

**FROM OVULATION
TO IMPLANTATION**

FROM OVULATION TO IMPLANTATION

Proceedings of the VIIth Reinier de Graaf Symposium,
Maastricht, the Netherlands, 30 May-2 June 1990

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VIIth REINIER DE GRAAF SYMPOSIUM
FROM OVULATION TO IMPLANTATION

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THE REINIER DE GRAAF SYMPOSIA

I	1973	Noordwijkerhout	The contributions of Reinier de Graaf to reproductive biology
II	1975	Amsterdam	Corpus luteum function
III	1978	Maastricht	Non-luteal ovarian function throughout life
IV	1981	Nijmegen	Follicular maturation and ovulation
V	1984	Nijmegen	Gamete quality and fertility regulation
VI	1987	Nijmegen	Neuro-endocrinology of reproduction
VII	1990	Maastricht	From ovulation to implantation

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PREFACE

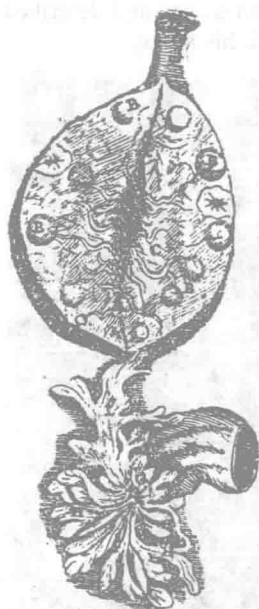
Reinier de Graaf (1641–1673) was one of a group of young Dutch physicians and anatomists who provided evidence that the '*female testis*', appropriately named *ovarium* by Fabricius, is a pivotal organ for reproductive function in the female. In his '*De mulierum organis generationi inservientibus tractatus novus*' Reinier de Graaf indicated that this organ is indeed an ovary, and described for the first time the follicles which are now associated with his name.



Fig. 1: Reinier de Graaf dissecting a corpse in his study (detail of a drawing by J. Verkolje; Museum Boymans-van Beuningen, Rotterdam, with permission).

However, de Graaf contributed more to our knowledge than the Graafian follicle. In his '*De virorum organis generationi inservientibus*' he drew attention to the functional anatomy of the male reproductive organs.

In one of the less known sections of his work he described the discovery of a tubal ovum, and advanced evidence that embryonic development starts already in the Fallopian tube. Reinier de Graaf reported, in 1672, his studies of the contents of the rabbit oviduct at different intervals after copulation. He discovered no eggs in the oviducts of animals killed during the first two days following mating, but on the third day he found little spheres, which appeared to have migrated to the uterine cavity on the subsequent day. When he died at the age of only 32 years at Delft, Reinier de Graaf had shown his genius by contributing important observations on the role of the ovary and the testis in reproduction, on the ovum and its transport through the Fallopian tube to the uterus, and on that glandular substance in the ovary which he named '*corpus luteum*'.



TABULA DECIMA-SEXTA

EXHIBET TESTICULUM SEU OVARII MULIERIS CUM ANNEXO
TUBARUM EXTREMO.

Fig. 2: Female internal genital organs as depicted by de Graaf in his '*De mulierum
organis generationi inservientibus tractatus novus*'.

To commemorate de Graaf, the *Reinier de Graaf symposia* have been organized in the Netherlands since 1973. Over the years, they have grown to become a forum for the mutual exchange of knowledge between clinicians and scientists in the rapidly expanding practice of clinical reproductive medicine and biology. After Noordwijkerhout (1973), Amsterdam (1975), Maastricht (1978), Nijmegen (1981, 1984,

and 1987) the 7th Reinier de Graaf symposium focused on the theme '*From ovulation to implantation*', for the second time in Maastricht, from May 30 till June 2, 1990.

Topics discussed were: the mechanism of ovulation, fertilization, gamete and embryo transport and development in the Fallopian tube and in the peritoneal environment, corpus luteum function and implantation.

This book offers an account of the state of the art lectures presented by leading authorities of international acclaim at this symposium and of selected free communications and poster presentations. It puts on record the most recent developments in this fascinating field of reproductive research that was inspired by Reinier de Graaf, now more than 300 years ago.

We have to thank so many people for their help. Our colleagues in the local organizing committee, Peter Bouckaert, Gerard Dunselman and Jolande Land made it into a sheer pleasure to organize this symposium. We thank the authors for delivering their contributions so promptly as to make the rapid publication of this volume possible. We are indebted to Liesbeth Eichelsheim for her organizational skills and her excellent managing assistance, and to Nicolle Sangers-Jeurissen and Ria Huppertz for their secretarial help. The organization of this 7th Reinier de Graaf symposium has been made possible by an educational grant from Wyeth laboratories.

Maastricht, August 1990

J.L.H. Evers

M.J. Heineman

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THE 'REINIER DE GRAAF LECTURE'

THE SELECTION OF THE FOLLICLE OF THE MONTH

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INTRODUCTION

In all mammals a very small minority of the oocytes formed during fetal life are eventually ovulated¹. The mechanism by which these lucky few survive the winnowing process of atresia is still unknown although it is clearly essential that in each species the number of eggs ovulated match the number of offspring which can be supported throughout pregnancy and infancy. Thus in primates a single offspring has a much better chance of surviving and there are evolutionary selection pressures to favour the emergence of a single ovulatory follicle. In many domestic animals, eg. sheep, man has selected strains with high ovulation rates for commercial purposes and it is possible within the same species to study animals with ovulation rates ranging from one to six^{2,3,4}. In rodents on the other hand, there are advantages to producing larger litters and, hence, mice and rats have evolved a mechanism by which up to 12 preovulatory follicles develop.

In this paper I will consider this mechanism of selection of the preovulatory follicle(s) in primates including man and sheep. While the monovulatory status of primates and sheep makes them good models for man, much of our fundamental knowledge about the dynamics of oogenesis and particularly the mechanism of cellular differentiation of the follicle arise from rodent models^{5,6,7}. The growth and differentiation of the follicle is designed to ensure that a mature healthy oocyte capable of being fertilized is ovulated at the appropriate time. Throughout folliculogenesis important maturational changes occur in the oocyte which ensure that by the time of ovulation the egg is capable of being fertilized. The somatic cells of the follicle (granulosa and theca) play an essential role in this maturation but this process is outside the scope of this present review.

Two main hypotheses have been developed to explain the process of follicle selection^{8,9}. One theory supposes that waves or cohorts of follicles leave the pool of primordial follicles and that the follicle which will ovulate has already been predetermined during the process oogenesis. The second hypothesis assumes that recruitment from the pool of primordial follicles