Regnier de Graaf (1641-1673) [1]

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Regnier de Graaf [4], a Dutch physician and anatomist, was born 30 July 1641 in Schoonhoven, the Netherlands. Though he published papers on both pancreatic and male reproductive anatomy, he is best known for his discovery of the mature ovarian follicles as well as his contributions to the general body of knowledge surrounding the female mammalian reproductive organs.

De Graaf studied for several years in Holland beginning in 1660, first at the University of Utrecht [5] and later at Leiden University. At Leiden, he was a student of both Franciscus Sylvius [6] and Johannes van Home [7] and studied alongside such historical figures as Niels Stensen [8], Frederik Ruysch [9], and Jan Swammerdam [10]. His early friendship with Swammerdam later soured due to a highly turbulent and hostile argument over priority and academic credit. The year 1664 saw the release of de Graaf?s first known publication, a paper on pancreatic secretions, saliva, and bile. In 1665 he traveled to France to continue his education and received his MD from the University of Angers [11] later that year.

After receiving his MD, de Graaf returned to the Netherlands and established a medical practice in Delft. Though he worked as a practicing physician and his business was successful, he also continued to engage in private research, and it is this research that ultimately led to the anatomical discoveries for which he is famous.

De Graaf did some dissection and research on the male reproductive organs [12], but his 1668 treatise on the subject was largely a summation of existing knowledge. He is much better known for his investigation of the female mammalian reproductive organs, specifically the identification of the ovarian follicles that now bear his name. The discovery of the ovarian structures that would later be labeled Graafian follicles [13] was a significant step forward in the field of reproductive biology [14], but de Graaf?fs research was plagued by several misconceptions stemming mostly from the lack of microscopic equipment at the time.

Interestingly, all de Graaf?fs work took place more than 150 years before Karl Ernst von Baer [15] first identified the ovum [16] in 1827. Though the egg [17] had not technically been discovered at the time de Graaf was doing his research, reproductive anatomists and biologists of the time were conceptually aware of it. De Graaf deduced its existence from his knowledge of ectopic (tubal) pregnancies, and he was aware of the unidentified object?fs path of travel. However, he mistakenly believed that the egg [17] actually consisted of the ovarian follicle itself, which he thought detached from the ovary [18] and entered the Fallopian tube. Though de Graaf?fs theory was incorrect, he did realize that the structure traveling down the Fallopian tube was significantly smaller than the supposed parent follicle, an inconsistency he was never able to explain. With the help of highly improved microscopic equipment, future scientists would reveal that the Graafian follicles [13] actually rupture, releasing the mature egg [17] into the tube.
Much of de Graaf’s work on the female procreative system is still relevant today, due largely to the fact that his knowledge was derived directly from the physiological dissection and examination of humans\(^{[19]}\) and other mammals. His illustrations—very specific, detailed, and anatomically correct, especially compared to others of the time—remain particularly useful. De Graaf was one of the first anatomists to adopt the term “ovary”, which had been recently suggested by Swammerdam and van Horne. Among de Graaf’s notable accomplishments was his comparison of pre- and post-mating ovaries; the structural differences he noted led to his realization of the morphological changes that accompany the ovary’s functioning. He was also the first to discover the glandular origin of the \textit{corpus luteum}\(^{[20]}\) (the mass of cells secreted from an ovarian follicle after \textit{ovulation}\(^{[21]}\)), an important milestone in the history of \textit{endocrinology}\(^{[22]}\).

De Graaf was remarkable for several reasons, not least of which is the fact that his numerous scientific contributions were all made before his thirty-third birthday. He died at the age of thirty-two on 21 August 1673 in Delft, the Netherlands, of unknown causes. Some unconfirmed speculation has suggested that his death might have been due in part to the combined stress of the ongoing dispute with Swammerdam and the death of his three-week-old son in April 1673. Regnier de Graaf’s research and discoveries contributed greatly to the modern understanding of the female mammalian reproductive system.

**Sources**


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**Subject**

Graaf, Reinier de, 1641-1673 \(^{[23]}\) Reproduction \(^{[24]}\)

**Topic**

People \(^{[25]}\)

**Publisher**

Arizona State University. School of Life Sciences. Center for Biology and Society. Embryo Project Encyclopedia.

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