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Preface

During the writing of a book about the Mt. Desert Island Biological Laboratory,[1] I discovered that Warren and Margaret Lewis had a major impact on that laboratory and the emerging field of cell physiology during the early and mid-twentieth century. With scientific or personal connections to such luminaries as Hans Spemann, Thomas Hunt Morgan, Ross G. Harrison, Leonor Michaelis, and Joseph Needham, they were at the dawn of cell biology as it evolved from static anatomy to functional physiology. Warren had formal training in William Osler's medical school at Johns Hopkins and was certainly the accepted leader, but Margaret (who left a Ph.D. program to marry Warren) was the one who brought tissue culture to their research program, for which they were best known. Her collaborations with an array of nascent research leaders led to ground-breaking publications in hematology and cancer causes and treatment. Throughout their long careers (which spanned over 50 years), they collaborated and also worked independently, producing a substantial body of research literature and a library of videos of cells moving, dividing, and engulfing their surrounding medium. This is the story of their personal and professional lives.

Gainesville, FL, USA David H. Evans

[1] D H Evans, *Marine Physiology Down East: the Story of the Mt. Desert Island Biological Laboratory* (New York, NY: Springer New York, 2015), pgs. 151–152.

Introduction

At a dinner in 1955, celebrating the lives and scientific work of Warren and Margaret Lewis, a parade of internationally known colleagues offered their thoughts about the couple:

> We remember lunch in the laboratory; the happy conversation; the early lesson of the risk of loose statements (and not only biological ones—has anyone ever exploited reference books, including the Encyclopaedia Britannica, as has Dr. Warren Lewis with such devastating effects on the inaccurate, but so good humouredly); the risk of burning the toast or getting an unpopular cheese when it was one's turn to do the chores. All these, and many other, memories remain with us. But most of all the pleasure of Dr. Warren in photographing a living egg of the pride of Dr. Margaret in thriving tissue culture. Together and alone you have advanced biological knowledge, and are universally admired for the manner in which you have done so. (Dixon Boyd, M.D. (and Mrs. Boyd), School of Anatomy, Cambridge, England)
>
> I shall never forget the morning you came in and discovered that my partner and I, who were then dissecting 'lowers' and had opened the abdominal cavity, had nonchalantly severed both vagi as they came through the diaphragm and had not bothered to work out their distribution at all. Your withering scorn, expressed in no uncertain terms, made us both wish that the ground beneath us would open up and swallow us whole. I was therefore all the more surprised the following autumn when you asked me to be a student demonstrator in gross anatomy. (Alan M. Chesney, M.D., Dean Emeritus, Johns Hopkins University Medical School)
>
> Some of us have had the great good fortune of having known and worked with you personally and therein have benefited immeasurably from your great understanding and extraordinary humanity. Truly, the lives and careers of those who had had such enviable opportunity bear the indelible stamp of your influence so strikingly characterized by its warmth, its simplicity, its friendliness and its penetrating critique. Influence such as yours. . .is indeed immortal and we are truly glad for it. (Wiley D. Forbus, M.D., Duke University School of Medicine)
>
> One of my earliest memories of Woods Hole, in the twenties, is of you two walking arm in arm, in the evening, out along the Nobska Point Road. I asked someone who you were, and was answered in a manner which made it plain that you were something very special. One of my earliest memories of this medical school is of you two presiding over your laboratories in the New Hunterian, handling your cultures with loving care and with the touch of magicians. (Allan L. Grafflin, M.D. Johns Hopkins School of Medicine)

> I am delighted to have the opportunity of sending. . .a message of warmest greetings to Dr. Warren H. Lewis and Mrs. Margaret Lewis upon the occasion of his 85^{th} birthday. As one whose work has lain in the borderline between experimental morphology and biochemistry, the contributions of the Lewises have been familiar to me for more than thirty years, and one of the happiest recollections of my wife and myself concerns our visits to their home by the edge of the water at Salsbury Cove. Representatives of the great generation of American biologists, long may they flourish! (Joseph Needham, DPhil., Cambridge University)
>
> Your capacity of identifying problems which cried out for study and of devising exquisitely suitable methods of approach to their solution proves your right to be included in that small and select group of great leaders in the field of cell biology. Your quiet never-ceasing thoroughness, the endless reliance upon your own hands and minds and your apparent disdain of applause and public recognition have set examples, the influence of which cannot be over-stated. Your world of biological science, deeply in your debt, is now, in congratulating you, really thankfully congratulating itself for its possession of you through all these years. (Alfred N. Richards, M.D. University of Pennsylvania)

These warm remembrances show the personal and professional esteem of the Lewises. Their story defines the early history of biomedical research on the structure and function of living cells, which they so carefully cultured in their unassuming laboratories in Baltimore and Salisbury Cove.

Acknowledgments

This book could not have been written without the list of publications for Warren in Cormer's biography,[2] as well as the list of Margaret's publications (as well as other documents) in the Lewis family archives in Salisbury Cove. Using these lists, and with access to all the publications through the University of Florida's Interlibrary Loan system, I was able to download and read each of their publications. And the ubiquitous *Wikipedia* provided access to readable explanations of biological terms, as well as numerous biographies of scientists who were associated with Warren and Margaret. The Lewises' daughter Margaret Nast's reminiscences in the Centennial Book about the MDIBL[3] provided insights into the Lewis family and their lives in Maine. Dr. Maggy Myers (granddaughter) and Margaret Lewis (great-granddaughter and fourth generation Margaret) kindly provided personal insights and numerous documents, and Margaret played a significant role in what became Chaps. 1 and 2. Without their help, this book would not have been possible.

Finally, I could not have made it through this last of my books without the love, support, and encouragement of my wife, Jean. She has "been there" for more than 60 years.

[2] G.W. Corner, "Warren Harmon Lewis, 1870-1964; a Biographical Memoir." *National Academy of Sciences, Biographical Memoirs* 1967 (1967): 321–58.

[3] M N Lewis, W R Lewis, and J L Myers, "Growing Up with the Lab," in *A Laboratory by the Sea. the Mount Desert Island Biological Laboratory*, ed. F N Epstein (Rhinebeck, NY, 1998), 73–85.

Contents

Chapter 1
Warren Lewis: Early Life, Educational Background, and Early Research

Warren Harmon Lewis was born in Suffield, CT on June 17th, 1870 to John Lewis and Adelaide Eunice Harmon, the first of their three children. The Lewis family moved to Chicago 7 months later, where John began his law practice. Warren's brother John and sister Helen were both born in Chicago, in 1872 and 1876, respectively. John was a partner in the law firm Tuley, Stiles, and Lewis, and the family lived in Oak Park, an affluent suburb just to the west of Chicago.

Warren attended the Oak Park public schools as a child, doing well in his courses. In 1885, when he was in the eighth grade, his scholarship average was 91, and his teacher noted his deportment as "good." His grades remained mainly in the 90s and his deportment "good" and "fair," through his time at Oak Park Public High School. He attended the Chicago Manual Training School for his junior and senior year, where he continued to do well in all his courses: Math, Science, and English. He graduated in 1889. His scrapbooks[1] record a popular young person, filled as they were with calling cards and invitations to receptions and birthday parties. In his high school years he attended many programs: musicals and orchestras. It was as a young person that he became interested in botany. His family would recall that he was given a copy of Asa Gray's[2] Manual of Botany as a young teen, and spent his high school years collecting plants that he diligently pressed and kept organized in a chest.[3]

The family history portions of this chapter were written with the help of the Lewis's great granddaughter, Margaret Myers. She is the daughter of the Lewis's grandson, John (son of Jessica Lewis Myers, the youngest daughter of Warren and Margaret).

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[1]The scrapbooks are in the Lewis family archives, in their summer cottage on Spruce Point, Salisbury Cove, ME.

[2]Gray, considered "the most important American botanist of the 19th century." See: https://en.wikipedia.org/wiki/Asa_Gray

[3]Letter from the Lewis's daughter, Jessica Helen Lewis Myers to George Corner, dated October 11, 1965. Corner was Warren's biographer for the National Academy of Sciences (see Footnote 14, below). In Lewis family archives.

D. H. Evans, *Pioneers in Cell Physiology: The Story of Warren and Margaret Lewis*, Perspectives in Physiology, https://doi.org/10.1007/978-3-031-11894-4_1

Warren entered the University of Michigan in 1890. He may have been attracted to UM because of the legacy of Asa Gray, who had been the first faculty member appointed to the Botany department. Warren's family seemed positive about his decision to enroll and his ability to succeed. "Should discouragement come to you never give up," his maternal grandmother, Caroline (who still lived in Suffield, CT), wrote, "persevere and all will come out right...I don't think you really need caution in regard to your *goaheaditveness* [sic]. I think it already implanted in your makeup, an inherited gift [that] goes a good way back. . ."[4] In his first semester, Warren took French, German, Math, and systematic Zoology. He had a membership at the University Lawn Tennis Association and continued to fill his time with concerts and other events. His professors looked upon him fondly. A math instructor called him "one of the very best students in my classes." And, perhaps unsurprisingly, he excelled in botany, as well as other areas of science.[5] In October of 1893, Frederick Charles Newcombe, an instructor in botany with a particular interest in plant physiology, wrote that Warren was "regarded by all the instructors as one of the best in the class, and showed marked ability, doing all his work thoroughly."[6] He branched out from Botany, focusing also on Biology. In January of 1894, Warren borrowed $200 from his father to purchase a microscope. The agreement specified that he would pay back the money "on demand."[7]

Warren also came under the influence of Jacob Reighard, who had returned to his alma mater in 1886, after graduate work at Harvard and 2 years as a private tutor and a year of high school teaching, not an uncommon pathway for a young zoologist in the late nineteenth century. By Warren's senior year, Reighard was a Professor of Animal Morphology.[8] After graduation in 1894, Warren remained at UM, as an Assistant in Zoology, presumably under Reighard's tutelage. Two years later, in 1896, Warren entered the Johns Hopkins University School of Medicine, in only the fourth class of students. The medical school had been established in 1893, 17 years after the university had been founded with a bequest from the estate of the American philanthropist and abolitionist Johns Hopkins. In addition to Hopkins, the medical school was also underwritten by several wealthy daughters of Baltimore's businessmen, who insisted that the new medical school be open to students of both sexes, making the new Hopkins program the first co-ed medical school in the USA.[9] The new medical school gained immediate eminence because four outstanding physicians were recruited at the outset: William Henry Welch (Dean), William Osler (medical practice), William Stewart Halsted (surgery), and Howard Atwood Kelly

[4] Letter from Caroline to Warren, October 26, 1890. In Lewis family archives.

[5] WHL's scrapbook.

[6] *Ibid.*

[7] *Ibid.*

[8] A Franklin Shull, "Jacob Ellsworth Reighard," *Science (New York, NY)* 95, no. 2466 (1942): 344–46.

[9] A brief history of the Johns Hopkins University School of Medicine can be found at: https://en.wikipedia.org/wiki/Johns_Hopkins_School_of_Medicine

(gynecology). The four are immortalized in John Singer Sargent's *The Four Doctors*, commissioned by Mary Elizabeth Garrett, one of the founding donors of the medical school.[10]

Because of his background in morphology, Warren entered the Anatomy Department, led by Franklin P. Mall, who had also been educated at the University of Michigan, earning an MD in 1883.[11] While doing postdoctoral research in Leipzig, Germany, Mall started a collection of human embryos, which became the major resource for his subsequent anatomical studies, as well as Warren Lewis's early research.[12] Upon joining Mall's laboratory, Warren must have immediately encountered Mall's two junior faculty associates: Charles R. Bardeen and Ross G. Harrison,[13] both of whom would go on to make major contributions to anatomy and embryology in the early twentieth century. Immediately after graduation in 1900, Warren joined Mall's department as an Assistant, along with medical classmates Florence R. Sabin and John B. MacCallum. Each member of this group (except MacCallum, who died at an early age), in later years, became President of the American Association of Anatomists, and four of them (Bardeen, Harrison, Sabin, and Lewis) were elected to the US National Academy of Sciences.[14]

Within a year, Warren had published his first paper, on the anatomy and development of the human pectoralis major muscle. Using tissue from cadavers "from the dissecting room, from bodies embalmed with the carbolic acid derivative," he was able to unravel the "peculiar twist in the sternocostal portion of the pectoralis major muscle," as well as delineate its development by dissecting some of the human embryos that Mast had collected.[15] This collection also provided the embryos for Warren's second publication that year. Working with Dr. Bardeen, he described the

---

[10] http://jssgallery.org/Paintings/The_Four_Doctors.htm. To read more about the four founding physicians, see: https://www.hopkinsmedicine.org/about/history/history5.html. Osler is probably the best remembered, because he pioneered what became known as internal medicine, outlined in his 1892 text, *Principles of Internal Medicine* and also established the first medical residency program. For an excellent biography, see: *William Osler: A Life in Medicine*, by Michael Bliss.

[11] As was common in the nineteenth century, Mall started his research career in Europe, studying morphology in Heidelberg and Leipzig (where he met Welch). After a fellowship with Halstead at Johns Hopkins, Mall held academic positions at Clark University and the University of Chicago, before accepting the chair of the Department of Anatomy at Hopkins in 1893. See: https://embryo.asu.edu/pages/franklin-paine-mall-1862-1917, as well as https://en.wikipedia.org/wiki/Franklin_P._Mall

[12] For a discussion of the acquisition and importance of this collection, see: F P Mall, "The Value of Embryological Specimens," *Maryland Med J* XL, no. 3 (1898): 29–33 and F P Mall, "A Contribution to the Study of the Pathology of Early Human Embryos," *Johns Hopkins Hospital Reports* IX (1900): 1–68.

[13] See: https://en.wikipedia.org/wiki/Charles_Russell_Bardeen and https://en.wikipedia.org/wiki/Ross_Granville_Harrison

[14] G.W. Corner, "Warren Harmon Lewis, 1870-1964; a Biographical Memoir." *National Academy of Sciences, Biographical Memoirs* 1967 (1967): 321–58.

[15] W H Lewis, "Observations on the Pectoralis Major Muscle in Man.," *Bull Johns Hopkins Hosp* 12 (1901): 172–77.

development of the limbs, body-wall, and back in the early human embryo, using serial sections embedded in wax plates, a technique which had been perfected in Mall's laboratory.[16] They found that "during the first two months of embryonic life, therefore, are developed the rudiments of the muscles, nerves, blood-vessels, and skeletal structures characteristic of the back, the body-wall and the limbs. Adult conditions are reached by an increase in size and complexity of the various organs and by relative shifting of parts." The paper was published as the first report in the first volume and number of the *American Journal of Anatomy*, which had been founded by Mall and three colleagues the year before "to collect into one place, and present in a worthy manner, the many researches from our investigators, now scattered through many publications at home and abroad." The plates at the end of the Bardeen and Lewis paper presented exquisite drawings of the reconstructions of the serial plates and gross dissections of the embryos (e.g., Fig. 1.1).

This first paper with Bardeen was followed up by a second report, published in early 1902, on the development of the human arm, again using Mall's human embryo collection.[17] Once again, the drawings and diagrams of the dissection were extremely detailed, but artistic (Fig. 1.2). Since Warren was the only author, one must conclude that the drawings were his. Warren's detailed study of human development culminated in a comprehensive review, published in 1904 in the multivolume *Reference Handbook of the Medical Sciences*, which "embrac[ed] the entire range of scientific and practical medicine and allied science."[18]

Warren spent the summers of 1895 and1901 at the Marine Biological Laboratory at Woods Hole, MA. The MBL was the descendent of the short-lived marine station on Penikese Island (one of the Elizabeth Islands, near Woods Hole), overseen by Harvard's Louis Agassiz,[19] probably the leading biologist of the period. Another MBL precursor was the Annisquam Laboratory (north of Boston), started by Alpheus Hyatt, a student of Agassiz's. In 1888, Hyatt moved to Woods Hole and served as the first President of the MBL's Corporation. Within a decade, the Laboratory became a center for the study of the biology and physiology of marine organisms, particularly development of invertebrates, with such luminaries as Edmund Beecher Wilson, Thomas Hunt Morgan, Edwin Grant Conklin, Ross Granville Harrison, and Jacques Loeb.[20] During the 1901 summer at the MBL, Warren worked with Loeb,[21] studying the effect of the very poisonous compound

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[16] C H Bardeen and Lewis W H, "Development of the Limbs, Body-Wall and Back in Man," *Am J Anat* 1, no. 1 (1901): 1–36.

[17] W H Lewis, "The Development of the Arm in Man.," *Am J Anat* 1, no. 2 (1902): 145–183.

[18] W H Lewis, "Development of Foetus," in *Reference Handbook of the Medical Sciences*, ed. A H Buck, 2nd ed., vol. 8, (New York, 1904), 450–57.

[19] See: https://en.wikipedia.org/wiki/Louis_Agassiz

[20] J Maienschein, "Agassiz, Hyatt, Whitman, and the Birth of the Marine Biological Laboratory," *Biol Bull* 168, no. 3 (June 1985): 26–34.

[21] Loeb was an established physiologist at this point, with an appointment at the University of Chicago. He was best known for his research on animal tropisms, toxic and antitoxic effects of ions,

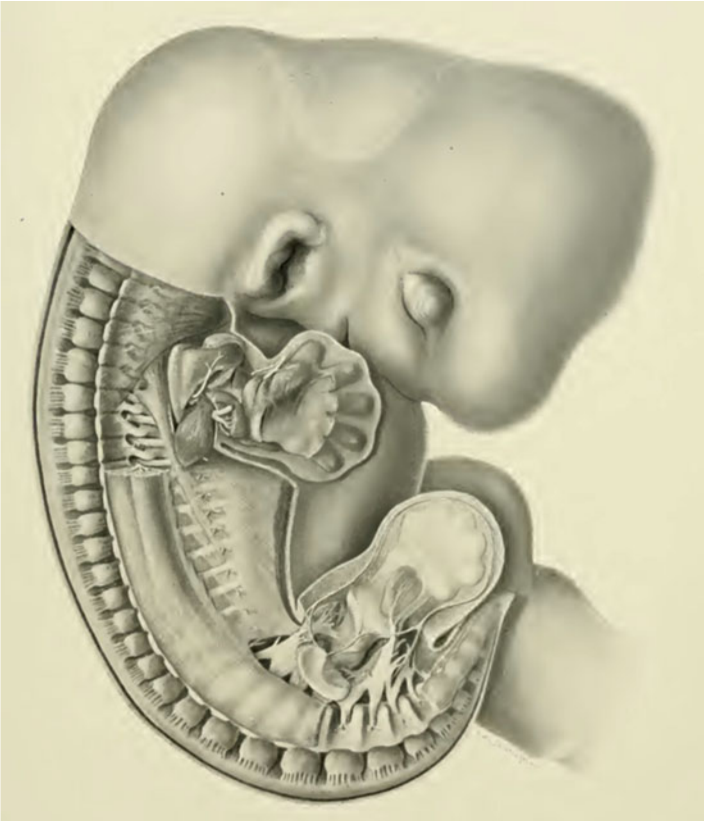

Fig. 1.1 Drawing of a lateral view of human embryo, age about 5 weeks. Screen shot of Plate V from: C H Bardeen and Lewis W H, "Development of the Limbs, Body-Wall and Back in Man," *Am J Anat* 1, no. 1 (1901): 1–36

potassium cyanide on the life-span of unfertilized sea urchin eggs.[22] This was Warren's first foray into cell and developmental biology, a significant change from mammalian morphology. Loeb had previously found that shed urchin eggs died quickly, while fertilized eggs started to divide and develop into embryos. He concluded from these studies that there are "two kinds of processes going on in the egg—a mortal process and a second which leads to cell division and further development. The latter process inhibits or modifies the mortal process." The research with Warren set out to determine if the mortal process could be delayed, by "agencies which inhibit catalytic phenomena without permanently altering the

artificial parthenogenesis, and heteromorphosis ("the replacement of an injured or removed organ by a different organ"). See: https://en.wikipedia.org/wiki/Jacques_Loeb

[22] J Loeb and W H Lewis, "On the Prolongation of the Life of the Unfertilized Eggs of Sea-Urchins by Potassium Cyanide," *Am J Physiol* 6 (1902): 305–17.

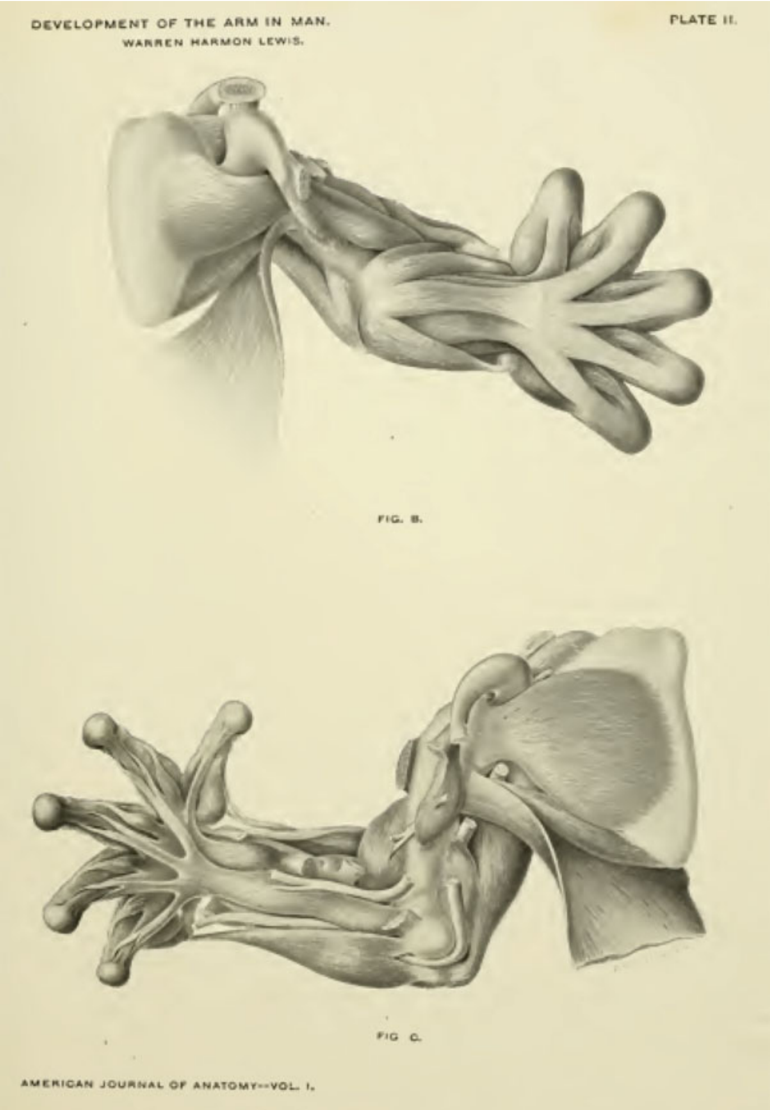

Fig. 1.2 Drawing of medial view of arms of two human embryos, age 5–7 weeks. Screen shot of Plate II from: Lewis W H, "Development of the Arm in Man," *Am J Anat* 1, no. 2 (1902): 145–183

constitution of living matter." Since potassium cyanide was known to inhibit "a number of enzymatic processes," they exposed unfertilized urchin eggs to various concentrations of the poison before fertilizing them. They found that control eggs (no poison) could reach the pluteus stage of development if fertilized within 23 h; eggs developed for longer periods would not develop to the pluteus stage and "as a rule, the eggs form a sticky and discolored mass." Eggs kept in cyanide solutions (0.001% was optimal), however, could develop to the pluteus stage even after 112 h of exposure. Higher concentrations of cyanide precluded any development. Lack of oxygen did "not prolong, or prolongs but little, the life of fertilized eggs." They also considered the nature of the "mortal process" of the normal egg. What was going on that resulted in death if no fertilization took place? They concluded that "no definite answer is possible at present," but posited that it might be "self-digestion" or, since the "nucleoproteids" of the cell nuclei may be "oxidizing agents," as the cell divides and the contents of the original nucleus "are scattered throughout the cell. It is easily conceivable that this periodic spreading or mixing of the contents of the nucleus and the cells may modify the chemical processes in the egg and check the mortal processes." This hypothesis is especially interesting because the importance of nucleoproteids (now termed nucleoproteins), such as proteins associated with DNA, was not known in the early twentieth century. We now know, of course, that nuclear DNA controls not only cellular division, but also the biochemical metabolism of cells.[23]

The summer working with Loeb at the MBL, must have shifted at least some of Warren's interests to more experimental approaches, because many of his subsequent publications examined processes associated with changing morphology (development), rather than morphology itself.

Returning to vertebrate development and morphology, and working in the laboratory of Professor Moritz Nussbaum in Bonn, Switzerland (presumably sometime in 1902), Warren showed definitively that the "wandering pigment cells" in the optic cup of the chick, as well as the pupillary muscle, are of ectodermal origin and, therefore, "must modify our idea of a rigid specificity of the outer germ layer."[24] This was one of the early suggestions that adult tissues, such as the vertebrate eye, might be composed of cells from more than one germ layer (ectoderm, mesoderm, endoderm), a concept that was becoming a major research topic in developmental biology, and of Warren's research.

By the spring of 1903,[25] Warren was studying the interactions between the developing amphibian eye cup and the overlying epidermis (skin). Warren's research had been prompted by an earlier (1901) study by Hans Spemann,[26] which had shown that the developing eye of the frog, *Rana fusca,* did not produce a lens if the early optic cup was destroyed by electrocautery. In addition, if the optic cup had not been destroyed completely, the lens formed only if the cup rudiment touched the

[23] For a brief introduction to the structure and function of DNA, see: https://biologydictionary.net/dna/ or https://en.wikipedia.org/wiki/DNA

[24] Warren Harmon Lewis, "Wandering Pigmented Cells Arising From the Epithelium of the Optic Cup, with Observations on the Origin of the M. Sphincter Pupillae in the Chick," *Am J Anat* 2, no. 3 (July 1, 1903): 405–16.

[25] Warren was promoted to Assistant Professor of Anatomy at Johns Hopkins Medical School that year. A year later, he was promoted to Associate Professor, a rate of academic advancement much faster than normal.

[26] See: https://en.wikipedia.org/wiki/Hans_Spemann

epidermis. These experiments suggested that lens development was dependent on optic cup development.[27] In a later review of this work, Viktor Hamburger translated,[28] from the original paper, Spemann's "intent" for this ground-breaking study:

> The complex apparatus of the vertebrate eye originates by a sequence of developmental processes which. . .are interlocked spatially and temporally. The following is an experimental contribution to the question of whether these developmental processes proceed dependently or independently of each other; that is, whether their spatial and temporal coordination is guaranteed by a causal interaction or by a harmony which dates back to earlier stages, and perhaps to the egg.

Warren Lewis had read Spemann paper (while in Nussbaum's lab in 1902?) and decided to approach the question a bit more directly the next year. He wrote: "By the use of the binocular microscope one can make minute dissections of the living amphibian embryo and can remove various organs, transplant them or alter the normal relations, and so alter the influences they exert on each other. We may thus determine certain correlations necessary to normal development."[29] This was one of the first demonstrations of the importance of microdissection under a binocular microscope. Warren was able to actually remove the optic cup (vesicle) before the lens had started to differentiate from the ectoderm (skin) in the frog *Rana sylvatica*. Like Spemann, he found that if the optic vesicle failed to regenerate, no lens developed. If the vesicle "regenerates sufficiently to come in contact with the skin a lens will form." If the regenerated eye cup "is deeply buried. . .a lens does not form." The next two series of experiments were ground-breaking. Warren found that if the optic cup was transplanted to a more caudal portion of the embryo, a lens developed if the transplanted optic cup touched the skin, but did not if the optic cup was buried more deeply and did not touch the skin. And he could show that skin transplanted from the abdomen of the frog to over the eye cup could develop a lens only if the transplanted skin touched the developing eye cup. He concluded that "the lens is absolutely dependent for its origin on the influence of the optic vesicle on the ectoderm" and "there is no predetermined area of ectoderm which must be stimulated in order that a lens may arise." The abstract ends with one of the earliest descriptions of what came to be known as "embryonic induction":

> We have here one tissue influencing another during the course of development, and from this a new structure, the lens, arises. It seems likely that there is a definite chemical reaction between certain substances of the optic vesicle and certain substances of the ectoderm cells, which results in the formation of new substances within the lens cells, and that these substances give to the lens its peculiar characters and mode of development.

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[27] H Spemann, "Uber Correlationen in Der Entwicklung Des Auges," *Verhandl Anat Ges* 15 (1901): 61–79.

[28] V Hamburger, *The Heritage of Experimental Embryology: Hans Spemann and the Organizer*, (New York, Oxford: Oxford University Press, 1988). 196 pgs.

[29] W H Lewis, "Experimental Studies on the Development of the Eye in Amphibia," *Am J Anat Suppl* 3 (1904): xiii–xv. For a short discussion of embryonic induction, see https://encyclopedia2.thefreedictionary.com/embryonic+induction

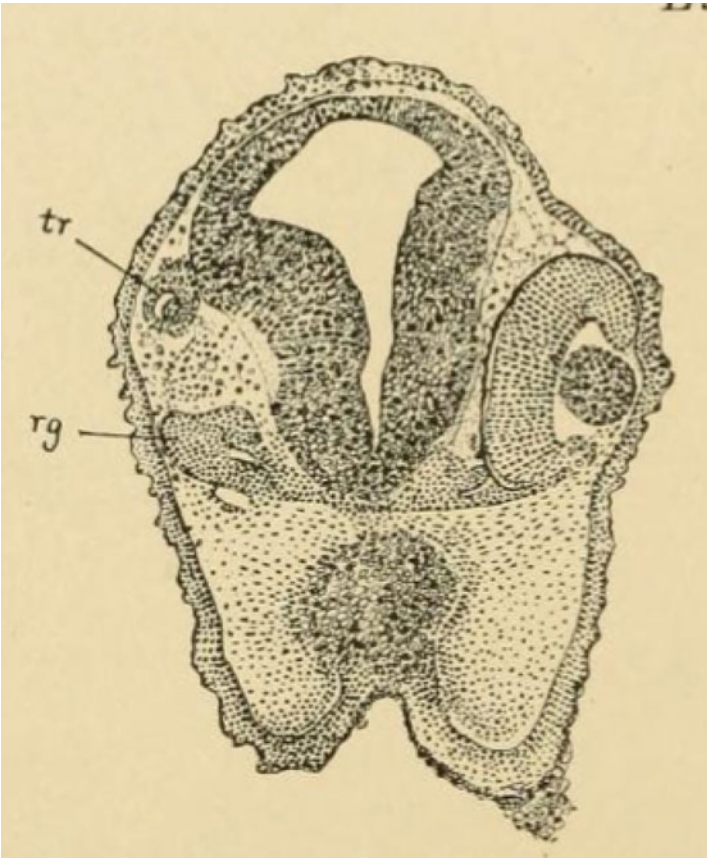

Fig. 1.3 Drawing of transverse section of an amphibian embryo in which the early optic cup had been surgically removed on the left side and then reinserted away from the ectoderm. Two days later, the embryo was sacrificed and the development of the lens on the left compared with that in the normal eye on the right side. It is clear that neither a regenerated eye cup (rg) nor the transplanted eye cup (tr) had stimulated the production of a lens, as seen on the right side. Screen shot of Fig. 3 in W H Lewis, "Experimental Studies on the Development of the Eye in Amphibia. I. on the Origin of the Lens. *Rana palustris*.," *Am J Anat* 3 (1904): 505–36

In a subsequent publication (also published in 1904), Warren gave a much more complete description, with illustrations, of this work.[30] He noted that he had used two species of frogs (*R. sylvatica* and *R. palustris*) to do the transplantation studies, to take advantage of the different pigmentation in their skin. In addition to describing the extirpation (Fig. 1.3) and transplantation (Fig. 1.4) experiments outlined in the 1904 abstract, he demonstrated that "the all-important influence of the optic vesicle

[30] W H Lewis, "Experimental Studies on the Development of the Eye in Amphibia. I. on the Origin of the Lens. *Rana palustris*.," *Am J Anat* 3 (1904): 505–36.