UNIVERSITY OF PORT HARCOURT

A TRIBUTE TO THE

CORPUS LUTEUM

AN EPHEMERAL ORGAN OF MAMMALIAN REPRODUCTION

An Inaugural Lecture

By

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DEDICATION

To my dad, who passed on as this lecture was being written.

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I most sincerely thank my parents for their foresight to send me to school and the selfless sacrifice they made during those, sometimes, difficult early years. This was the best gift they ever gave me.

I gratefully acknowledge the encouragement and excellent teaching I received from Mrs Thelma Brian in my formative years in Government Secondary School, Kuru, a woman who made learning such a delight. Of all my teachers, she sticks to my memory and I've not met a teacher like her since I left G.S.S. Kuru. Prof. Duro J. Adegboye, then of Ahmadu Bello University, Zaria, was both an inspiration, a teacher, and a friend and was a key person who sharpened my love for academia and my quest for the unknown. I sincerely thank him for all he did.

I am most grateful to Dr B. D. Murphy formerly of the University of Saskatchewan, a brilliant scholar whose work attracted me to Canada for graduate studies. In those years I worked in his lab, I learned from him how stimulating research can be. Two wonderful compatriots, Joe Mudiare and B. Ezenwa provided the much needed emotional and friendly support during those challenging years in the Prairie. Thanks, Joseph and Bertram. I also thank my "Canadian brothers" Darian Reed, Norman (Norm) Loendorff, Claude Daust and Tim Huntley who made me felt at home in their country. Unfortunately I seem to have lost them in this rather complex digital world!

My boundless gratitude goes to Dr. Mary M. Buhr, then of the University of Manitoba, who, not only made my dream of a doctorate degree come through, but provided selfless support when all appeared hopeless. I could never thank you enough, Mary.

I wish to thank all members of my Department of Animal and Environmental Biology, University of Port Harcourt, especially my

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I take nothing for granted so, to anyone whose name is not here, but who has at any time shared with me moments of joy, of honour, or triumph over human challenges, or moments of disappointment and reflection, I say many thanks, because you made a difference!

Finally I thank my lovely wife, Elizabeth for her support and my children Jennifer and Jessica for the joy they *always* bring regardless of what the world outside looks like.

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INTRODUCTION

My inaugural lecture this afternoon is in the area of Reproductive Physiology. Physiology is a branch of the biological sciences dealing with the function of organisms (Advance English Dictionary) so when applied to reproduction in mammals, it is the study of the mechanism, factors controlling, and the application of human technology in the reproduction of mammals, both domestic and wild. My lecture is on one of the most important but perhaps underestimated female organ of reproduction: the corpus luteum (CL). I first encountered the CL in the lab of the eminent scholar Dr. Bruce D. Murphy, a physiology professor at the University of Saskatchewan, and I am proud to say, even today, that my first mature work as a scientist was in the area of the CL. So, today I am paying a little tribute to an old "friend", the corpus luteum.

The name "corpus luteum" which literally mean "yellow body" (pl. *corpora lutea*) was introduced by Marcello Malpighi (1628-1694) in 1681 (cited by Tomac, et al., 2011) which was described in illustrated detail by Reinier De Graaf (1641-1673). De Graaf observed correctly, that the number of corpora lutea corresponded to the number of offspring an animal produced (cited by Tomac, et al., 2011; Niswender, et al 2000). Prenant later studied the histology of the CL and concluded that it was a gland that produce some "internal secretion" that regulate pregnancy. Although this was true, it wasn't until 1901 that the true biological function of the CL was elucidated when workers confirmed the role of the CL in pregnancy in the rabbit. It was observed that removal of the ovaries or all corpora lutea from pregnant rabbits "resulted in abortion or resorption of the embryos" (Tomac, et al, 2011). Other studies that further supported the role of the CL in pregnancy soon followed: Some of these were (1) treating rabbits whose ovaries have been removed (ovariectomized) with corpora lutea extract, (2) crystallizing and characterizing the active factor in the CL which was named progesterone (review: Niswender, et al. 2000), which literally means a substance that "favours pregnancy".

The CL is a temporary organ in all mammals and in size it is relatively small compared to other reproductive structures in the female mammal. But the knowledge that its function underlies every successful pregnancy in placental mammals and that its application is one of man's agricultural innovations makes it a fascinating organ indeed. What I have presented here is not a review of the scientific work that has been done on this organ, but an introduction of the organ to this audience, and the scientific benefits we can derive from the knowledge of its function.

A Brief History of the Science of Reproduction

One of the characteristic features separating living from non-living matter is that given the right conditions, living organisms can reproduce their own kind. This is an attribute given to them by God at the beginning of time when He created Adam, then added Eve. After creating all the creatures on land and the seas, in Genesis 1:22 He

"blessed them and said be fruitful and increase in number. . ."

We are also told in Gen. 7: 2-3 that when enraged by human wickedness, God decided to wipe off all living things from the face of the earth but to give the man opportunity to start over again, He instructed Noah to put in an ark

"seven pairs of every clean animal, a male and its mate, and a pair of every kind of unclean animal, a male and its mate, and also seven pairs of every kind of bird, male and female, to keep their various kinds alive throughout the earth." (Web Bible, Noteless)

The implication of this injunction is clear to us: that the perpetuation of the species requires a male and a female. A search through the Bible will show similar references to procreation in other areas.

Vice-Chancellor Sir, from these Biblical passages, it is clear that reproduction is one of God's most important gift to living things.

Therefore its study is not only an academic exercise, but a service to God. The lecture topic today: "A Tribute to the Corpus Luteum, an ephemeral organ of reproduction in mammal" will highlight an aspect of this extraordinary attribute of living things, as it applies to mammals.

Why we need to study reproduction in mammals:

- *Animal reproduction is at the heart of animal husbandry* and its application is one of the major factors controlling the availability of animal proteins in the form of milk, meat, and eggs. The management of both domestic and wild animals by man has enabled him, from ancient times, to be able to provide food in times of scarcity. In addition, understanding animal reproduction prepares the ground for the application of reproductive technology such as artificial insemination, embryo transfer, in vitro fertilization and many others that have made the West self-sufficient in animal proteins.
- *For genetic improvement of animals:* The ability to alter natural reproductive processes in animals through management and human technology has enabled man to improve many aspects of animal reproduction such as the production of lean meat (meat containing less fat) and higher milk production.
- *Enables the preservation of the species.* The strongest impulse in any living organism is self-preservation and reproduction is nature's second strongest impulse. Careful application of reproductive technology helps man to preserve the species and prevent their extinction. (Bearden and Fuquay, 1984).

The term "reproduction" was not in use until 1749 when it was introduced by Buffon (Cobb, 2012; Roger, 1997). Prior to this time, "generation" was used in place of "reproduction" when referring to issues of procreation and production of new offspring (Cole, 1930, cited in Cobb (2012). The whole subject of reproduction itself, whether in humans or animals, has fascinated man since the beginning of civilization. Man wondered how a tiny mammalian egg, barely visible to the naked eye, could give rise to a complete

animal of millions of cells. This fascination gave birth to several theories and opinions on the formation of a living being dating back to the time of Aristotle. Revered today as the father of Biology by many, believed that the factor responsible for the formation of the new animal was in the blood (Gosden, 2013). He divided animals into two kinds: the "bloodless" which included the insects and similar groups that "generated spontaneously", and the others for which mating was necessary (Cobb, 2012, Gosden, 2013). According to him, the female provided the substance that gave rise to the embryo or offspring while the male gave it form (Cobb, 2012), identity or individuality. The male contributes the seminal fluid formed in the seminal ducts (not the testes) whereas the uterus in female mammal or the oviduct (reptiles, birds and fishes) contributes the substance that forms the embryo and that this material is the menstrual blood (Gosden, 2013). By then, of course, the spermatozoa had not yet been discovered so the process of fertilization was virtually unknown. In the absence of a more convincing opinion, Aristotle's view gained wide acceptance across Europe and across religious divides.

William Harvey (1578-1657) in 1651 published a book "On the Generation of Animals" in which he wrote that the "egg" was important to *generation*, a crucial point that, unfortunately lacked experimental proof at that time (Cobb, 2012). His effort to support his conviction with experimental data failed when he could not show eggs in the female "testicles" (the female ovaries) in his dissections of the red deer (Cobb, 2012). This forced him to change his view about the involvement of the egg and suggested that a new life was made in the uterus but in a way that did not involve the female "testicles", a view that more or less supported the Aristotelian view which then persisted. The issue of the involvement of the egg in animal production was finally settled with the work of Swammerdam in 1669 with his observation that insects were not spontaneously generated as Aristotle had thought, but that they came from eggs (Cobb, 2012).Even after the germ cells (the sperm and egg) were discovered with the invention of the microscope in the

17th century, the significance of the germ cells was not immediately known.

In 1672 Regnier de Graaf (who earlier discovered the pancreatic juice) published a book titled "*de mulierum organis generattioni inservientibus tractatus novus*" "New treatise concerning the generative organs of women" (Gosden, 2013, Cobb, 2012) in which he explained that what was referred to as "female testis" by his predecessor van Horne and others, was, in fact, an ovary and from his account of the ovarian follicle, the large, antral follicle was named the Graafian follicle after him. Credited today as one of the founders of the mammalian reproduction, he thought that the corpus luteum developed from the follicular wall before the follicle ruptured.

A few years later van Leeuwenhoek with the aid of the light microscope (1677) discovered the male germ cell, the spermatozoon, and in 1683 published an article rejecting de Graaf's discovery, denying the existence of the ovum. According to him, the spermatozoon was the sole contributor to the offspring; it was *the* spermatozoon and not the ovum, that contributed to the formation of the new organism, an essentially Aristotelian concept. Two opposing views then emerged with those who held de Graf's view referred to as the "ovulists" or "ovists" while those that favoured van Leeuwenhoek's view were called the "spermists".

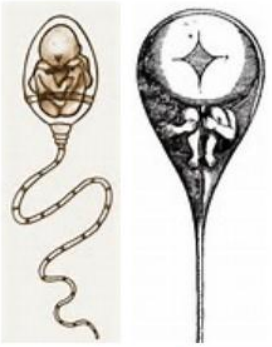


Fig. 1. A preformed man, a homunculus, in the head of a spermatozoan. (www.bing.com/images)

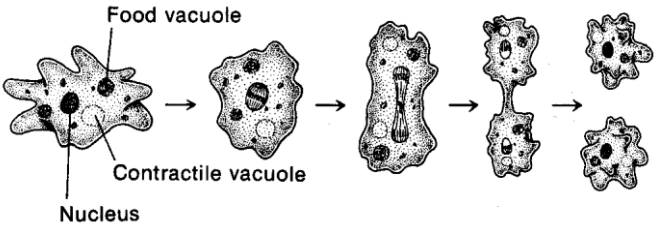
This popular and widely-held view in the 18th century espoused the theory of *preformation*in which the adult animal already existed in a miniature form with complete features such as arms and legs, folded in a squatting position in either the head of the sperm or in the egg of the female, depending on which side you were on. This miniature form of a human being was called a "homunculus" whereas the animal form was an "animalcule" One of the spermists, Nichola as Hartsoeker in 1695 was said to have published an illustration of a completely formed, miniature man, a "homunculus" in a squatting position at the head of the spermatozoa (fig. 1), which he claimed to have observed in a seminal fluid (Neill, 2006). This drawing that became iconic of the spermist view, can be found in many zoology books and on the internet today. Both groups believed that the body of the female only help to nurture the animal into a fetus. Other views were also held until 1759 when the German embryologist Kaspar F. Wolff, studying the chick embryo, showed that there was no preformed chick in the egg.

While we smile at these developments because the facts appear very obvious today, we should also remember the conditions these scientists worked in at that time and the sleepless nights they must have endured in search for the truth.

In the following section, I will highlight the main aspects of reproduction in the female mammal that will prepare the ground for our discussion of the central role the corpus luteum plays in reproduction and the perpetuation of the species.

Modes of Reproduction

Animal reproduction is a complex and sometimes bewildering phenomenon. In its simplest form reproduction occurs by a simple division in which the organism divides into two (Villee, et. al. 1978.)



Binary fission in Amoeba (Villee, et. al. 1978)

producing two individuals that are alike, both genetically and morphologically (fig. 2). This type of reproduction, typified by Amoeba, is called **asexual** because it does not involve the union of gametes from two parents. Asexual reproduction could also take other forms, such as budding, in which a new individual grows on the body of the parent (Agu, 2005) as in hydra, (fig. 3),

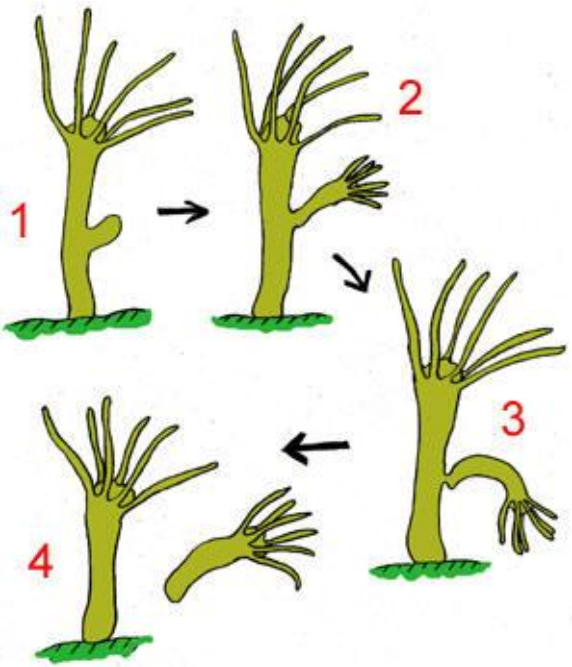


Fig. 3. Budding in Hydra (www.bing.com/images)

fragmentation, in which a piece of the parent breaks off and grows into a new organism as in corals, and, spore formation (Agu, 2005.). Some flatworms reproduce asexually by regeneration in which the worm divides into two leaving one piece headless and the other tailess and each piece then grows the missing parts-the tail or the head.

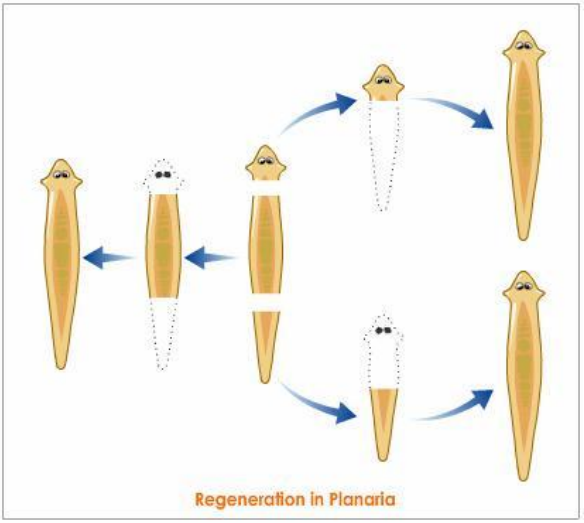


Fig. 4. Regeneration in flatworm. (www.bing.com/images)

In parthenogenesis, offsprings are formed from unfertilized eggs, a method of reproduction favoured by the plant-sucking insect, the Aphid (Agu, 2005).

Asexual reproduction is mostly limited to lower organisms, the type without backbones called invertebrates, and does not occur naturally in mammals, although some consider identical twinning as a type of asexual reproduction since it involves, in some cases, binary fission of blastomeres (Hickman, et. al. 2001).

Fig. 5: Aphid reproducing asexually (www. en.wikipedia.com/)

One of the functions of reproduction is to pass on superior genes to the offspring so that it can easily adapt to new, and perhaps more challenging environment. Therefore a major disadvantage of asexual reproduction as indicated above, is that the offspring is genetically identical to the parent. This lack of genetic variability implies that the offspring cannot adapt to new environments that require new genes for survival and therefore, cannot evolve.

In contrast with asexual reproduction, sexual reproduction involves two parents, each contributing a specialized reproductive cell, a gamete, which fuse to form the zygote. The egg is typically large, with or without a store of nutrient in form of a yolk to support the developing embryo. The male gamete is typically smaller than that of the female and motile, adapted to swimming actively to the female gamete, the ovum. Sexual reproduction may take one of three forms (Sherwood, et. al. 2013):

- Oviparity: (egg-bearing). The young develops in and hatch from eggs released from the body of the mother most non-vertebrates, fishes, and reptiles, and birds reproduce this way.

- Ovoviviparity: The young ones are produced from eggs (that may not have shells) and use yolk to develop partly or fully within the body of the mother. The young may also hatch inside the mother to emerge live.
- Viviparity: The production of live young that develops using maternal blood nutrients through an organ, the placenta.

To ensure maximum chance of offspring survival reproduction in viviparous mammals require a complex and highly regulated system that requires fine-tuning at various critical periods. This complexity of factors isn't quite as advantageous as it may seem because it can reduce the chances of offspring survival.

Fig. 6: Starfishes reproduce asexually by fragmentation and regeneration (www.bing.com/images)

The form of reproduction in higher animals such as mammals, that is the focus this lecture, is called **sexua**l reproduction which requires the contribution of gametes from both parents, the male and the female. The two sexes have a genetic composition that makes them either male or female: the female has XX sex chromosomes while

the male has XY (Saladin, 2009). From experimental data available, it is now clear that the genes that determines whether or not a testis is produced in the fetus depends on the regulatory gene on a portion of the Y chromosome (Neill, 2006).

To fully appreciate the structure and function of the corpus luteum, it is necessary to familiarize ourselves with the mammalian female reproductive system from which the CL arises and acts. A brief discussion of the reproductive system of the female mammal is therefore, presented below.

THE MAMMALIAN FEMALE REPRODUCTIVE SYSTEM

The reproductive structure of the female comprises of the ovary, the uteri (sing. *uterus)*, cervix, and vagina. The uteri are usually two: a left and a right one, but may fuse to give various shapes (Bearden and Fuquay 1985) as discussed further below.

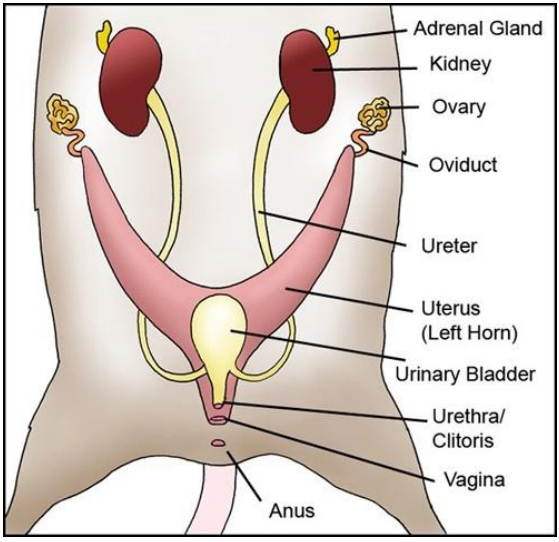


Fig. 7. Reproductive structures of the female rat. (www.bing.com/images)

The paired **ovaries** are the primary reproductive organs of the female because they produce the female gamete, the ovum (pl. *ova*) or egg and the female hormones estrogen and at specific times, progesterone. (Bearden and Fuquay, 1984, Mescher, 2010). At birth the ovaries contain variable number of tiny capsules called primary follicles, each about the size of the head of a pin. Structurally, a primary folliculeis a germ cell with a single layer of follicular or granulosa cells. With each estrous cycle the number in this pool of follicules diminish as they grow, mature, and ovulate. For example, an old cow may have just 2500 follicles left out of a starting number of about 75,000 (Bearden and Fuquay, 1984).As follicles grow, the granulosa cells around the potential ovum increases in number so that a secondary follicle has two or more layers of granulosa cells. As growth continues, a cavity or antrum forms also in the middle of the follicle so that it is now referred to as an antral follicle.

The follicle contains the potential ovum and for an animal that produces one offspring in each pregnancy such as the sheep, and the cow (monotocous animals), one dorminan to vum is produced at each ovulatory cycle. Others such as the rat and mouse, and indeed most rodents (polytocous animals), produce several ova in each estrous cycle and therefore several young ones are produced at a time.

The **oviduct** (also called the *fallopian tube*) are a pair of convoluted tubes that delivers the egg from the ovary to the uterus. They open near the ovary at one end and are continuous with the uterus at the other. The oviducts are the site of fertilization and initial divisions of the embryo prior to its implantation in the uterus.

The next segment is the **uterus**: the site for implantation and growth of the embryo until birth, as earlier noted. Its shape varies from one mammal to another as stated above, but the basic structure is the same in all of them. They all have a body, a cervix demarcating it from the vagina, and usually two horns. In general, mammals such as rodents and pigs that give birth to many young at a time have longer uterine horns and a shorter uterine body than those (such as

the sheep, cattle and goats) that usually produce fewer offsprings or twins.(fig.6). When completely separate, each horn of the uterus has its own cervix, forming a *duplex* uterus (Bearden and Fuquay, 1984) as in rodents and rabbits and other small mammals. When the lower portions

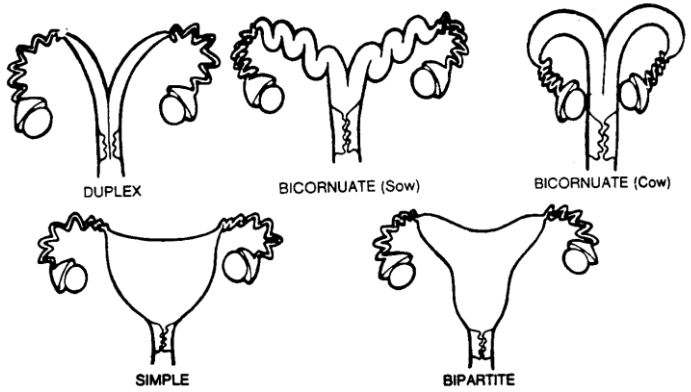


Fig. 8. Shapes of mammalian uteri. (Bearden and Fuquay, 1984)

are fused and both uteri have a single cervix, the condition is a *bipartite* uterus found in the mare (the female horse) and characterized by a prominent uterine body anterior to the cervix. In a *bicornuate*uterus, found in the pig, cow, goat and sheep, the lower two-thirds of the uteri are fused whereas the remaining portions remain separate. It is characterized by two long horns and a small uterine body anterior to the cervix and implantation occurs in the lower fused portion. In the fourth type referred to as a *simple* uterus, found in primates such as monkey and man, the uteri are fused into a single structure with no uterine horns. Implantation occurs in the fused part, (Bearden and Fuquay, 1984) commonly called the *womb*.

The **cervix** in all cases, is the narrow posterior end of the uterus that prevents the entrance of foreign agents and micro-organisms into the

uterus. To maintain pregnancy the cervix must remain tightly closed and can only open at term when the young is to be born.

The **vagina** is the channel between the cervix and the vulva. It conveys the semen into the uterus and expands to allow the birth of the fetus. The common opening for the vagina and the urinary system is the external opening of the female reproductive system is called the **vulva.**

Now that we are familiar with the female reproductive system, we will now discuss how the corpus luteum arises from this system, and why this ephemeral organ is unique.

A "Hormonal Orchestra" heralds the Corpus Luteum

The preparation for the birth of the CL is initiated by cyclic and predictable changes brought about by varying levels of *hormones* in the body of the animal. Hormones may be regarded as chemical messengers within the body, produced by specific glands called *endocrine glands*, into the blood stream and carried to their target organs where they exert physiological effects. The hormones regulating the reproductive processes that lead to the formation of the corpus luteum originate from the brain, the pituitary gland and the gonads. The stimulus that prompts the reproductive endocrine system to begin secretion of reproductive hormones comes from the hypothalamic region of the brain (Fox, 2011). This command centre produces the Gonadotrop in-releasing hormone (GnRH) that "instructs" the anterior part of the pituitary gland to produce hormones that affect the functioning of the ovaries. The reproductive hormones produced by the pituitary gland are collectively called **gonadotropins** or gonadotropic hormones because their target organs are the gonads. The two gonadotropins are: *luteinizing hormone* (LH), *follicle-stimulating hormone*, (FSH) and a third hormone not usually a gonadotropin but also reproductively active called *Prolactin*. Other reproductive hormones originate from the placenta at various stages of the reproductive cycle as well (Fox, 2011) depending on the species. The

gonadotropins LH and FSH have specific functions in reproduction and the functional life of the corpus luteum.

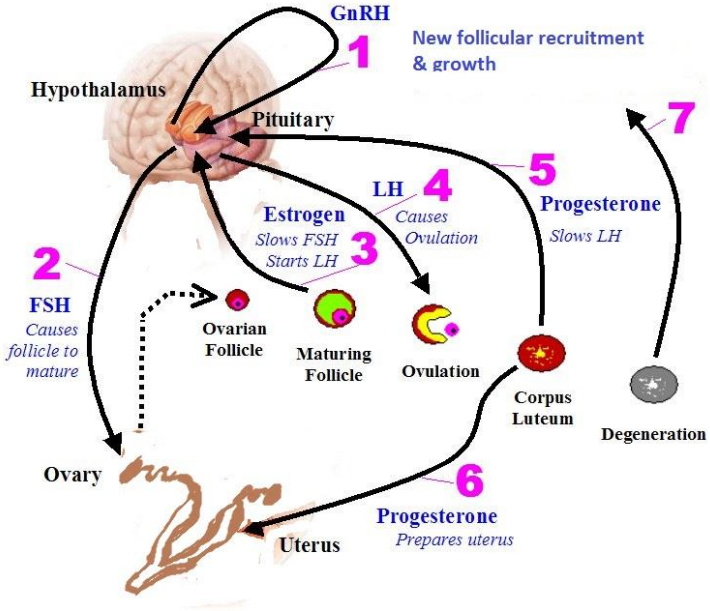


Fig. 9: The reproductive hormones and their functions. (Modified from www.fertilityinstructor.com/hormones)

Follicle stimulating hormone in the female induces the development and growth of the follicles from the primary to the ovulatory stage, leading to the formation of the corpus luteum. **Luteinising hormone** in the female induces ovulation of large antral follicles, the primary signal for the formation of the corpus luteum (www. Fertilityinstructor.com/hormones; review: Murphy, 2000).The levels of the hormones are finely regulated by a feedback system in which a hormone modulates the level of the one that induces its secretion. This phenomenon is part of what makes reproduction a unique and bewildering physiological phenomenon. The changing hormonal levels makes reproductive events a cyclic

phenomenon called the estrous cycle when the CL is produced.

The Estrous Cycle

Most mature sub-human mammalian females, are not ready to mate with the males at all times. There are periods when they are receptive to the male and periods that they are not, the two periods alternating with each other. The time a female will accept a male for mating is called the **estrus** or heat period, beginning from when the female attains puberty or sexual maturity, and occurring periodically thereafter throughout the reproductive life of the animal, accompanied by noticeable changes in the female. The visible signs of estrus depends on the species of mammal in question so no generalizations can be made here but these changes, which may be observed by an expert, include changes in posture, frequent urination, restlessness, and a desire to associate with the male. The period of non-receptivity on the other hand, is called the **anoestrus** period.

Table 1: Average reproductive cycles of some domestic animals.

S/No	Animal	Estrous cycle length	Length of estrus *	Ovulation	Length of pregnancy
1.	Cow	21 days (polyestrus)	18 hrs	11 hrs after end of estrus	280-282
2	Sheep	17 days, (seasonal)	29 hrs	Near end of estrus	148 days
3.	Pig	21 days (polyestrus)	48-72 hrs	35-45 hrs after start of estrus	115 days
4.	Mare	21 days (Seasonal, polyestrus)	4-8 day	3-6 days after estrus	335 days
5.	Bitch	6 months	9 days	4-24 days after start of estrus	63 days
6.	Queen	17 days	9 days	Induced	63 days

*Within the estrous cycle, the female accepts the male only during estrus. (http://repository:uobabylon.edu.iq/2010_2011/3_31907_200.pdf)

Estrous cycles vary in length from one animal to another, each cycle divided into four phases namely *proestrus, estrus, metestrus*, and *diestrus* (Zenclussen, et. al. 2014) in those animals that do not experience menstruation. Distinct physiological changes accompany these stages which may be summarized as follows:
During **proestrus**, one or several follicles, depending on the species, start to grow. The growing follicle or follicles secretes the hormone estrogen which initiates the development of the uterine wall called **endometrium.** The duration of this phase depends on the species but it is generally shorter in smaller species than larger ones (Table 2). **Estrus** is the period of sexual receptivity when the female would allow mating with a male. In many species the female shows visible signs of receptivity to the male at this time, the duration again varies from one animal to another but it is generally shorter for small mammals than larger ones. Ovulation occurs during the estrus period as indicated in Tables 1 and 2.

The time it takes the growing follicles to reach ovulatory stage vary from one animal to another but, invariably, the goal of the process is the same: ovulation and the release of the ovum. The ripe follicle first migrates to the outer wall of the ovary where the follicular wall thins out such that the pressure from the follicle causes a noticeable bulge of the ovarian wall (White and Porterfield, 2013). Ovulation occurs at this time, either spontaneously or after coitus in induced ovulators,

In the laboratory mouse and rat, a microscope-slide preparation of the vaginal wall at this time shows flat, squamous, non-nucleated cells (fig 4). **Metestrus**, the third phase of the estrous cycle

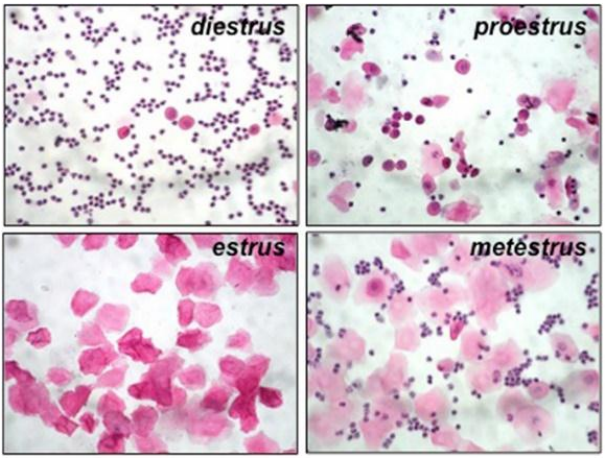


Fig. 10: Hematoxylin-eosin stain of vaginal lavage at each stage of the estrous cycle of the mouse. *Diestrus*: only leukocytes with a few nucleated epithelial cells; *Proestrus*: mostly nucleated and a few cornified cells with some leukocytes; *Estrus*: only cornified epithelial cells present. *Metestrus:* Cornified cells with some leukocytes. (Zenclussen, et al, 2014)

shows a brief corpus haemorrhagicum, the newly formed CL with blood in its cavity, caused by the trauma of ovulation. It transforms quickly into a fully formed CL that secretes progesterone whose main function is to maintain pregnancy as further elaborated below. If pregnancy does not occur, the CL regresses, progesterone production ceases and the uterus returns to a resting condition called **diestrus.**

Table 2. Duration of estrus in some domestic animals.

	Cow	Sheep	Pig	Horse
Estrous cycle (days)	21	17	21	21
Proestrus (days)	3-4	2-3	3-4	2-3
Estrus (hrs)	12-18	24-36	48-72	4-8
Metestrus (days)	3-4	2-3	2-3	2-3
Diestrus (days)	10-14	10-12	11-13	10-12

http://repository:uobabylon.edu.iq/2010_2011/3_31907_200.pdf

Prior to ovulation, estradiol is the main steroid hormone produced by the ovary, secreted by the granulosa and theca cells. The **theca interna** cells possess enzymes that can convert cholesterol to androgens but not the enzymes to convert androgen to estradiol. (review: Niswender, et al. 2000). The granulosa cells then convert the androgen to estradiol. Following the preovulatory surge of LHthe signal for luteinisation, the granulosa and theca cells acquire enzymes enabling them to synthesize progesterone, and enzymes that allows the conversion of cholesterol to progesterone. (review: Niswender, et al. 2000). Whereas the newly luteinized cells of domestic mammals are mixed, those of primates remain separated, with the theca-lutein cells at the periphery of the granulosa-lutein cells in the middle of the CL (review: Murphy, 2000)

Ovulation, the birth of the Corpus Luteum.

We need to look at the structure of the tertiary follicle just before ovulation to appreciate the nature of the subsequent changes that forms the CL. As the follicle progresses towards ovulation, it grows in size because of the proliferation of granulosa cells surrounding the potential ovum, and the formation of a cavity full of fluid the *liquor folliculi* or follicular fluid (Fig. 9). This liquid also contains the estrogen produced by the granulosa cells and at this stage the follicle is called a tertiary or Graafian follicle (Frandson, et al. 2009), surrounded by two layers of

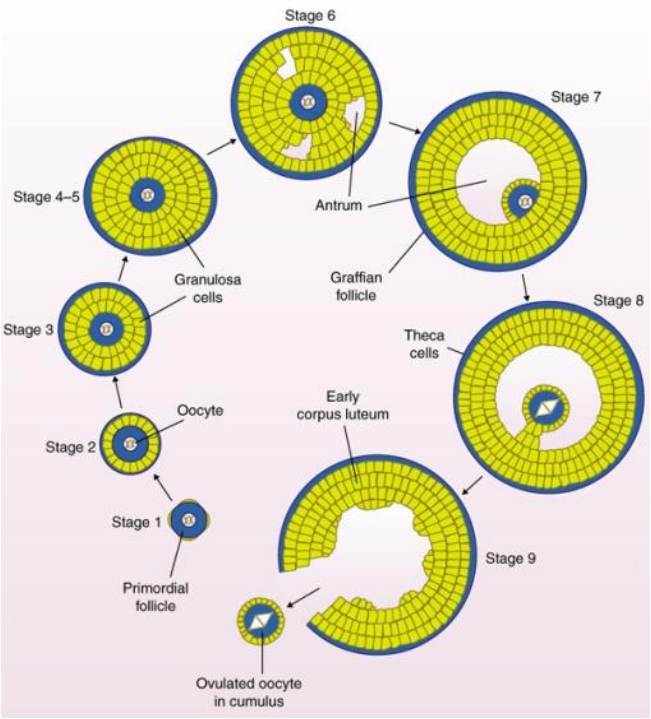


Fig. 11: Diagram of the stages in the development of mammalian follicles. (www.bing.com/images).

Cells: the outer theca external and the inner layer, the theca interna both of which are supplied with blood through capillaries. The two layers are separated from the granulosa layer by a basement membrane that prevents the invasion of the vascular system into the ovum compartment (review: Niswender, 2000; Irving-Rodgers, et al. 2006). The potential ovum rests on a mound of granulosa cells, the *cumulus oophorus* and surrounded by the **corona radiata**, the granulosa cell layer in immediate contact with the potential ovum. Both the theca interna and granulosa cells contribute to the estrogen in the *liquor folliculi*.

Ovulation is the release of a "ripe egg" or ovum from the ovary when a follicle breaks open. (fig. 11 and 12). This usually occurs towards the end of the estrus period (Table 2), expelling the follicular fluid, some granulosa cells, and the potential ovum into the body cavity close to the opening of the oviduct. Some of the corona cells still stick to the potential ovum but are eventually shed, either before or after fertilization, depending on the species (Bearden and Fuquay, 1984.). Following ovulation, the granulosa layer that surrounded the egg before it ovulated is thrown into folds in what was previously the antrum, and become converted into a hormone-producing gland, the **corpus luteum**. The basement membrane also degrades allowing other cell types to invade the new CL (Ogiwara, et al. 2005). The theca cells also become part of the new CL as the connective and vascular tissue around them proliferate while the granulosa cells also grow in size (review, Niswender, et. al. 2000) The main function ofthe hormone, progesterone, is to ensure that the pregnancy, if it occurs, is maintained (Bachelot and Pinart, 2005).

Among the domestic mammals, sheep and goats typically ovulate 1 to 2 ova per heat period but may occasionally produce 3 and may be capable of being fertilized from 10 to 25 hours. The number of offspring produced by a mammal usually indicates how many eggs ovulated during that heat period. Once released, the egg is collected by the funnel-shaped structure near the ovary, and taken into the fallopian tube where fertilization is expected to occur. If fertilization does not occur, this gland producing progesterone will die out, or, as they say, regress.

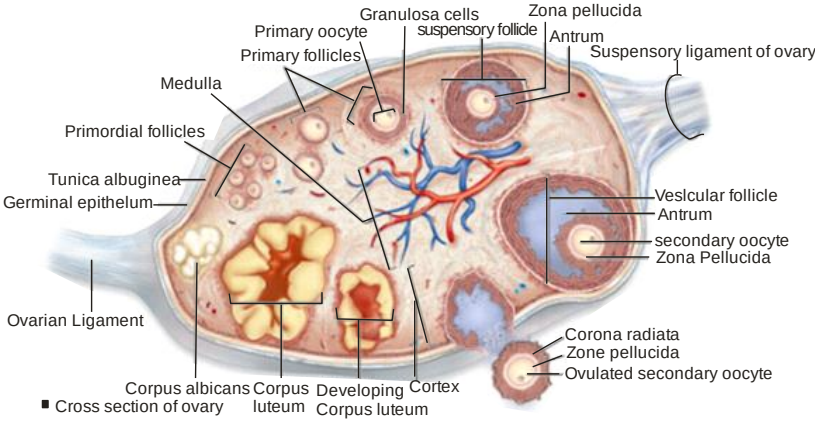


Fig. 12: Growth of mammalian follicles and the formation of the corpus luteum (Modified from Mescher, 2010)

Ovulation may occur in one of two ways: either spontaneously or by artificial means. When spontaneous, it requires no intervention beyond natural processes but when induced, especially in small mammals by cervical stimulation, it is referred to as induced ovulation. In the rat, hamster, the mouse and the guinea pig for example, the CL forms spontaneously after a spontaneous ovulation but the rabbit, ovulates in response to coitus or any such stimulation. A mouse, hamster, and the rat may also ovulate in response to a *sterile* coitus (that is, no male gamete is involved) in the form of cervical stimulation during estrus, followed by formation of a normal CL. But because there is no fertilization and therefore no implantation, the resulting pregnancy is referred to as pseudo pregnancy. literally meaning “false pregnancy” In the mouse and rat pseudo pregnancy lasts 13 days but in the hamster, it lasts 9 days (Hilliard, 1973).

Table 2. Pregnancy duration in some mammals

Animal	Pregnancy length (days)
Rat	21
Mouse	21
Guinea pig	68
Hamster	16
Cat	62
Ferret	42
Dog	62
Goat	151
Sheep	148
Cow	280
Pig	113

Modified from factophile.com (17/2/15)

The cell types in the CL

The CL of most mammals studied possess, among other cells "fibroblasts, endothelial cells, pericytes and components from the vascular system (Review, Niswender, et al, 2000) and two steroidogenic cell types, referred to as **small** and **large** cells, differing in morphological and functional characteristics (Agu, 1990). It is now known that the theca cells differentiate into the small cell type whereas the granulosa cells differentiate into the large cell type. Evidence supporting the two cell populations came from various experimental procedure such as differential density centrifugation (Lemon and Loir, 1977), antibody-binding experiments (Alila and Hansel, 1984) and biochemical, electron microscopic, and morphometric studies (Fields, et al. 1985). The large cell type (granulosa in origin) are more conspicuous but less numerous than the small cell population (Fitz et al, 1982; Agu and Buhr, 1989, 1990, 1998). Antibodies to granulosa cells bound the luteal large cell type whereas antibody to theca cells bound predominantly small luteal cells from bovine CL (Alila and Hansel, 1984) demonstrating the follicular origin of these CL cells. The sizes reported in the literature for both cell types vary but the small cell

type in the sheep are between 12 and 22µm while the large luteal cells are between 22µm and 50µm in diameter (Review, Niswender, et al., 1994).

How the CL synthesizes progesterone:
Cholesterol, much of which is produced in the liver (Krisans, 1996) and shipped to organs that need it through the blood stream in the form of lipoproteins (Niswender, et. al., 2000) is the substrate for the production of progesterone by the CL. (Agu and Buhr, 1989). The CL uses lipoproteins in the form of low density lipoprotein (LDL) and high density lipoprotein (HDL) (Rajkumar, et. al. 1987; Agu and Buhr, 1989) circulating in the blood. However, when lipid supply is inadequate due to inadequate synthesis of cholesterol, poor nutrition, or other factors, the CL is capable of synthesizing cholesterol *de novo* from acetate (Niswender, 2000; Cook and Nalbandov, 1968; Cook, et al. 1967)

Low density lipoprotein is taken in by receptor-mediated endocytosis (Fig. 11), (review: Niswender, et al, 2000). Once inside the cell, the LDL dissociates from the receptor, is broken down and the free cholesterol becomes available to the cell to make a number of cellproducts: it can be turned into cholesterol ester and stored until the cell needs it or used to produce new cell membrane, or progesterone (Niswender, et al., 2000). When progesterone is required, the cholesterol is converted first to pregnenolone then to progesterone (Fig. 11).

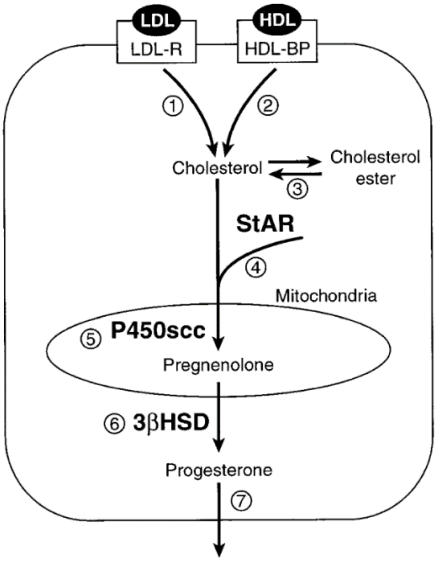


Fig. 13: Pathway for the synthesis of progesterone by luteal cells. (review: Niswender, et al., 2000)

The CL is important in the regulation of both the estrous and the menstrual cycle and the maintenance of pregnancy because it is the source of progesterone that is necessary for the maintenance of pregnancy in all eutherian mammals. It is reported, for example, that embryo mortality in cows is about 30% implying that about 30% of all fertilization is lost resulting in about $1.4 billion dollar loss annually to cattle producers in the United States (Ayalon, 1978). Lack of adequate progesterone, and by implication, luteal insufficiency has been cited as one of the factors responsible for the loss (Sreenan and Diskin, 1983.) The importance of this temporary ovarian structure, the corpus luteum, becomes apparent when we consider the functions of progesterone: Progesterone stimulates and maintains the endometrial functions for embryonic growth, implantation, placentation and development to term, as the following outline shows:

- It stimulates proliferation of decidua (cells of the wall of the uterus) for the purpose of implantation of the embryo. Impaired progesterone production leads to low fertility in mice (Labelle-Dumais, et. al. 2007) and embryonic loss in mammals because it is essential for endometrial growth and fetal survival (Kanghah and Kor, 2013).
- Progesterone blocks pulses of GnRH from the hypothalamus (Kasa-Vubu, et al. (1992) and reduces receptors for GnRH in the pituitary (Law, et al. 1990) thereby reducing the amount of LH produced due to GnRH stimulation (Janovic and Conn, 1996) partly because of the reduced population of GnRH receptors.
- Progesterone induces quiescence in the uterus by prolonging the resting electrical potential of endometrial cells to prevent uterine contractions that could prematurely expel the fetus. (Parkington, 1983)
- It reduces calcium ion uptake (which is required for smooth muscle contractions) by the cells of the uterus to prevent contractions of the uterine wall (Batra, 1986.).
- Progesterone also reduces uterine contractions by blocking the ability of the hormone estradiol to induce α-adrenergic receptors that leads to uterine contractions (Bottari, et. al. 1983).
- The hormone also stimulates the glandular system of the endometrium to produce uterine milk to "nurse the embryo" during that critical period between initial attachment and the formation of the placenta in most ruminants.
- It induces the maternal immune system to be prepared to accept what is essentially a foreign body, the conceptus, so that it is not rejected by the mother. Progesterone also prepares the endometrial cells to accept the foreign conceptus by surrounding it with specialized cells which secretes molecules that protect the conceptus.
- Progesterone supplementation has been associated with increased embryo growth and elongation and production of a protein interferon-tau in sheep and cattle, required for successful pregnancy in these species (Knickerbocker, et al 1986).

Supplementation has also be associated with higher pregnancy rate in cattle (Carter, et al. 2008) and sheep (Ashworth, et al., 1989). Conversely, animals with low concentration of progesterone soon after ovulation show retarded development of the conceptus, and a reduction in interferon production (Mann and Lamming, 2001)

- Glucose is a major nutrient for conceptuses (Rieger, et. al. 1992). Increase in uterine concentrations of glucose and several amino acids in cattle (Hugentobler, et. al. 2010) and sheep (Satterfield et al. 2010) required for fetal growth and survival have been associated with increased levels of progesterone.
- Progesterone favours efficient body metabolism in the pregnant animal. This is particularly useful if the nutrient is limited, insufficient, or expensive to get.
- Progesterone also induces maternal behaviour such as nest building, which is particularly evident in rodents and smaller mammals.

Hormonal Support for the CL

The corpus luteum, in order to continue functioning, like most reproductive phenomena, requires hormonal support. Such a hormone is called a luteotropin or luteotropic hormone. Which hormone is luteotropic varies from one animal to another but all of them serve the purpose of maintaining the secretory function of the corpus luteum as long as necessary. The CL of the ferret (Agu, et al. 1986, Rajkumar, et al., 1987)and the rat (Astwood and Evans, 1941) for example, requires the support of the hormone prolactin and luteinizing hormone to continue synthesizing and secreting progesterone. Therefore prolactin is luteotropic in the rat and the ferret where as sheep (Niswender et al, 2000) and cow CL respond to luteinizing hormone stimulation. The CL of the rabbit and the pig need estradiol support, and in fact in the rabbit estradiol is the ultimate luteotropin capable of maintaining the CL of even hypophysectomised (pituitary gland surgically removed) animals. (Bill and Keyes 1983)

Luteolysis: Who Kills The Corpus Luteum?

It is one of the ironies of life that your most trusted ally could be your worst enemy. The uterus whose interests the CL spends its short life to protect, is the source of the demise of the CL!

It is now known that the uterus produces a substance, prostaglandin F2alpha that terminates the lifespan of the corpus luteum of the estrous cycle if pregnancy does not occur. Early evidence from the labs of several workers (Connor et al, 1976, Moeljono, et al, 1976, Rampacek, et al, 1979) and others (review by Pate, et al, 2011) have demonstrated that PGF2alpha is the luteolytic factor and the uterine endometrium is identified as a source of the luteolytic factor. The progress that led to this conclusion was made through experiments involving removal of the uterus (hysterectomy) of pigs (Anderson, et al 1961, du Mesnil du Buisson, 1961,), auto transplantation of luteal phase tissue in early or mid-cycle (Spies et al, 1960, or chemical destruction of the endometrium (Anderson et al. 1961). In each case it was reported that the CL persisted in the absence of the uterus. In addition, total removal of the uterus maintained the CL for up to 30 days (du Mesnil du Buison, 1961) but when more than one-quarter of the uterus was retained, the CL found on day 40 or 55 of gestation were those on the opposite side of the uterine fragment. These early studies demonstrated that a uterine factor caused luteal regression, a fact that is now well established.

The mechanism by which PGF2a induces luteolysis has been extensively studied, all of them suggesting that luteolysis involves a functional (cessation of progesterone production) and morphological (cellular breakdown) regression (McCracken, et. al., 1999). Some evidence shows that it deprives the organ of blood supply thereby starving it of nutrients, oxygen supply, substrates for sustained synthesis of progesterone, and perhaps, luteotropic support and other essential requirements to continue functioning (review, Niswender, et al, 2000). This condition eventually leads to both functional and anatomical atrophy of the CL. Prostaglandin F2a may also act by producing a "luteolytic mediator called Endothelin-I which

constricts the blood vessels in the CL, reducing its blood supply and progesterone output (review, Niswender, et al. 2000). Evidence also support the fact that PGF2a directly reduce the CL steroidogenic cell populations (both large and small cells) during luteolysis.

That the Corpus Luteum May Not Die: Maternal Recognition of Pregnancy.

When pregnancy does occur, it is imperative that the corpus luteum must continue to produce adequate amount of progesterone to keep the conceptuse(s) in place in the uterus. This means that the normal cyclic regression of the CL in all species where pregnancy does not occur must be prevented (Roberts, et al. 1999). To remain viable, the conceptuse must also ensure that the implantation sites receives adequate blood supply from the mother so that gas and nutrients are available to it. The early embryo, therefore, must intervene so that the CL is kept alive for its own sake. This is essentially the purpose of maternal recognition of pregnancy: a signal from the conceptus or conceptuses (in the case of litter-bearing mammal) that tells the mother not to allow the CL to die, because they are around. Mammals have not collectively evolved one mechanism for rescuing the CL and so they have different means of doing this. In anthropoid apes and man, luteolysis occurs as a result of intra-ovarian mechanism which many believe may be due to a local effect of PGF2α. Premature luteolysis is avoided by blood-borne chorionic gonadotropin (CG), a protein hormone produced by the implanting trophoblast cells (Hearn, et al. 1991) which exerts two functions: it is luteotropic because it induces the CL to produce more progesterone, and it is luteoprotective because it protects the CL from the luteolytic effects of PGF2α (Hearn et al, 1991; Auletta and Flint, 1988).

Rodents such as rats and mice do not produce CG and so they use a different mechanism to prevent luteolysis. The placenta and the deciduum produce placental lactogens and "prolactin-like" hromones at mid-pregnancy that take over the function of pituitary prolactin.

Luteolysis in all ungulates is due to uterine release of PGF2α late in the estrous cycle (Geisert, et al. 1994) but the mechanism of preventing premature CL regression is not the same in all of them. In the pig, the concept uses produce the hormone estrogen between days 11 and 12 after ovulation but it is generally believed that other factors may be involved, in addition to estrogen, to ward off luteal regression in the pig. PGF2α is still produced by the endometrium, but instead of releasing it into the blood, it is channelled into the uterine lumen and metabolized.

In cattle and sheep, the signal informing the mother that the conceptuse is present is a trophoblastic protein, a glycoprotein belonging to the class called "interferon" (Roberts, et al. 1996). Ovine and bovine interfere on tau are released between day12 and 13 and 14 and 16 in sheep and cattle respectively, after ovulation with similar actions. Though not directly luteotropic, they dampen the release of PGF2α so that it does not exert its luteolytic action.
All these signals must be accurately timed and must be received by the mother so that CL regression is prevented in time.

PRACTICAL APPLICATION OF THE FUNCTION OF THE CORPUS LUTEUM

In developing countries like Nigeria, a major challenge is that the agricultural system is mainly based on subsistence farming in which individually owned farms are managed by a system of agriculture that has not improved in many generations. Animal farming is also poorly managed and productivity from such establishments is not enough to serve a growing population that cannot afford adequate animal protein in their diet. For example, data published by Ademosun (2000) and cited by Ekine et al (2012) suggests a total meat consumption of 810,000 tons for an estimated population of 110 million Nigerians. If these figures are correct, and still relevant it implies an average of 22g of meat per person per day whereas Food and Agriculture Organization (FAO) recommends 35g of animal protein per person daily. Dairy milk production also lags behind demand. Data published in 2013 (http://starafrica.com/news) shows that Nigeria dairy milk production is about 400 million litres per annum whereas the total demand for milk is over 1 billion litres. Meanwhile Nigeria spends about $426 million annually on importation of liquid and powdered milk.

All these put together imply that Nigerians are taking inadequate level of animal proteins in their diets and that unless action is taken to improve productivity, the situation will get worse with rising population. We need to apply reproductive technology to improve our dairy output.

Reproductive technology involves the application of human technology to reproduction that aims at improving the natural processes already inherent in the biological system. This requires the intervention of man in the reproductive process so that the output per period is maximized. This has many advantages, one of which is that animal protein in the form of milk and meat can reach more people, the quality of the meat so produced can be improved, and farmers will get more return for their labour.

The knowledge that regression of a CL allows another ovarian cycle to start (Niswender and Nett (2005) and that the corpus luteum can be regressed artificially to provide opportunity for another estrus in animals that are not pregnant (Diaz, et. al. 2011) is a major discovery in agricultural technology. It has made technologically advanced countries self-sufficient in food and has virtually eliminated incidence of severe malnutrition that we are familiar with on television. This is because the output from one farm alone can serve a sizeable portion of the population and not just the farmstead or community where it is located.

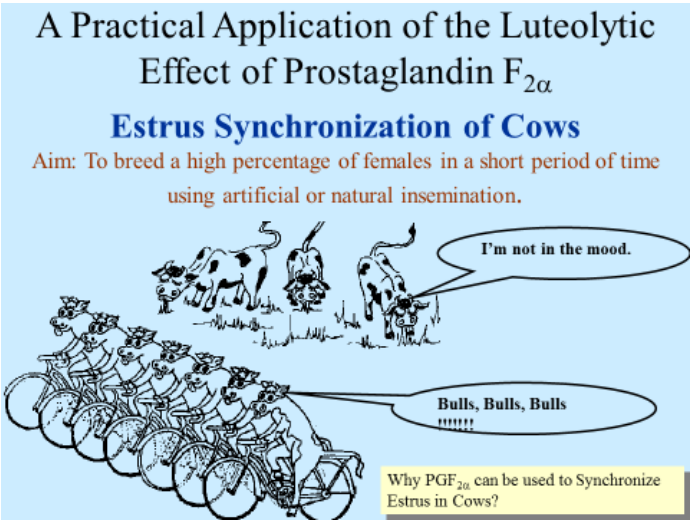


Fig. 14. Estrus and ovulation synchronization in dairy cows. (www.slideshare.net)

Estrus synchronization is a protocol that enables many animals to be bred at a pre-determined time, usually by artificial insemination (fixed time-AI) rather than breeding based on when the animal comes to natural standing heat (www.minnesotafarmguide.com/news) When applied to cows, this is particularly useful because it is not always possible to detect estrus in cows, to know when they should

be bred because they may not show overt signs of receptivity. Fixed time-AI is, therefore, useful to farmers because it is not necessary for the farmer to detect estrus through observation of individual animal (Yamada, et al.1999).All females in the herd can be inseminated as a group, not individually as nature permits. Furthermore, animals can be fed and cared for in groups instead of separately, which saves labour and time, and the effort required on the farm.

Fix time-AI also helps to keep the period of offspring production (calving) on the farm to a specific time when farm resources can best be used. And because off-springs are produced at the same time, the producer gets a uniform group of young ones that can be raised to marketable weights together. This is not only an economic advantage but the producer can serve a greater population than when animals are raised individually according to natural processes.

Furthermore, the process ensures that all females are provided an opportunity to conceive with an AI treatment or natural mating. Several protocols are used in fixed time AI but all of them have the same goal: to synchronize the estrous cycle and ovulation among the animal in question and thereby maximize the number of animals that can be pregnant at the same period. Any of the two protocols given below can be used in an AI programme:

1. Producers can use a short time of heat detection during which he checks for animals in heat. These are then inseminated while a fixed time-AI (discussed below) is used for those that fail to show heat (http://animal-husbandry:blogspot.com)
2. The producer may also decide to apply fix time-AI on the entire herd by using PGF2a or its analogue with GnRH treatment regardless of the ovarian stage of the animal.

When GnRH is used, the process involves, first, an administration of GnRH or its analogue to the animals regardless of the phase of the ovarian cycle. This causes ovulation because it induces the release of LH. Ovulation removes the inhibition of FSH by the hormone

inhibin produced by the dominant follicle. As this inhibition is lifted, FSH is released once again which causes a second wave of follicular growth that is synchronized across the animals treated (Yamada, et. al. 1999). An injection of PGF2a 7 days later causes the first crop of CL to regress and a new dorminant follicle to grow towards ovulation. Ovulation of this dominant follicle is synchronized therefore AI can be performed within the following 24 hours that results in a high conception rate.

In the ovulation synchronization protocol developed by Pursley (1995) GnRH (100 µg) is administered to all animals in the herd regardless of their stage in the estrous cycle. GnRH so injected releases the LH necessary to cause ovulation of the dominant follicle to give way for a new follicular wave. For animals in which a new follicular wave is on course, the stage of the cycle will not be affected. A week (7 days) later, PGF2αor its analogue is injected intramuscularly to regress any active corpus luteum. The 7-day interval from the GnRH injection gives any corpus luteum emanating from the GnRH-induced ovulation to grow to a sufficient size to respond to PGF2α. Two days (48 hr) later, a second injection of GnRH (100 µg is given intramuscularly to cause ovulation of the dominant follicles from the first treatment. The cows may then be bred by natural or AI 24 hours later.

PGF2a and GnRH have definite roles to play in these protocols. When administered to female animals PGF2a destroys the CL that may exist at that time (depending on the ovarian status of the animal) thereby eliminating progesterone production. This allows the animal to get into heat again. GnRH in the above example performs two functions: when given at an appropriate time in an AI program it can induce growth and maturation of the follicle or induce ovulation to allow insemination to take place. PGF2a and GnRH are therefore used together in a fix time-AI to control follicular growth, CL regression and ovulation.

All methods in estrus synchronization use PGF2a at or near the end of the protocol because a female will not show estrus or ovulate if it has a viable CL. Sometimes it may be necessary to administer progesterone prior to PGF2a injection (www.minnesotafarmguide.com/news) either in the form of MGA or intravaginal insert which prevents females whose CLs are undergoing natural regression from going into heat after the CL has finally regressed. By so doing these females do not go out of synchrony with the other females. Once the progesterone is removed, the animals will go into estrus shortly after that, that is, estrus has been synchronized. Once estrus is synchronized, AI is performed on a day chosen by the farmer (in fixed time-AI) resulting in better pregnancy rate. Table 3 shows an example of estrus synchronization with a combination of PGF2a and GnRH as described, followed by a fix time-AI (Yamada, et al, 1999.). Ovulation synchronization can also be practised on sheep and goats to improve yield in their respective breeding seasons.

Table 3: Reproductive performance following OVSYNCH (Ovulation synchronization)

S/No	No. of cows treated	OV	CO
1	No. of cows treated	185	151
2	No. of cows inseminated	153	151
3	No. of cows conceived	82	33
4	Conception rate percent	53.6 **	21.9

** Significantly different from Control (Modified from Yamada, et al. 1999)

Management of the CL has other uses as well

Other Management Uses of the Corpus Luteum:

Abnormal CL occurs when the CL fails to produce the level of progesterone required to support gestation or its lifespan is abnormally long or short. Depending on the nature of the abnormality the cause can be diverse. Inadequate luteinisation, a condition where the CL is not properly formed may cause it to

produce less than normal level of progesterone. The cause of this condition has be suggested to be due to insufficient LH surge, (Schramm, et al, 1983) which provides the primary signal for luteinisation (review: Murphy, 2000) and environmental stress.

Uterine disorders such as intra-uterine embryonic death, endometritis, pyometra (MacLachian, et al. 1987) and negative energy balance (Zulu, et al. 2002) can cause a prolonged luteal phase when the CL fails to regress when it should. A prolonged luteal life as a result of persistent CL is undesirable because it reduces the reproductive performance of the animal affected by preventing regular estrous cycle. The knowledge that the CL can be induce to regress provides us with a tool to induce parturition either for farm management or health reasons (Taverne, 2001)

The knowledge can also be used to treat several forms of dystocia (difficulty in giving birth) in animals caused by several complications such as incomplete dilatation of the cervix, uterine quiescence, (Taverne, 2001) or intra-uterine fetal death. When we induce luteolysis at such a time, progesterone production ceases and the uterus and cervix may relax to enable evacuation of the uterus

My Modest Contribution to Knowledge in this Area

In response to previous reports that pre-pubertal pigs mated after gonadotropin-induced ovulation show high incidence of abortion, I investigated the basal levels of progesterone production by CL from this animal model in vitro in the presence of steroidogenic substrates LDL and HDL. In the process I have also successfully separated the two cell types in the CL of the pig CL and tested their progesterone producing capacity.

I have also studied and published the effect of PGF2 on the two cell types in the pig separately and in the presence of the substrates required by the cells to produce progesterone. The role played by LH in steroidogenesis by the two cell types of the pig in vitro have also been studied, presented at a conference, and published.

I was the first to report that prolactin is under tonic inhibition by the neurotransmitter dopamine in the ferret and that prolactin is required by the ferret corpus luteum to synthesize and secrete progesterone. In other words, that prolactin is luteotropic in the ferret. I also published that the ferret CL also requires LH in addition to prolactin to synthesize and secrete progesterone. That is, that this animal has what I refer to as a luteotropic complex. I also studied and published that elevation of prolactin in vivo using dopamine antagonist enhanced the level of progesterone the CL produced in vitro. That increasing or decreasing prolactin levels in vivo respectively increased or decreased the ability of the luteal cells from the treated animal to take up substrates for progesterone production. The work concluded that prolactin may play an important role in regulating the binding site of LDL to luteal cells for progesterone production and therefore regulate the uptake of substrates for steroidogenesis.

Other efforts in the area of luteal function investigated the pattern of release of prolactin, one the luteotropic hormones in the ferret (Agu, et. al., 1986), the role of unbalanced diet during pregnancy on neonatal characteristics (Daodu and Agu, 2001).

Vice-Chancellor Sir, in the Department of Animal and Environmental Biology, we are currently investigating the effects of environmental contaminants and household applications such as organochlorines, organophosphates, and carbamates pesticides on various aspects of mammalian reproduction. We are also asking such questions as whether exposure of adult animals compromises the reproductive potential of off-springs in the next generation.

Conclusions and Recommendations

Vice Chancellor, Sir, in this lecture I have tried to introduce us to an organ of mammalian reproduction, though short-lived, and weighing substantially less than most components of mammalian reproductive structures, is a primary requirement for successful reproduction itself. The corpus luteum may be regarded not only as a reproductive organ, but as a tool for agricultural advancement and nutritional

benefit of man because it is a driving force in animal husbandry. Given the tremendous advantage of applied reproductive technology over subsistent agriculture, and the general world trend in agriculture, I wish to recommend:

- That animal reproduction should also be part of a Secondary School curriculum because it will arouse the interest of the young minds in Agriculture as a profession, which the country badly needs.

- That a course in animal reproduction and application of reproductive technology be included in the curriculum of Zoology and Animal Science students to be taught jointly by the two Departments. This is because of the critical role of animal reproduction in Agriculture.

- That the Federal Government should establish ovulation synchronization and artificial insemination centres in all the states of the Federation as part of the extension services of the Federal Ministry of Agriculture. It is a worthwhile investment that will, over time, eliminate the need for importation of dairy products. This will also provide jobs for University graduates in Agriculture.

Vice Chancellor, Sir, in the words of G.W. Corner," The greatest reward of the Scientific Investigator is that no matter what his success or failure he knows he can serve. . . by keeping on asking questions. If he cannot answer them someone else will and in the end truth is achieved and mankind advanced a little farther toward the light."

Vice Chancellor Sir, ladies and gentlemen, thank you for listening!

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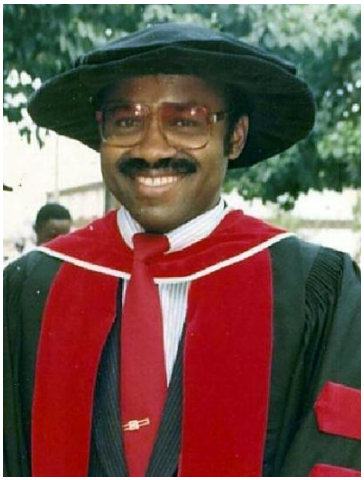

PROFESSOR GABRIEL OGABA AGU
B.Sc (Hons.) *ABU*, M.Sc. (*Saskatchewan*), Ph.D. (*Manitoba*)

THE 122ND INAUGURAL LECTURER OF THE UNIVERSITY OF PORT HARCOURT.

Early Life and Education

Gabriel Ogaba Agu was born a second child of late Mr Alfred Agu Otse and Mrs Orefi Agu, in Agila, Ado LGA in Benue State. He received his primary education from Methodist School Agila and Wesley School Utonkon. Thereafter he proceeded to Government Secondary School, Kuru, near Jos, in the then Benue Plateau State, for post primary education in 1970. In his first year in G.S.S. Kuru, he came first position in a class of 64 students, a standard he maintained until he graduated with his WASC certificate with a Division I in 1974. Ogaba was baptized in 1970 and was Christened Gabriel, a name suggested by his highly religious father.

In 1974 he was admitted to do Higher School Certificate (HSC) in the prestigious Government College Keffi, and while there he received another admission to Federal School of Arts and Science Ogoja under the headship of the late Dr Sanya Onabamiro. He left Keffi for Ogoja and after his HSC programme, gained admission to Ahmadu Bello University, Zaria in October, 1976 to read Zoology. He graduated three years later with a Second Class honours, Upper Division and as the best graduand that year. Ogaba was posted to Sokoto State for National Youth Service.

Career and Work-life

From the Youth Service Ogaba secured appointment with the School of Biological Sciences, University of Port Harcourt for the position of Graduate Assistant in August 1980. After a while, he proceeded to the University of Saskatchewan where he obtained his M.Sc. in Animal Physiology in 1984. He was later admitted to the University of Manitoba, Winnipeg, for the Ph.D. programme. While there he secured the Commonwealth Scholarship to enable him complete the Ph.D. degree in mammalian reproductive physiology in February, 1990.

Ogaba Agu returned to Nigeria on February 13, 1990 and resumed duties at the University of Port Harcourt. He rose through the ranks and became Professor of Reproductive Physiology in 2006.

Administrative, Public and Community Service

Gabriel Ogaba Agu has served in various capacities including: Faculty of Science representative on Board of Faculty of Education (1992-1999); Assistant Secretary, ASUU (1994-1997).
Head of Department of Animal and Environmental Biology (2006 – 2008);

Chairman, Faculty of Science Business Committee (2012-date); Chairman, Departmental Workshop Committee (2012); Member, University Public Health Committee (2001-2005); Associate Editor,

Journal of Applied Sciences and Environmental Management (1998-date); Editor-in-Chief, *ScientiaAfricana*, the International Journal of the College of Natural and Applied Sciences (2010-date); Senate representation on the Delta Series Editorial Board (2014-date); Treasurer, Senior Staff Club (1997-2001); and

Professor Agu has also served the wider community in several instances. He is a consultant to Nigerian National Petroleum Corporation (NNPC), Rivers State Environmental Protection Agency, Niger Delta Network for Environmental Management and Nigerian Liquefied Natural Gas (NLNG), Bonny.

He has served as External Examiner to Cross River University of Technology, Calabar. He is a visiting Professor to the Kogi State University, Anyigba. He has also assessed colleagues for promotion to the rank of professor in the University of Uyo, University of Lagos, and University of Gabarone, Botswana.

Professor Agu has published several journal articles, books and chapters in books. His articles have appeared in Biology of Reproduction, General and Comparative Endocrinology, and Canadian Journal of Animal Science.

Family Life

Ogaba fell in love with one of his students - former Miss Elizabeth Chima from Iselekpitime, Delta State and married her in (2008). The union is blessed with two lovely daughters, Jennifer and Jessica.

Mr. Vice Chancellor Sir, distinguished ladies and gentlemen, permit me to therefore formally present to you;

This erudite and well-travelled scholar; a teacher whose hand writing is rather printed in an unusual style; this man who could fall in love with his former student and was faithfully committed to culminate into marriage; a detribalised Nigerian; an epitome of gentility and humility; a consultant of repute; a former Head of Department of

Animal and Environmental Biology, an ASUU activist; the Editor-in-Chief of the *ScientiaAfricana*; the man of his words. Professor Gabriel Ogaba Agu as the 122rd Inaugural Lecturer to deliver his lecture.

Professor Benjamin C. Ndukwu
(Professor of Plant Science & Biotechnology; the 96th Inaugural Lecturer, University of Port Harcourt)