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HERBERT MCLEAN EVANS

1882—1971

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*A Biographical Memoir by*  
GEORGE W. CORNER

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*Biographical Memoir*

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*Robert M. Evans*

## HERBERT McLEAN EVANS

*September 23, 1882–March 6, 1971*

BY GEORGE W. CORNER

HERBERT McLEAN EVANS, anatomist, endocrinologist, and bibliophile, was born in Modesto, California, September 23, 1882. His father, Clayburn Wayne Evans, a native of Alabama, was the leading physician and surgeon in the then-small town; he is said to have been the first in the upper San Joaquin Valley to do abdominal surgery. Herbert Evans's mother, née Bessie McLean, came of a Virginia family. Her father practiced medicine in Modesto, and her brother, Robert McLean, was professor of surgery and dean of the San Francisco medical faculty of the University of California. Dr. C. W. Evans was a man of vigorous rather than polished character; Bessie McLean Evans and her brother Robert were persons of refined manners and tastes. Herbert Evans thus began life in a strongly medical family and with a varied store of traits and temperaments.

He attributed much of his early interest in science, literature, and history to a cultivated high school principal in his home town and the excellent library at the school. This exposure to books in boyhood was fortunate, for with his family background and strong pressure from his father it was inevitable that the young man should enter the medical profession and that his college education (at Berkeley) would be directed to that end, at the expense of cultural interests. Indeed, his father seems to

have been dubious about letting him have more than the two years of premedical preparation then required; and young Evans himself concentrated the rest of his college years on science. Among his teachers, one who especially won his admiration was the celebrated paleontologist John C. Merriam, who during Evans's senior year in college took him on a field trip to Idaho. Evans's first published contribution to science, about the time of his graduation from college, was the description of a fossil fish spine from the Triassic of Idaho, which Merriam encouraged him to study.

In college, Evans distinguished himself sufficiently to be, at the commencement of 1904, one of the two students then customarily chosen to deliver brief graduation addresses. He spoke on the importance of biological research for human welfare. In the autumn he enrolled in the medical school of the university, in whose Berkeley laboratories he pursued the courses of the first year of professional study. The professor of anatomy was Joseph Marshall Flint, a surgeon who had done some anatomical research at Johns Hopkins and a stimulating lecturer; his associates were Irving Hardesty, a productive histologist, and Robert Orton Moody, a competent teacher of gross human anatomy.

The next summer Evans boldly took two steps that were quite contrary to his parents' judgment. In the first place he decided not to continue the study of medicine at the University of California, but instead to go to the School of Medicine of Johns Hopkins University where, his father feared, his leaning toward science might turn him away from the practice of medicine. The other, equally bold step was to marry his college sweetheart, Anabel Tulloch, like him tall and handsome, and in her way as spirited and impetuous as he. Since her family also strongly disapproved the match, the young people were married privately and departed for Baltimore.

At that time married medical students were unheard of at Johns Hopkins and most other medical schools. Fearing that he might not be admitted, Herbert concealed his marriage from the admissions office. He and Anabel set up housekeeping at some distance from the school, where in a poor city neighborhood the bride from California's broad and verdant spaces was cooped up and separated from her husband all day long, among unintellectual neighbors, seeing nothing of his associates and activities, feeling lonely and neglected. Years afterward each of them separately spoke to the writer of this memoir about that strange interlude, he with an expression of remorse, she with a trace of lingering resentment, but each realizing that their sacrifice had helped to put Evans on the way to professional achievement. After about a year, the birth of their daughter Marian in the Johns Hopkins Hospital ended the deception and Anabel's isolation, although as the wife of an impecunious and intensely busy student her lot was still far from easy.

During his medical year at Berkeley, Evans had taken the usual course in human anatomy with dissection. At Johns Hopkins, at that time, second-year students were given continuing instruction in that subject, but the professor—Franklin P. Mall, a shrewd and subtle judge of men—allowed Evans to spend his time in the laboratory more or less as he wished. Because Mall himself had engaged in research on the pattern of microscopic blood vessels in various organs and in embryos, Evans learned from him methods of injecting blood vessels with colored fluids to make them readily visible. Working with finer and finer glass cannulas, under the microscope, he became expert. His special status in the laboratory gave him much closer association with the departmental staff than he would otherwise have had. Mall, the most influential anatomist in the country, had gathered about him probably the strongest anatomical research group in the English-speaking world, including

Warren H. Lewis, Ross G. Harrison, and Florence R. Sabin—all of them destined, as was Mall, to become members of the National Academy of Sciences.

One day the school's professor of surgery, the austere scientific William H. Halsted, came to Mall for help with a clinical problem. A patient of his, following an operation on the thyroid gland, had developed acute tetany. Knowing of other surgical mishaps of the same kind, Halsted rightly conjectured that he had inadvertently either removed the inconspicuous but indispensable parathyroid glands along with the thyroid, or had tied off their blood supply. He felt that with more exact knowledge of the small arteries supplying the parathyroids, operations could be planned to conserve the glandules. Mall arranged for Evans to take on the problem under Halsted's supervision. By injection and careful dissection of the branches of the thyroid arteries in a few cadavers, Evans solved the problem, and thus his name appeared with Halsted's at the head of an authoritative little article that appeared in *Annals of Surgery* in 1907 while the junior author was still a medical student. In the same year Evans published in the *American Journal of Anatomy* a very creditable article on the blood circulation in the walls of large lymphatic vessels, illustrated with his own drawings made in the style of the great Johns Hopkins medical artist Max Broedel. About the same time he had begun research on embryonic blood vessels. Before taking his medical degree he completed a study of the earliest vessels in the limb buds of chick embryos, which he published in full in 1909. Another significant accomplishment while a medical student was his demonstration of the growth of lymphatic vessels into a malignant tumor, published in 1908.

While Evans was thus exhibiting his remarkable talent for anatomical investigation, Franklin Mall missed no occasion to foster his training for a professional career. He not only encouraged Evans's research, but had him write book reviews for

the *Anatomical Record*, then being published from Mall's laboratory, and finally gave him a quite extraordinary opportunity for so young a man. In 1907, Mall was organizing, jointly with Franz Keibel of Freiburg, Baden, Germany, their great *Manual of Human Embryology* (1910, Philadelphia and Leipzig), to be written by leading investigators of Germany and America. When a European embryologist who was to contribute a section on the blood-vascular system was unable to do so, Mall entrusted the task to Evans. Too ambitious merely to compile what was already known, Evans prepared himself for the assignment not only by studying the literature and then examining well-understood human embryos in Mall's collection but also by making original observations on the little-known earliest development of the aorta and the other great vessels. By extremely skillful injection of chick embryos, working under the microscope, he proved—against the supposition of Hochstetter and others—that these ultimately large channels begin, as do the peripheral arteries and veins, as a network of capillaries. This fundamental observation was the basis of Evans's authoritative contribution to the Keibel-Mall *Manual*, Chapter XVIII, Section III.

From the first, Evans felt little interest in the clinical courses at Johns Hopkins, particularly when they took his time from such exciting activities as injecting embryonic blood vessels. He cut classes without regard to consequences. A preposterous story got abroad that he was granted his medical diploma only on his promise that he would never practice medicine. He himself contributed to the persistence of such legends by his own, equally apocryphal statement\* that he was expelled from the medical school at the end of his third year for incompetence in surgical bandaging, obstetrical manikin exercises, and prescription-writing and was only restored to academic status with the help and advice of Dr. William H. Howell, then dean of the school. No doubt he did neglect such practical routines, but in

\* *Bulletin of the Johns Hopkins Hospital*, 68, 300 (1947).

sober fact the records of the medical school do not mention any disciplinary action ever taken with respect to H. M. Evans,\* and he was graduated in medicine in 1908.

Immediately afterward he joined Mall's department as assistant in anatomy and by this step confirmed, as his father had been fearing for some years, that he would not return to Modesto to assist with and later take over the older man's practice. To the senior Dr. Evans this was a heavy blow, for he thought practice far more important than research. It was undoubtedly the feeling that his father undervalued his choice of career that instilled in Herbert Evans an urgent desire to impress his parents by success in his chosen work and in later life to win the highest academic honors.

While Evans remained at Johns Hopkins, Mall arranged several times for him to go to Germany in the summer vacations. During a stay at Freiburg he was fascinated by the novel experiments of the surgeon Erwin Goldman on intravital staining of animal tissues by acid azo dyes (e.g., trypan blue). With a young Freiburg chemist, Werner Schulemann, he began experiments to find out whether the spectacular coloration, inside and out, of living rats, mice, and rabbits by injection of such dyes is a physical or chemical phenomenon. Continuing the work for some years, he found that these dyes do not truly dissolve in the body fluids, but are dispersed as extremely fine particles, forming a fluid suspension. When injected under a rat's skin, the dyestuff gets into the bloodstream as submicroscopic aggregates that the macrophage cells of connective tissues take up and then store in their cytoplasm. The recognition of this important class of cells and their role in the storage of particulate matter was much forwarded by Evans's work. Among the numerous dyes he and Schulemann studied, one now called Evans blue proved

\* Information kindly supplied by Mary E. Foy, Registrar, School of Medicine, Johns Hopkins University.



useful in a method of measuring the blood volume of living animals and human surgical patients.

As a member of Mall's staff, Evans was busy with teaching, with his work on vital staining, and with studying the blood vessels of pig and chick embryos as well as of human embryos on the rare occasion when one was received in a sufficiently fresh state to be injected with india ink. In 1913, on obtaining funds from the Carnegie Institution of Washington for the support of his large collection of human embryos and to develop research in that field, Mall created the department of embryology of the Carnegie Institution. This was first housed in the Johns Hopkins anatomical laboratory and later in part of an adjacent new building. Evans, who was given a Carnegie appointment concurrently with his Johns Hopkins post, then devoted a good deal of his time to the sectioning of early human embryos and to reconstructing them in wax from the sections—"A wearisome thing to do," he said, "compared with making the living embryo pump india ink as though it were blood to show the multitudinous vascular channels."

This strong inclination to experimental rather than purely morphological research was a partial cause of Evans's dropping a major project that Mall had suggested, a descriptive study of the human embryo during the period of somite formation. Another reason was that when Evans finally left Baltimore, Mall was unwilling to let him take along, even for his temporary use, the rare and precious serially sectioned embryos necessary for the study—one or two of which, at least, Evans had himself collected and laboriously sectioned during Mall's summer absences. Evans was disappointed and hurt by what he regarded as his chief's ungenerosity. However, a few years later when Mall died in the prime of life with the rift between them still unhealed, Evans was deeply grieved. As a kind of penance for his part in the disagreement, he proposed to write a biography of Mall, hinting

that this would be a profound analysis of a distinguished scientific mind (as indeed it might well have been), but in time the plan was forgotten. Evans's work on the embryos, however, was not lost. Several years later G. W. Bartelmez of the University of Chicago took up the study of the somite stage of human development, first studying the Carnegie embryos in Baltimore, then going to Berkeley to secure Evans's collaboration and the use of his notes and drawings. The result was an important monograph in the Carnegie *Contributions to Embryology* (1926) under their joint authorship.

In 1915, when Evans was in his thirty-third year, President Benjamin Ide Wheeler of the University of California offered him the chair of anatomy at Berkeley vacated by the departure of Flint in 1907 and of his acting successor, Irving Hardesty, in 1909. Since then, the direction of the department had reverted to the worthy pedagogue Robert O. Moody, under whom Evans a dozen years before had studied gross human anatomy. Research had practically ceased. Even routine teaching had suffered because of Moody's frail health and the illness of another member of the small staff. Philip E. Smith was the only man left in the department who was in good health and had sufficient experience to teach gross and microscopic anatomy. During the year before Evans's advent, Smith and his wife, who had done some postgraduate work in biology, had carried almost the entire teaching load, to the detriment of the research program in experimental embryology that Smith had brought with him from Cornell.

To build up the department, Evans took with him from Johns Hopkins two young people who had shown competence for anatomical research—Katherine J. Scott (now Katherine Scott Bishop), a medical graduate of 1915, and George W. Corner, who was just completing an internship in the women's clinic. "Gynecologists ought to know more about the female reproductive cycle," said Dr. Evans to Corner. "Come to Berkeley

with me and do your gynecology for a while on rats and rabbits." At Berkeley, recognizing Philip Smith's great abilities, Evans arranged for him a much-lightened teaching schedule and in every possible way facilitated the research that ultimately won for Smith an international reputation and the chair of anatomy at Columbia University. It was during this early period that Smith perfected his operation of hypophysectomy in the rat, which became an invaluable procedure in research on the pituitary gland. Associate Professor Moody, perhaps a little surprised by the inrush of all this youthful enthusiasm, retained charge of gross anatomy, with Smith and one of the newcomers helping him.

With the staff thus fully manned, the reorganized department resumed its work in the autumn of 1919 in a small frame building, once the university's printing shop, that had been adapted for the teaching of human anatomy when the San Francisco earthquake and fire of 1906 forced the transfer of pre-clinical classes to Berkeley. Evans took teaching quite seriously, in his own way, which was tinged with the pride of intellect he never concealed. His course in histology was radically new in its extensive use of fresh and experimentally prepared tissues along with the traditional fixed and routinely stained sections. In the class laboratory he was usually to be seen at the microscope beside one of the better students. With the general run he was tolerant; with the duller minds, barely so and occasionally sarcastic. He did not believe in lecturing on gross anatomy, a finished science, but his lectures on microscopic anatomy were superb from the standpoint of his staff, for whom they constituted a postgraduate course. As for the medical students, he was heard to say that he aimed his lectures at only the four or five best students in the class (of forty), tacitly implying that the assistant professors and instructors could take care of the rest.

For the best ten percent the instruction (or, it might be more correct to say, the freedom to learn) provided by this brilliant

professor opened new vistas in medical science. Years later Elmer Belt, a member of the first class Evans taught at Berkeley and now California's most distinguished urologist, wrote of Evans and his young associates that "The effect of their scholarship and idealism upon the freshman class in medicine was electric. Each of us realized how great an opportunity it was to enter the study of medicine under their guidance and for us the study of medicine became an obsession. The routine work of gross dissection and histology was time-consuming but most of us, in addition, were stimulated to take up a separate problem in research. We were thus led to seek out and read recent contributions to the literature concerned with our special subjects. This pursuit inevitably led us to doubt didactic textbook statements unless verified by our own personal observations. This atmosphere of doubt and verification prevailed through the department and led to intense application. For most of us this was our first taste of scholarly research." \*

Departmental administration was for Herbert Evans a duty reluctantly borne. His compulsive urge to work intensively at research led him to put off administrative routine, the writing of articles against deadlines, and other less congenial tasks until the last minute. Thus the course of departmental affairs was interrupted from time to time by minor or even major crises. One of these in the early Berkeley days, somewhat mysterious to Evans's associates, evidently caused him deep concern. He and his secretary for several days were intently busy, occupied with account books and the adding machine. Evans's brother, a businessman familiar with accounting, was called in; there were urgent messages to and from the university bursar's office. Probably the professor had overrun his budget. On another occasion he was overtaken by the deadline for an article long promised

\* Elmer Belt in *There Was Light: Autobiography of a University, Berkeley, 1868-1969*, ed: Irving Stone, Doubleday & Co., Garden City, New York, 1970, p. 354.

to an eastern scientific journal. In despair he retired to his study at home, sent for the secretary and her typewriter, and dictated hectically for three or four days. Typed sheets were sent up to the laboratory to be proofread by an assistant professor; the manuscript was assembled at home as the last pages were being typed, while Mrs. Evans sat in the family car at the door, ready to dash to the Berkeley Southern Pacific station to get the parcel on the Overland Limited for Chicago and the East.

Despite harassing episodes such as these, Evans had a wife still willing to yield her impetuosities to his, junior colleagues anxious to be helpful, and a devoted secretary and thus was able to keep the Berkeley department of anatomy happily productive and himself moving from one achievement to another. Resuming work on the vital staining of connective tissue cells, he quickly produced in collaboration with Katherine Scott a monograph (1921), beautiful in its clarity and certainty, on the differential reactions of macrophages and fibroblasts to particulate matter such as the acid azo dyes.

While still in Baltimore Evans's attention had been directed to the ovary by the observation that in mice vitally stained with trypan blue the moribund cells of atretic follicles were heavily laden with dye particles. Following this up at Berkeley he sought information about the ovarian cycle of rodents from Joseph A. Long of the zoology department, a quietly persistent worker who for years had been studying the estrous cycles of albino mice and rats. The length of the cycle in these animals was still a puzzle because the outward signs of estrus in them are very inconspicuous, as compared with those of household and barnyard animals. Joseph Long, by an ingenious but (as it turned out) inadequate method, had set it tentatively at eleven days. About this time (1916) Charles R. Stockard and G. N. Papanicolaou published a study of the estrous cycle of the guinea pig. They had revived a forgotten observation that the lining of the vagina undergoes periodic changes produced (as we now

know) by action of the ovarian estrogenic hormone. Such changes are revealed by microscopic examination of cells scraped from the vagina. With this simple and expeditious method Evans and Long, working together in the anatomical laboratory, soon found that the female rat has a quite regular cycle of about five days and that the occurrence of estrus and the time of ovulation can be determined by the vaginal test. This exciting discovery, obviously opening the way to a vast field of research in the physiology of reproduction, stimulated Evans to furious further activity in which the gentle and studious Long was caught up. Long's chief, the senior professor of zoology, was annoyed by Long's frequent absence from his own laboratory, and both Mrs. Long and Mrs. Evans were even more disturbed by their husbands' lateness at dinnertimes and absences at weekends. The writer of this memoir was the embarrassed witness, in the rat room late one afternoon, of a dramatic entrance of the two ladies with a loud peremptory demand that their respective husbands should quit work at once and go to their homes where they belonged at that time of day.

The outcome of Evans's collaboration with Long was a monograph, now a classic in its field, published in 1922, *The Oestrous Cycle in the Rat and Its Associated Phenomena*. Evans drafted it but, in deference to Long's prior work, put his colleague's name first on the title page. The book has had a very great influence, partly because of the attention it directed, in conjunction with Stockard's and Papanicolaou's study of the guinea pig, to the ovarian-uterine cycle as a general phenomenon. It made available for experimentation on the cycle the albino rat, a mammal that is inexpensive, hardy, and easy to house, feed, and handle. From this work stemmed directly the discovery, next to be discussed, by Evans, Scott-Bishop, and Burr, of vitamin E, and almost as directly the isolation of the ovarian estrogenic hormone by Edgar Allen and E. A. Doisy at St. Louis; and the work helped greatly to stimulate the whole

advance of our knowledge of the steroid hormones and the general chemistry of steroids. Not only did the monograph attain international fame; so also did the animals whose activities it described, for the Long-Evans standardized strain of white rats with gray hoods is currently specified in many accounts of research on the physiology of the rat.

Once having developed a standard strain of experimental animals and a practical method of following their cycles, Evans proceeded with various colleagues to attack major problems in the physiology of reproduction. First of these was the question of dietary factors in the cycle. That fertility could be impaired or abolished by inadequate diet was well known. With Katherine Bishop he established a standard diet of known composition on which their rats maintained regular estrous cycles, then proceeded to experiment with various dietary deficiencies. In 1923 they announced the existence of a hitherto unrecognized dietary factor that is essential for reproduction; in its absence female rats, although they grew well and in maturity ran regular cycles, could not carry their young to birth because early in pregnancy they suffered breakdown of the placentas and resorbed their fetuses. Male rats, if their food lacked the same ingredient, became sterile by deterioration of the sperm-forming cells of the testes. This dietary factor, essential for reproduction, Evans and Bishop found is fat-soluble, is present in green leaves (lettuce), and occurs in especially high concentration in wheat germ. With a chemist, George O. Burr, Evans obtained a partially purified extract from wheat-germ oil. The active ingredient acquired the designation "vitamin E," as the next in a series after E. V. McCollum's antirachitic vitamin D. In the next few years biochemists elsewhere carried the purification further and identified the factor as an alcohol; in 1936 Evans, with the biochemists Oliver H. and Gladys A. Emerson, prepared a product pure enough to yield the empirical formula  $C_{29}H_{50}O_2$ , which he named "tocopherol." During the course of these experiments

with varied diets Evans and his co-workers at the time (Burr, the Emersons, Samuel Lepkovski, and others) were also among the first to recognize the importance of fatty acids as dietary constituents.

Evans's attention was next drawn to the hypophysis (pituitary gland) and its remarkable endocrine effects. It had recently dawned upon the medical profession that a form of gigantism, acromegaly, results from pituitary overactivity, usually caused by a tumor of the gland. Evans's admired teacher in medical school, Harvey Cushing, had been experimentally removing the gland from dogs, with striking effects on growth. When Evans took over the Berkeley anatomy department Philip Smith, already there, was becoming expert in extirpating the rudiment of the anterior lobe of the hypophysis of frog tadpoles, causing remarkable repressive effects on growth, on pigmentation, and on the development of the thyroid and adrenal glands. In 1920 Evans began experiments with extracts of the mammalian anterior lobe, at first with J. A. Long, and in 1922 they announced that, by injecting an alkaline extract of ox pituitaries into young rats, they had produced such enhanced growth that some of the treated animals grew far heavier than the largest untreated rats in the colony. This was the first essential step toward recognition of the pituitary growth hormone.

The extracts also delayed the onset of sexual maturity and lengthened the estrous cycle or completely suppressed it. In the ovaries of treated female rats an excessive amount of luteal tissue was formed by luteinization of the ovarian follicles. This observation was the basis of the subsequent search for a specific luteotropic hormone of the anterior pituitary lobe.

Henceforth, the isolation and identification of the several hormones of the anterior pituitary was to be for forty years the main theme of Evans's research. Because, however, of his practice—in his maturity—of always working with one or more collaborators, he stepped aside not infrequently to attack, with



one or another of them, problems not closely related to the pituitary endocrines. One of these ventures was with Olive Swezy, a research associate several years his senior, in the neighboring department of zoology. They jointly published reports on two important topics. One of these was the old question of whether or not in mammals the formation of egg cells (ova) from the germinal layer of the ovaries continues after the birth of the female infant and on through adult life. After much debate, it had been generally accepted that all the ova in the ovaries of a sexually mature woman or other mammalian female are formed during the fetal period. The opposite conclusion of Evans and Swezy (1929, 1931), based largely on study of the rhesus monkey, that ova are formed after birth and in sexual maturity, has not been confirmed by subsequent workers carefully examining similar material. Their other chief topic was the number of chromosomes in man. For this study Evans personally obtained exceptionally well-preserved material by attending, at San Quentin prison, executions of criminals whose bodies were not to be claimed by relatives. Swezy did most of the counting, from thin serial sections. The currently available method of displaying the chromosomes and examining them in bits of tissue selectively stained and then flattened by gentle pressure was not then known. The count of 48 chromosomes in each cell, published by Evans and Swezy, was unfortunately incorrect; it is now certain that 46 is the correct number. In 1969, to a gathering of scientific friends, Evans explained that semidetached portions of two chromosomes had been counted as separate units.

Another, more successful sideline was a descriptive account of the canine estrous cycle, published in 1930 as a joint monograph with H. H. Cole. For this research Evans was himself prepared by a study of the early embryology of the dog, done while still at Baltimore, where by greasing the palms of dog-pound attendants he was permitted to mate bitches in heat at stated

times before they were put in the gas chamber. A few carefully preserved jewel-like blastocysts thus obtained remained for years in vials on his shelves at Berkeley; he never published the embryological findings. References to other joint investigations with various members of his group will be found in the bibliography appended to this memoir.

Evans's principal collaborator in the continuing research on the pituitary hormones was Miriam E. Simpson, who after an outstanding record in Evans's department as a medical student and in other preclinical departments at Berkeley transferred to Johns Hopkins for the latter half of the medical curriculum, took her M.D. there in 1923, and returned immediately to Berkeley as a member of the department of anatomy. For about a decade their efforts were centered largely on the relations between the pituitary gland and the ovaries. In his work with J. A. Long on the growth hormone, Evans as stated above had found in 1921 that their extracts of the anterior lobe strongly affected the ovaries of experimentally treated female rats, causing persistence of the corpora lutea and filling up immature follicles with lutein-type cells. The rhythm of the female reproductive cycle was, of course, seriously deranged by such alterations. This was the first direct experimental demonstration of an action of the anterior pituitary on the gonads. Here, then, was apparently a second hormone of that organ: its activity and its chemical structure must be distinguished by further research from those of the growth hormone.

Shortly afterward workers elsewhere found that pituitary extracts would stimulate growth and maturation of the ovarian follicles. For some years it remained uncertain whether the luteotropic hormone (LH) and the follicle-stimulating hormone (FSH) were one and the same. A further complication was the finding by others that the urine of pregnant women contains a substance that when injected into female animals, causes hyperemia of the ovaries, growth of the follicles, and, in some

species, ovulation. This is the basis of the Ascheim-Zondek and Friedman tests for pregnancy. For some time the similarity of action of the urinary and the anterior pituitary hormones was quite confusing. To this problem Evans and Simpson devoted much attention during the earlier years of their collaboration, finally demonstrating that the urinary gonadotropin (since shown to be produced by the chorionic part of the placenta) and the pituitary FSH are different substances.

In 1929 the two collaborators published another significant discovery, that something in their pituitary extracts caused hypertrophy of the mammary glands in virgin rats. This gave a strong hint of still another hormone of the anterior lobe. The hint was confirmed in 1933 by Stricker and Grueter of Strasbourg, who by injecting Evans-type pituitary extract caused rabbits actually to secrete milk; by G. W. Corner at Rochester, New York, who proved that previous action of the corpora lutea is not required for this effect; by Oscar Riddle of the Carnegie Institution at Cold Spring Harbor, New York, who isolated and almost completely purified the lactation hormone (now called prolactin); and by Abraham White of Yale University, who completed the purification.

While Evans, with his collaborators, had thus been engaged since 1920 in the characterization and isolation of the pituitary gonadotropic (follicle-stimulating and luteinizing) hormones and in obtaining the earliest evidence for a mammatropic hormone, investigators elsewhere had recognized that two other organs are also targets for the action of anterior pituitary hormones. Philip Smith's skillful ablation of the pituitary rudiment of frog tadpoles, done in Evans's laboratory, as already mentioned, had revealed that in tadpoles so deprived the thyroid gland does not develop. When Smith succeeded in performing hypophysectomy in the rat, a similar finding reinforced the suspicion that a thyreotropic hormone of the anterior pituitary was waiting to be identified. Actual isolation of such an agent in

crude form was accomplished in several American and European laboratories in 1929. About the same time several workers observed deficient development of the cortex of the adrenal gland in hypophysectomized animals. J. B. Collip of Toronto and his associates, in 1933, were the first to isolate an effective if only partially purified adrenotropic substance.

By the mid-1930's the six hormonal products of the anterior lobe of the pituitary gland now generally recognized as distinctive substances had been isolated in various degrees of purity, namely those for growth (somatotropic, STH), follicle stimulation (FSH), stimulation of lutein and interstitial cells (LH, ICSH), lactation (prolactin), stimulation of the thyroid gland (TSH), and stimulation of the adrenal cortex (ACTH). These hormones have been extremely difficult to separate, to purify, and to characterize chemically, for they are proteins and hence exceedingly complex in molecular structure. Furthermore, they are effective in very small dosage, and it is therefore difficult to know when a preparation of any one of them is free of contamination by another. As Evans and his associates attempted to identify them and distinguish their functional activity, their progress, like that of other workers, was slow and confusing. One well-known American endocrinologist, Oscar Riddle, insisted for a long time that Evans's growth hormone was identical with prolactin. As Evans himself has said, he and his colleagues published again and again statements that they had "purified" the follicle-stimulating hormone, as indicated by tests available at the time, only to find out themselves or learn from others that with different tests or different dosages their "pure" preparations still produced effects that must be ascribed to another of the anterior lobe endocrines. Even at the present writing, when some of the amino acid chains constituting these potent proteins have been identified, one of Evans's former co-workers, C. H. Li, attributes the growth effect and the mammatropic

effect to the same group of amino acids, while another of the group, W. R. Lyons, disagrees.

Because of these perplexities, the biographer and historian find it difficult to chart the course of discovery in this area of research and to assign credit to any one man or group of co-workers for one or another item in an ever-changing pattern of knowledge. We shall do ample justice to Herbert Evans when we say that for thirty years he led his able associates in productive study of each and all of the anterior pituitary hormones. When he first began to experiment with pituitary extracts, nothing was known about the endocrine activity of the anterior lobe of the pituitary gland except that in some vague way it exerted control over bodily growth and was somehow essential to the reproductive function. When he retired from active research, worldwide investigation had recognized the six hormones, characterized their activities, and to a large extent revealed their chemical structure. Evans was involved in some way in almost every aspect of this great advance.

The names of many who worked at his side are recorded in the long list of joint publications appended to this memoir. One of them has written that because this was a period of group research in Evans's laboratory, the contributions of individual members might well be obscured or even forgotten, but none of those who took part in this large and bold enterprise would ever forget Evans's own contribution through wise choice of personnel and the provision of facilities for work, or his conferences in which divergent views were analyzed and conclusions reached.

The work of Evans and his group could not long be accommodated in the little gray building where he began at Berkeley in 1915. In 1930 the department of anatomy and with it his research laboratories were removed to the newly built Life Sciences Building, further west on the Berkeley campus. In the same year the University of California created an Institute of

Experimental Biology and in recognition of Evans's achievements in research appointed him its director, thus providing for him and those he had gathered around him far ampler space and superior equipment. With the new appointment went the specially endowed Herzstein Professorship of Biology.

The progress of research in the new laboratories was interrupted temporarily in 1932 when Simon Flexner, Director of the Rockefeller Institute (now Rockefeller University) in New York City, invited Evans to spend a year at the Institute as a guest investigator. Evans's rising reputation for endocrinological research perhaps sufficiently explains this rather unusual invitation, but he believed, as did many of the Institute's permanent staff, that it had been arranged to test his eligibility to succeed to the directorship. Flexner, sixty-nine years old, would soon have to step down. Evans at fifty was of suitable age and obviously possessed the scope and courage to deal with difficult scientific problems and the ability to lead group research. He had just finished a two-year term as president of the American Association of Anatomists. Before scientific audiences he spoke with impressive manner and style.

Evans took with him to New York Miriam E. Simpson and Richard Pencharz, then junior members of his Berkeley group. At the Rockefeller Institute he added a pharmacologist, E. L. Gustus, and a biochemist, Paul R. Austin. Gustus recalls still his admiration of Evans's broad knowledge of science in general, his charm, and his encouragement of the younger men. In a personal communication Austin describes the characteristic drive and intensity of research under Evans's direction: "Dr. Evans impressed everyone with his infectious energy and enthusiasm. He sent a technician to the Institute ahead of the rest of his group to get a rat colony started. . . . This colony was soon supplemented by purchase of rats from outside suppliers so that at our peak of activity we had 700 21-day-old rats available every

Monday morning for our assays. . . . As you will guess, the situation was pretty hectic at times and there were occasions when the rats drove the program rather than have the program limited by the rats. But we did get a lot of work done with a small group in the short period of eight or nine months."

The group, in fact, made significant progress in the purification of the follicle-stimulating hormone of the pituitary gland and in clarification of the synergism between this agent and the pituitary luteinizing hormone (which they were then calling "interstitial cell stimulating hormone").

The minutes of the Board of Scientific Directors of the Rockefeller Institute do not reveal anything about this visit, and none of the senior staff of that time survive to tell why nothing more came of it, if indeed it was a trial run for the brilliant Californian. In all probability Simon Flexner and his advisers doubted whether Evans could subordinate his own program of research to the broader duty of leading the distinguished and diversified Institute.

Few of Evans's fellow scientists knew that he was an ardent collector of rare books, especially the great classics of medical, biological, and physical science. His adoption of such an avocation, ordinarily far beyond the means of a professor, is easily understood in the light of his aspiration to cultural distinction, long hampered by his lack of classical education. As a young man in Baltimore he was already sufficiently interested in the history of his profession to publish one or two brief reviews of new books in that field. As he matured, even if he did not read the Greek of Galen, the Latin of Vesalius, or the antique French of Ambroise Paré, he came to relish the sight and feel of the volumes in which the works of these heroes of science were enshrined and steeped himself in historical and bibliographical lore until he could talk freely with bibliophiles and historians of science. His urge to collect books could not be indulged, how-

ever, for lack of the necessary money, until he was well established in his professorship and the family exchequer was strengthened by parental bequests.

His remarkable career as a bibliophile (bibliomane would hardly be too strong a term) has been described since his death by Jacob I. Zeitlin, the well-known Los Angeles dealer in rare books and manuscripts.\* Evans began serious collecting about 1930. His earliest purchases were financed, it seems, by borrowings from his wife Anabel's patrimony. By 1934 his first collection was sufficiently important to be exhibited at the Berkeley Faculty Club by the History of Science Club of the University of California. A small catalog he prepared for the exhibit shows that he had interested himself especially in books embodying notable individual discoveries, the formulation of scientific laws, and announcements of important hypotheses. According to Zeitlin the catalog was a pioneer effort to compile a selected list of the most significant books in the history of science. It is still a valuable guide for advanced collectors and dealers. Zeitlin considers it largely responsible for the great increase in American demand for books in the history of science during the past thirty-five years and the consequent increase of prices.

Evans did not keep this first collection very long. Domestic difficulties requiring reimbursement of Mrs. Evans forced him to sell it. Almost at once he began another, of first editions in the sciences, accompanied by a collection of bibliographic reference books on the subject. This too was sold, to settle the estate of his wife, who died soon after their estrangement and divorce in 1932.

Somehow Evans found the means to continue collecting, periodically getting himself in debt and selling off the books. Each time he received payment for the latest collection, says Zeitlin (through whose hands most of them passed), "He would

\* Jacob I. Zeitlin, "Herbert M. Evans, Pioneer Collector of Books in the History of Science," *Isis*, 62, 507 (1972).



plunge into another passionate campaign by letter, cable, telephone, and overnight drives or air flights to all parts of the world, to try to recapture the treasures he had parted with a few days before."

The history and present whereabouts of the seven successive scientific collections show how widely this obsessive urge has ultimately served the scholars of our country, for almost all these books, estimated to number more than 20,000, are now in the possession of universities or other scholarly owners.

Mr. Zeitlin tentatively lists the medical and scientific collections as follows:

1930 (?): Classics in the Medical Sciences. Purchased by Dr. and Mrs. James Waring, Finley L. McFarland, and Mrs. Dora Porter Mason. Presented to the Denver Medical Society, Denver, Colorado.

1950: First Editions in the Sciences, together with a Reference Collection on the History and Bibliography of Science. Purchased from the conservator of the estate of Mrs. Anabel Evans by Zeitlin & Ver Brugge and John Howell:Books, on behalf of Lessing J. Rosenwald, and presented by him to the Institute for Advanced Study, Princeton, New Jersey.

1953: First Editions in the Sciences, together with a Reference Library on the History and Bibliography of Science. Purchased by Zeitlin & Ver Brugge. Described in several catalogs. Many of the outstanding items were acquired by the Burndy Library and by E. L. DeGolyer for the DeGolyer Collection at the University of Oklahoma at Norman, Oklahoma.

1957: First Editions in the Sciences. Purchased by Bernard M. Rosenthal and John Fleming for Louis Silver of Chicago and presented to the University of Chicago. Some duplicates and out-of-scope works were sold off by John Fleming. (One of these, Semmelweis, *Die Aetiologie, der Begriff und die Prophylaxis des Kindbettfiebers*, 1861, Zeitlin purchased back for Dr. Evans, the second time this book had passed from his hands to Dr. Evans's.)

1961: First Editions in the Sciences. Sold by Zeitlin & Ver Brugge and John Howell:Books, as agents for Dr. Evans, to Samuel A. Barchas of Tucson, Arizona.

1962: First Editions in the Sciences, together with a Collection on the History and Bibliography of Science. Sold by Zeitlin & Ver Brugge and John Howell:Books, as agents for Dr. Evans, to Lew D. Feldman, acting for the University of Texas, Austin, Texas.

1967: First Editions in the History of Science and a Collection on the History and Bibliography of Science. Purchased by John Howell:Books, San Francisco, and Zeitlin & Ver Brugge, Los Angeles, and dispersed in a number of catalogs of both firms. The major part of the collection is now at the University of Utah, Salt Lake City, Utah.

In addition to the medical and scientific books, Evans formed and disposed of two large collections of western Americana, two collections of Japanese prints, one of the prints of Jacques Callot, and a general library of poetry, art, and the humanities.

Dr. Evans was tall and broad-shouldered. His mobile features expressed alert interest in people and things about him, mingled now and then with a quizzical glance or the subtle reflection of an *arrière pensée* that might have meant anything from mockery to disdain. In friendly conversation he was gay, sometimes extravagantly enthusiastic. He liked especially to talk with intelligent women, who responded warmly to his deferential manner. In more formal conversation and in talk about scientific matters or book-lore, though expressively courteous, he could not conceal an air of superiority of which he may not always have been conscious, an air evinced by allusions to facts or personalities beyond his hearers' acquaintance, introduced in such a way as to suggest that one really ought to know about them. The same urge to be recognized as a cultivated person caused him, in his writings, to employ a high and sometimes high-flown literary style. As would be expected of a man always

expending his full energies at the highest level of individual talent, he would not busy himself with the organizational routines of the scientific profession. He frequently attended the annual meetings of the American Association of Anatomists, presenting the results of his research at the scientific sessions and heartily enjoying the sociability of these gatherings, but when he was president of the Association (1930–1932), he left the routine business to be handled by the vice president. Duty required him to take the chair at the executive session, but he did not inform himself of the agenda and was quite unabashed when he had to be coached by the secretary sitting beside him on the platform.

Dr. Evans's three marriages marked cardinal phases of his life. Anabel Tulloch, the bride of his student days, exhibited as much independence and impetuosity as he had when in disregard of family pressure, he boldly set out on a scientific career. But as shown by episodes narrated earlier in this memoir she did not willingly endure the stresses of marriage to a man so intensely dedicated to science. The daughter born of this marriage was greatly loved by her father and deeply mourned when she died in young womanhood.

Evans's second wife, Marjorie E. Sadler, was a highly competent research worker in his laboratory, fully qualified to tolerate the exigencies of his scientific activity. They were married in 1932 when his career in endocrinological research was at its crest. This union also ended in divorce. A daughter, Gail Evans (Mrs. Rolfe LaForge), no less beloved than was her half-sister, resides at Mill Valley, California.

The wife of Evans's later years, Dorothy F. Atkinson, was at the time of their marriage in 1945 acting director of the department of English at Mills College, Oakland, California. The third Mrs. Evans was prepared by her training and career to sympathize with her husband's interest in the history of science and his zest for collecting books and prints. Her humanistic studies gave her, indeed, a gentle superiority over his less-deeply rooted

literary and artistic qualifications, and her mature years gave her confidence to smile at his exuberances. No doubt, also, he had mellowed domestically. They lived quietly and happily together in their Berkeley hillside home, amid old books and objects of art, until her death in January 1969.

In 1970 a severe stroke terminated Dr. Evans's intellectual activities and ended his hopes of amassing yet another distinguished collection of rare books. He lingered until his death on March 6, 1971.

Dr. Evans received and appreciated many honors from the learned world, more than ample to justify the choice of a career that he had made with filial concern in young manhood.\* They include honorary degrees from universities on three continents, among them the Sorbonne, the University of Geneva, San Marcos de Lima, and his own *almae matres*, California and Johns Hopkins. He was elected a member of the National Academy of Sciences of the United States (1927) and was a foreign member of the Royal Society of London and other learned societies in Europe and South America. Appointments to numerous endowed lectureships in the United States, England, and Scotland testify to the admiration of fellow scientists and their desire to have their students see and hear this notable investigator and discoverer.

\* The record in *Journal of Reproduction and Fertility*, 19, 1-49 (1969), of an interview with Dr. Evans arranged by Sir Alan Parkes of Cambridge a few days after Evans's eighty-fifth birthday contains, besides a very interesting and revealing conversation, a *curriculum vitae* and a full list of honors, as well as a selected list of Dr. Evans's publications on endocrinology and the physiology of reproduction.

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## KEY TO ABBREVIATIONS

Am. J. Physiol. = American Journal of Physiology

Anat. Record = Anatomical Record

Cancer Res. = Cancer Research

Carnegie Inst. Wash. Contrib. Embryol. = Carnegie Institution of Washington, Contributions to Embryology

J. Am. Med. Assoc. = Journal of the American Medical Association

J. Biol. Chem. = Journal of Biological Chemistry

J. Nutr. = Journal of Nutrition

Mem. Univ. Calif. = Memoirs of the University of California

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