

## Carnegie Institution of Washington Department of Embryology <sup>[1]</sup>

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The Carnegie Institution of Washington's (CIW) Embryology Department was opened in 1914 and remains one of six departments in the CIW. The department quickly became, and remains, world renown for its many embryonic development discoveries. In 1913 Franklin P. Mall, Professor of Anatomy at Johns Hopkins Medical School, applied for a Carnegie grant to support his research with human embryos. Mall had a collection of over 800 human embryo specimens and was at the point of wanting to do more than just collect. He wanted to study normal and abnormal growth and so began categorizing embryos in a scientific fashion. It soon became apparent that Mall would need funding and a research venue. In 1914 Mall not only received a \$15,000 grant from Carnegie, but was also made director of the new Department of Embryology at the CIW. With money, new facilities, a fireproof vault for embryo specimens, and Carnegie's name above the institution's door, Mall brought his extensive embryo collection with him and began obtaining hundreds more human embryos to study. Over the next fifty years, the Department of Embryology would collect and permanently store more than 10,000 embryos.

At first, the Board of Directors of the CIW was undecided about where to locate the new Department of Embryology. Europe seemed to be a logical choice, given the number of well-known embryologists working in Germany. However, Mall's grant proposal steered the location to Baltimore, Maryland, a city that already had a department of public health, and Mall's plan of obtaining embryos from public health clinics (with the cooperation of health clinic physicians on site), was convincing. With research and technical help from George L. Streeter and Franz J. Keibel (both former students of [Wilhelm His](#) <sup>[5]</sup>), embryo modeler Osborne O. Heard, and scientific illustrator [James F. Didusch](#) <sup>[6]</sup>, Mall set out to catalogue the embryo collection and to establish norms for the sequence (stages) of early human embryo development. He began documenting his research by overseeing publication of [Contributions to Embryology of the Carnegie Institution of Washington](#) <sup>[7]</sup>, first published in 1915 and continued until 1966. In *Contributions* could be found the illustrations of Didusch, the photographs of [Chester F. Reather](#) <sup>[8]</sup>, and the embryo models of Heard. Their work, coupled with the writing of research scientists at CIW made *Contributions* a textual and visual standard in the international reproductive and embryological research community.

Embryology soon became a dominant American discipline as much of Europe saw itself entangled with WWI and the CIW increased its funding for research. After Mall unexpectedly died 1917, Streeter was hired to become the second Department of Embryology director. Under Streeter, the role of the Department of Embryology broadened from human embryo study to include rhesus macaque monkeys and tissue culture techniques. George W. Corner, a student of Mall's used Carnegie funding to develop the Carnegie monkey colony in 1925. The maintenance of the colony alone took up 18% of the department's budget and proved significantly more challenging compared to experimenting with flies, mice, and frogs. Monkeys

were used for several reasons. First, the embryos developed quickly. Second, only primates have a menstrual cycle associated with [ovulation](#) [9]. Thus, comparative anatomy utilizing monkey reproduction allowed researchers to begin their understanding of human [menstruation](#) [10], [ovulation](#) [9], and prenatal physiology.

Carl G. Hartman's laboratory documented the timing of monkey [ovulation](#) [9] and the changes that take place in the [uterus](#) [11] and [ovary](#) [12] prior to [menstruation](#) [10]. This led to a new scientific view of human fertility, as many of the discoveries about monkey reproduction held true for [humans](#) [13]. Streeter and Hartman discovered that maternal tissue begins preparation for [egg](#) [14] attachment before the [egg](#) [14] attaches to the [uterus](#) [11] and not after. Hartman continued his studies of the female menstrual cycle and soon was involved in publicizing the contraceptive method known as the "rhythm method".

Under Mall and Streeter's watch, the number of human embryo specimens at the department grew tremendously. Many of them were used to develop the formal classification of embryo development known as the Carnegie Stages—the global standard for human embryological research. Putting embryos in exact chronological stages had proven nearly impossible since one rarely knew exactly how old an embryo was when it was delivered to the embryologists. The Department of Embryology researchers and staff spent decades identifying twenty-three stages of early human embryo development, dependent on physical characteristics such as weight and crown-to-rump length. The growing Carnegie embryo collection also continued to serve as the basis for hundreds of research articles, many of them published in *Contributions*.

Streeter also oversaw the work of Warren H. Lewis and [Margaret R. Lewis](#) [15], who carried out early tissue culture studies. Their work became well known to both researchers and the public by their use of [time-lapse cinematography](#) [16] to record striking cellular activities never captured before on film. Monkey embryos were used in the Lewis' lab to make motion pictures of cleavage from the two- to eight-cell stage, while they used [rabbit](#) [17] embryos to document, for the first time, a record of mammalian [embryogenesis](#) [18] from [fertilization](#) [19] to [blastocyst](#) [20] formation. Much of the cinematography apparatus was not available for purchase but was built in-house by Heard and [Warren Lewis](#) [21].

Although not formally trained as an embryologist, [Elizabeth Ramsey](#) [22] discovered a fourteen-day-old human embryo while doing an autopsy on a young woman at a New Haven, Connecticut, hospital. This finding steered her to the CWI and a new field of study. Carnegie specimen number 6734, better known as the "Yale" embryo, arrived at CIW with Ramsey in 1934. Ramsey soon became curator of the Carnegie embryo collection and investigated the manner in which blood flows through the [primate](#) [23] [placenta](#) [24]. The application of her work to the field of obstetrics is noteworthy: prolonged labor contractions can have dire consequences for a [fetus](#) [25] due to curtailed circulation of blood through the [placenta](#) [24].

Streeter retired from the Department of Embryology in 1940 and was succeeded by George Corner, perhaps best known as a co-discoverer of [progesterone](#) [26]. As the department's third director, Corner brought an interdisciplinary approach to [embryology](#) [27] by incorporating physiology, biochemistry, and biophysics into [embryology](#) [27] research. Also under Corner the department collaborated with clinical researchers at Johns Hopkins to help discover the formation of cerebrospinal fluid, brain and spinal cord development, chromosome movement, and malignant cell [morphology](#) [28].

In 1956, [James D. Ebert](#) [29] an experimental embryologist transformed the way in which [embryology](#)

[27] would be done at CIW. Ebert became the department's fourth director and initiated change by aligning [embryology](#) [27] with the study of genetics. At the time, the department housed the world's most complete and unarguably the largest [collection of human embryos](#) [30] and human embryo models in the world. In the 1950s and 1960s the structure of DNA was defined and [genes](#) [31] were identified as major players in cellular [regulation](#) [32]. With the focus on [genes](#) [31] and DNA, the Department of Embryology was moved to the Homewood campus of [Johns Hopkins University](#) [33] in 1960. The relocation placed the department closer to the university's Departments of Biology and Biophysics and thus brought the fields of cellular and molecular biology into the world of the embryo. It also symbolized the move of [embryology](#) [27] from reproductive medical research to a molecular experimental platform. It was during Ebert's tenure that the Department of Embryology made several important contributions to the field of genetics. In 1976 Ebert resigned from the CIW to become director of the [Marine Biological Laboratory](#) [34] (MBL). [Donald D. Brown](#) [35] who had worked for the CIW during the 1960s and studied differential gene expression in *Xenopus* embryos, became the department's fifth director.

By the early 1970s the vast embryo collection was having fewer visitors and receiving less interest from embryologists. In 1973 the entire collection was shipped to the [University of California at Davis](#) [36] Medical School, along with Ronan O'Rahilly and [Ernest Gardner](#) [37], who maintained the collection while holding academic appointments at Davis. O'Rahilly and Gardner continued work on nervous system development and Carnegie stages. O'Rahilly retired to Europe in the 1980s and the embryo collection was once again poised for a move. In 1990 the collection was transferred to the [National Museum of Health and Medicine](#) [38] in Washington, DC, where it continues to be a resource for human [embryology](#) [27] studies.

[Allan C. Spradling](#) [39] and [Gerald Rubin](#) [40] became well known Carnegie researchers with their work on gene transfer in *Drosophila* [41] *melanogaster*. Spradling succeeded Brown as department director in 1994 and continued with his *Drosophila* [41] studies. In 2005 the Department of Embryology moved to the [Maxine F. Singer](#) [42] (Carnegie Institution President, 1988-2002) research building located on the Johns Hopkins Homewood campus.

The Department of Embryology today remains small; only eight research scientists and several staff associates or young researchers occupy laboratories in the new research building. The Carnegie research philosophy has always maintained that small groups are more flexible, require less oversight, and provide for an environment of collaboration. This emphasis on individual researchers and the freedom to pursue questions allows for new research programs and quick shifts in agendas. The Carnegie Institution's Department of Embryology remains one of the world's leading institutions for study of the embryo.

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