Book Reviews

The increasing frequency with which publishers are bringing out modern facsimile editions of classical medical works, either with or without editorial annotations and introductions, calls for special treatment in our review pages. It seems an excellent opportunity for revaluing the historical and scientific importance of these works. We therefore propose to notice them in a series of special essay reviews. The first of these is published below.

De Mulierum Organis Generationi Inservientibus 1672, by REINIER DE GRAAF. Facsimile with an introduction by J. A. van Dongen, Nieuwkoop, B. de Graaf, 1965.

It is indeed a pleasure to review this facsimile of Reinier de Graaf's famous book on the female organs of generation. The original work was published in 1672 in Leyden, a year before de Graaf's early death at 32, and it is now a very rare book. It forms one of the major landmarks in the development of ideas on the origin of life itself and is by far the most important of de Graaf's publications. The chapter on the ovarian or graafian follicle alone has assured his perpetual remembrance in the name which universal acceptance and long usage has elevated to that select group of eponyms which are no longer capitalized in spelling. Although it contains the first detailed and illustrated account of the ovarian follicle, this had already been described by Vesalius and Fallopius and their successors over a century earlier. Its real fascination and importance for both the biologist and the clinician is that for the first time it established experimentally that the female testis (as it was then called) of the mammal is the egg-producing organ and therefore analagous to the ovary of the bird. The discovery of the ovum within the follicle was made in 1827 by Van Baer, so completing the story.

Until the publication of de Graaf's book in the middle of the seventeenth century, the function of the ovary of mammals was uncertain. Aristotle had taught that the mammalian egg formed in the uterus from the menstrual blood and male semen. Galen modified this view, writing that female semen formed in the blood vessels of the female testis and then, after purification in this organ, passed into the uterus. There it combined with male semen to form the coagulum from which the embryo developed. The first real understanding of the function of the ovary came from the classical studies of Fabricius ab Aquapendente on the chick embryo. His observations led him to realize that the hen's ovary was the egg-forming organ and he named it the *ovarium*.

The idea that the female testis in the mammal might have a similar function began to gain ground in the seventeenth century and several independent observations to this effect were made. Swammerdam and Van Horne, working together in Leyden in 1666, described the ovarian follicles as ova in 1668 and planned a joint publication. During the same period the Danish anatomist Steno examined the organ in many mammals and also found the follicles in all cases. He came to the same conclusions and recorded them in his *Myologia* in 1667. Steno agreed to delay his own more detailed publication until Van Horne's account was published, but Van Horne died in 1670 before it was completed. Two years later de Graaf's book was published and

in it he gives the credit for these ideas to both Steno and Van Horne. However, Swammerdam was most offended by the publication, perhaps because he and Van Horne had failed to produce their own account. He issued a pamphlet which contained a bitter attack on de Graaf and claimed priority over him but he had left it too late; both the credit and the eponym went to de Graaf.

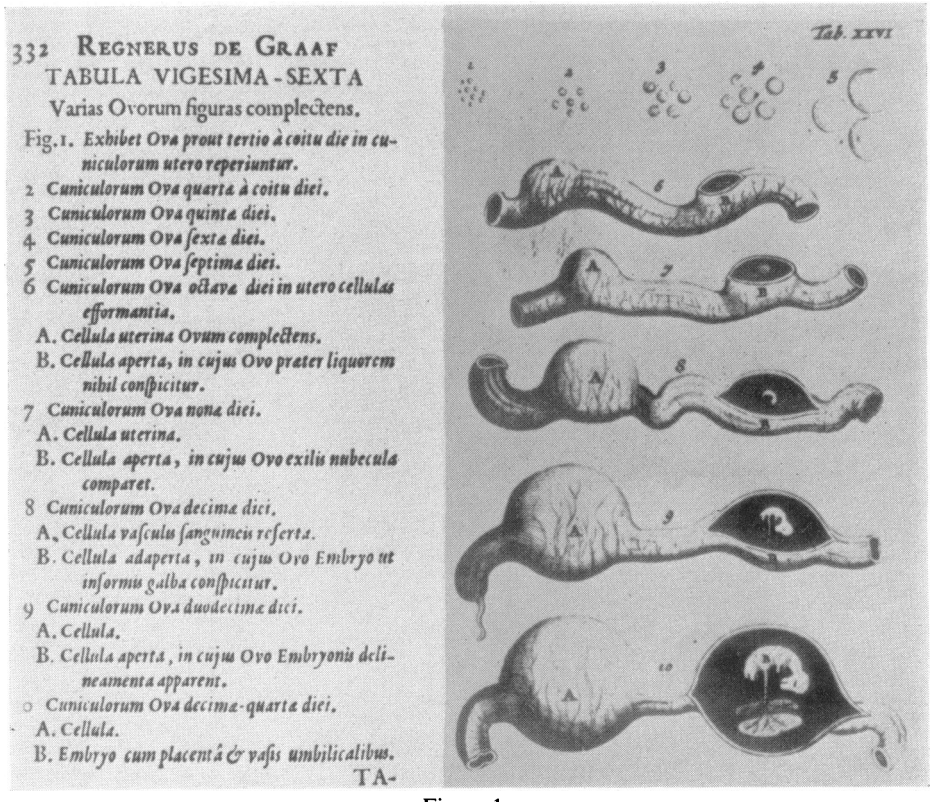
It is now clear that when de Graaf published his own book in 1672, the follicle had already been described in many works for over a century. In addition, the fundamental idea that the female testis was an ovary and that the follicles were the individual ova was already established.

What then was de Graaf's contribution to the story? Perhaps his greatest contribution, which alone justified the credit given to him, was that he applied scientific method to the problem; he devised a series of experiments, the results of which confirmed, at least in part, the hypothesis that the female testis of mammals was the egg-producing organ.

The story of this experimental approach to the problem is described in the final chapters and is by far the most exciting part of the book. The earlier chapters deal with detailed accurate descriptive anatomy of the female genital tract, with beautiful clear illustrations. Suddenly, however, his outlook changes. From being an accurate observer he becomes the true scientist. He moves from the Vesalian or descriptive method to the Harveian or experimental approach to his problem. He makes use of experimental animals to prove his thesis, and is fortunate in choosing the rabbit which ovulates shortly after coitus, and has a large blastocyst. He adopts the method which was first described in the Hippocratic collection for the study of the chick embryo, and examines the rabbit genital tract at timed intervals following observed mating. He examines the ovaries, the fallopian tubes and the uterus at six hours, twenty-four hours, twenty-seven hours, forty-eight hours, fifty-two hours, seventy-two hours and then daily up to twenty-nine days. His observations and the conclusions he draws from them establishes finally that the ovum originates in the ovary, passes down the tubes and then develops in the uterus.

He notes that the central cavity of the follicle is empty, and concludes that the egg has escaped. He searches the fallopian tubes and finds the blastocyst at seventy-two hours after mating, describing it as a minute ovum. He also records a correllation between the number of ruptured follicles in the ovary and the number of ova found in the fallopian tube on the same side. He notes that the wall of the ruptured follicle becomes thick and glandular, thus describing for the first time the organ later called the *corpus luteum*. His only error was the assumption that the whole follicle was the ovum, although he noted that the ovum in the tube (the blastocyst) was only one-tenth the size of the follicle in the ovary but was unable to account for this apparent reduction in size. In finding the early ovum on the third day, he succeeds where Harvey, conducting similar experiments in deer only a few years earlier, failed completely.

On the title page of de Graaf's book one of the putti is seen inspecting an ovary with a magnifying glass. This picture raises an intruiging speculation. On 28 April 1673, shortly before his death, de Graaf transmitted Leeuwenhoek's first letter to the Royal Society. Had de Graaf lived, his friendship with Leeuwenhoek might well



332 REGNERUS DE GRAAF

TABULA VIGESIMA-SEXTA

Varias Ovorum figuras complectens.

Fig. 1. *Exhibet Ova prout tertio à coitu die in cuniculorum utero reperiuntur.*

2 *Cuniculorum Ova quarta à coitu diei.*

3 *Cuniculorum Ova quinta diei.*

4 *Cuniculorum Ova sexta diei.*

5 *Cuniculorum Ova septima diei.*

6 *Cuniculorum Ova octava diei in utero cellulas efformantia.*

A. *Cellula uterina Ovum complectens.*

B. *Cellula aperta, in cujus Ovo præter liquorem nihil conspicitur.*

7 *Cuniculorum Ova nona diei.*

A. *Cellula uterina.*

B. *Cellula aperta, in cujus Ovo exilis nubecula comparet.*

8 *Cuniculorum Ova decima diei.*

A. *Cellula vasculo sanguineo referta.*

B. *Cellula adaperta, in cujus Ovo Embryo ut informis galba conspicitur.*

9 *Cuniculorum Ova duodecima diei.*

A. *Cellula.*

B. *Cellula aperta, in cujus Ovo Embryonis delineamenta apparent.*

10 *Cuniculorum Ova decima-quarta diei.*

A. *Cellula.*

B. *Embryo cum placentâ & vasis umbilicalibus.*

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Tab. XXVI

Figure 1

Table 26 from de Graaf's *De Mulierum Organis*, 1672, showing rabbit ova [blastocysts] at successive stages of pregnancy. No. 1 to No. 5 are ova found from the 3rd to the 7th day after witnessed mating. No. 6 to 10 show the developing rabbit embryo in-utero after implantation.

Figure 2

The title-page from de Graaf's *De Mulierum Organis*, 1672. It is of particular interest in that one of the putti is seen examining an ovary with a magnifying instrument.

have led to joint work on the microscopy of the follicle and perhaps even to the discovery of the ovum itself. As it was, the discoverer of the male germ cell lived on to denigrate the ideas put forward by de Graaf.

De Graaf's book is clearly of major importance in the history of generation. The success of his work depended on the use of the experimental method of Harvey rather than the descriptive method of Vesalius. In a recent essay Sir Peter Medawar has pointed out that modern scientific discovery depends on the hypothetico-deductive approach rather than on inductive processes. This is the method of de Graaf, and for this reason the book has a remarkably modern outlook. It is therefore a great pity that it is still not fully translated. The publishers are to be congratulated on this limited facsimile edition, but the work, as one of the classics of medical history, should now be freely available in an English translation including reproductions of the wonderful plates, for the benefit of all students of biology and medicine. The availability of such sources would do much to revive an interest in medical history today.

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J. G. BEARN.