insulin. Dr Best had encouraged the final purification of heparin by Charles and Scott (6) and collaborated with the Canadian surgeon Gordon Murray in early clinical trials (12). However, these two scientists might have been less than cordial to the discoverer of heparin. McLean seemed to have developed an antipathy toward Howell. On Oct 25, 1943, he wrote Dr McClure*: “In going over some old correspondence today, I came across a letter to me from Dr Howell, dated from Washington DC (when he was on the National Research Council), October 27, 1931. A part of one paragraph is as follows: ‘Doctor McClure of the Ford Hospital, Detroit wanted to use heparin as a routine procedure after all operations as a preventive of post-operative thrombosis, but it seemed to me that this was a risky idea, since if it were used immediately after the operation it might cause troublesome hemorrhage.’ That was in 1931! What a shame the idea could not have been developed by you instead of the Toronto and Stockholm Schools. As you know, I am writing a monograph on heparin, which includes the history of heparin; and if you should care to entrust to me the letter Dr Howell sent to you, it would be a valuable asset in clearing up the reasons why heparin was developed by foreigners.”

Dr McClure replied on Nov 19: “I am sorry to be so slow in answering your letter. I had hoped to have had time to look up Dr Howell’s original letter to me, but have not found it, though I remember it well. In spite of Dr Howell’s advice, I did try a heparin made, supposedly, as you have made it. This was used on two patients with very severe reactions so, of course, I never repeated it, especially in view of Dr Howell’s opposition.”

In 1980, I had some correspondence with Dr L.B. Jaques, a biochemist who was involved in the early heparin work in Toronto (13). He recalled that in 1939, McLean came to Toronto to visit Charles Best and Gordon Murray: ‘They ‘conveniently’ arranged to be out of town and Arthur Charles and I were deputed to meet him for Sunday lunch at the Royal York.” Jaques was impressed in a negative way with McLean, who gave him a long tale of woe that included a divorce.

A letter to me in June 1942 explained why he did not get to see the heparin exhibit in Cleveland. This letter was typed by him on personal stationery with the initials “[I, Mcl.” printed at the top. “Dear Doctor Lam: I thank you for your friendly letter and for the reprints; I am sorry that I did not have the pleasure of meeting you at Atlantic City. I had intended to go to Cleveland to meet you and see your heparin exhibit there; but at the last moment, my partner who is 70 years old, decided to go and I had to stay here and attend to the practice—he decides he had better not.”


THE THROMBOPLASTIC ACTION OF CEPHALIN

Fig 2

McLean’s autograph of the cover of a reprint of his original paper.
decides he will not go to any more conventions, then at the last minute thinks ‘Well! Maybe this will be my last, and I had better go.’ The Monday, June 8th, that the convention opened, he retired from practice (but not from the profits) so I was able only to arrive in Atlantic City a few hours before Macht’s paper and had to leave that night at 6:40 pm. I didn’t see much of the convention but I met a lot of old colleagues; and that is really worthwhile. . . . What luck to have Mrs Lam interested in your research with heparin. Mrs McLean, I fear, wishes heparin were still unknown. I sent you a reprint of my original article on heparin—I should have sent it to you and Mrs Lam (Fig 2). It was written under peculiar circumstances which I shall explain in a paper on the discovery of heparin.” As far as I know, Jay never finished that paper, and we will probably never know what he meant by the last statement.

A letter to Dr McClure dated Oct 25, 1943 had the letterhead “The Ohio State University, Columbus. Department of Research Surgery. Chairman’s Office, Kinsman Hall,” but Jay had typed the letter at home. On the back of the page was a long handwritten note: “George Curtis has appointed me associate professor here in his department and we have formally started on paper (ie, on the OSU treasurer’s book) the project with a $75.00 contribution to erect a separate building for surgical research—an Hunterian Laboratory. If you should know of any way of furthering this project, will you please write to George Curtis.” In his reply of Nov 19, Dr McClure said: “I am glad you are now an Associate Professor of Surgery. I talked to Julius Stone about it last week, and shall further commend the surgical department to Mr Kettering in hope that he will some time see fit to encourage more research in that department. . . . Can’t you come up to see us?”

Jay’s response on Nov 22, 1943, on plain paper: “I thank you deeply for your gracious letter of Nov 19. . . . The monograph and index and abstracts of all the heparin literature is a job in itself in addition to the research planned. Some of this (the laboratory experiments) I have interested other labs in undertaking for there are no facilities here for its execution. . . . Mr Stone was interested in heparin—in fact we thought he was going to finance the chemical work of which I am sending you a priority note we published in Science (14)—it will appear in full in the J Am Chemical Society; but he couldn’t and I got the Department of Chemistry, $15,000 from the Hoffman La Roche Company for this work.” The company he mentioned made heparin for clinical use under the brand name of “Liquaemin.” Handwritten on the margin; “Private practice has not been going so good. I am out on my own in a tough town to break into (since last Feb) and I get no salary as yet from the University, so I really can’t afford to travel just now. But I’ll get there if you think I could aid the laboratory project a little later. I should like to pay you a purely personal visit and chat about research.” This sad story is from a 53-year-old man who should have been at the peak of his career (Fig 3); it adds a bitter flavor to Harvey’s bland statement that Jay was “appointed Associate Professor of Experimental Surgery at Ohio State University, remaining there for four years, 1943 to 1947.”

By March 1944, his financial situation must have been better, because he did arrange the visit to Detroit. He called Dr McClure and asked if he could present a patient who had undergone treatment with irradiation at our weekly staff conference. The answer had been “yes” and would he also say something about heparin? He wrote me: “Dear Conrad Lam: I have just packed my bag for I am leaving tomorrow at 2 pm to attend a meeting of the Cleveland Radiological Society. I shall be at Henry Ford Hospital at 8 am Wednesday March 29 with the patient Mr Z. I wish you would be specific on the ‘early history’ of heparin. Can you prepare questions? I do not like to waste your staff members’ time with ‘reminiscences.’ Could you have a stenographer take down what I do say? Thanking for the invitation to speak a bit on heparin. Sincerely, Jay.”

On June 22, 1945, Jay had his day (or evening) in the sun. Lederle Laboratories, Inc, which had a preparation of heparin on the market, sponsored him in their nationwide series of broadcasts called “The Doctors Talk It Over.” I listened to the program and later received the printed transcript, which had the title “The Evidence for the Use of Heparin in Acute Coronary Thrombosis” by Jay McLean, MD, Associate Professor of Research Surgery, Ohio State University and Discoverer of Heparin.” He was interviewed by the radio personality Milton Cross. When Cross asked him to summarize, Jay showed surprising restraint: “The true evaluation of heparin in acute coronary occlusion must, of course, wait upon the results of clinical findings. We know the nature of heparin . . . we know that it has the power to prevent the formation of clots . . . we know that it can prevent a clot, once formed, from growing larger . . . and it is reasonable to suppose that it has the effect of dissolving a fresh clot . . . we can say that here heparin may prove of great value.”

In 1946, Jay was coauthor of a curious paper (15) that was a case report of ischemic complications following a fracture of the lower tibia. The claim that heparin therapy had reversed some of the gangrene was not supported by the evidence.

I have no record of the exact date, but I think it was in 1946 that McLean made his second visit to Detroit. On a Sunday afternoon, I got a call from him from a downtown hotel. He said he had an appointment to see

*Ed note: Charles F. (Boss) Kettering, inventor of the self starter for the automobile and vice-president in charge of research, General Motors Corporation.
Dr McClure in his home, and he had neglected to bring a necktie. Could I help him? I took him a tie, and I presume I drove him to the McClure home, although I do not remember the visit. I do know that the purpose of Jay's trip was to look for a job. Dr McClure was not interested.

Harvey's sketch states that in 1947 McLean was "Director of the Bureau of Cancer Control of the District of Columbia." In 1949 he went to Savannah where he was "Director of Radiation Therapy and consultant in Malignant Diseases" until his death on Nov 14, 1957. The Orientacion Médica article (11) states that (translation) "from 1949 until the moment of his death, he was director of the Savannah Tumor Clinic." Hopefully, the last seven years of his life spent in an area famous for southern hospitality were happier than those spent north of the Mason and Dixon line!

In this article, I have tried to answer my question, where was Jay McLean in the 25 years after the "discovery" of heparin? The answer seems to be that he remained hidden in obscurity until it became evident in 1939-1940 that the anticoagulant prepared in Canada and Sweden was a valuable therapeutic agent.

Although called "heparin," this anticoagulant is not the heparphosphatid or cuorin that McLean found had anticoagulant properties. For support for this statement, I can quote two authorities. The first is Professor Howell himself, who on Feb 19, 1924 wrote Dr Frank Hartman, head of the Department of Laboratories of the Henry Ford Hospital, "The material you obtained from Hynson, Wescott and Dunning is not a liver phosphatid prepared according to the findings of McLean. McLean was my pupil and was and is my friend. The work of his that you quote was done under my directions and according to my methods. The small portion of it bearing upon liver phosphatids had nothing to do with the subsequent preparation of heparin. This latter substance I discovered and isolated by a method worked out by myself and published an account of it in the paper by Holt and myself" (4). McLean would not have agreed nor have been pleased with this, because in an obvious effort to reinforce the connection of his name with heparin, he had a rubber stamp prepared and stamped the following on the covers or first page of the reprints of his 1916 report (1), which were autographed and sent to me and Dr McClure in 1941: "Cuorin and heparphosphatid renamed antiprothrombin(s) (Howell-Harvey Lecture of April 7, 1917) Antiprothrombin renamed heparin (Howell and Holt-Am Physiol. Dec 1918) see footnote p 318" (sic).

My other authority is L.B. Jaques of the original Canadian group. In 1978 he wrote an incisive short article "Addendum: The Discovery of Heparin" (16) He said "... it is still misrepresented in many current publications ... that 'heparin was discovered by Jay McLean in 1916 at Johns Hopkins.' This may be due to a misunderstanding of the nature of 'discovery,' or to a lack of the knowledge and experience with chemical extractions of tissues common among biochemists and physiologists of an earlier generation." After citing evidence from a biochemist's vantage point, Jaques concluded, "As McLean studied a phospholipid anticoagulant, he obviously did not isolate heparin (italics his) as it has been defined since 1922. Hans Selye has recently examined the meaning of 'discovery' in science. He points out that discovery is ascribed to an individual neither by being first in an accomplishment nor by correctness of ideas. Discovery in science is attributed to the individual whose work has led directly to development and application, as is true of history in general, eg, the discovery of America by Christopher Columbus in 1492. Hence, Jay McLean discovered heparin (no more and no less)."

Fig 3
Jay McLean in front of the Columbus (Ohio) Athletic Club, 1942 (courtesy of Dr Ben Wiltberger).
Jay McLean, Discoverer of Heparin

Ironically, the only real honor Jay ever received came six years after his death. At a symposium held in his honor, a plaque with this inscription was presented: “Jay McLean, 1890-1957, in recognition of his great contribution to the discovery of heparin in collaboration with Professor William H. Howell, this plaque is presented to Johns Hopkins Medical School by the Conference on Bleeding in the Surgical Patient—New York Academy of Science—May 3, 1963.” I wish fate had been kinder to my friend Jay when he was alive.

References