An Essay on

CERVICAL FACTOR IN REPRODUCTION

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By

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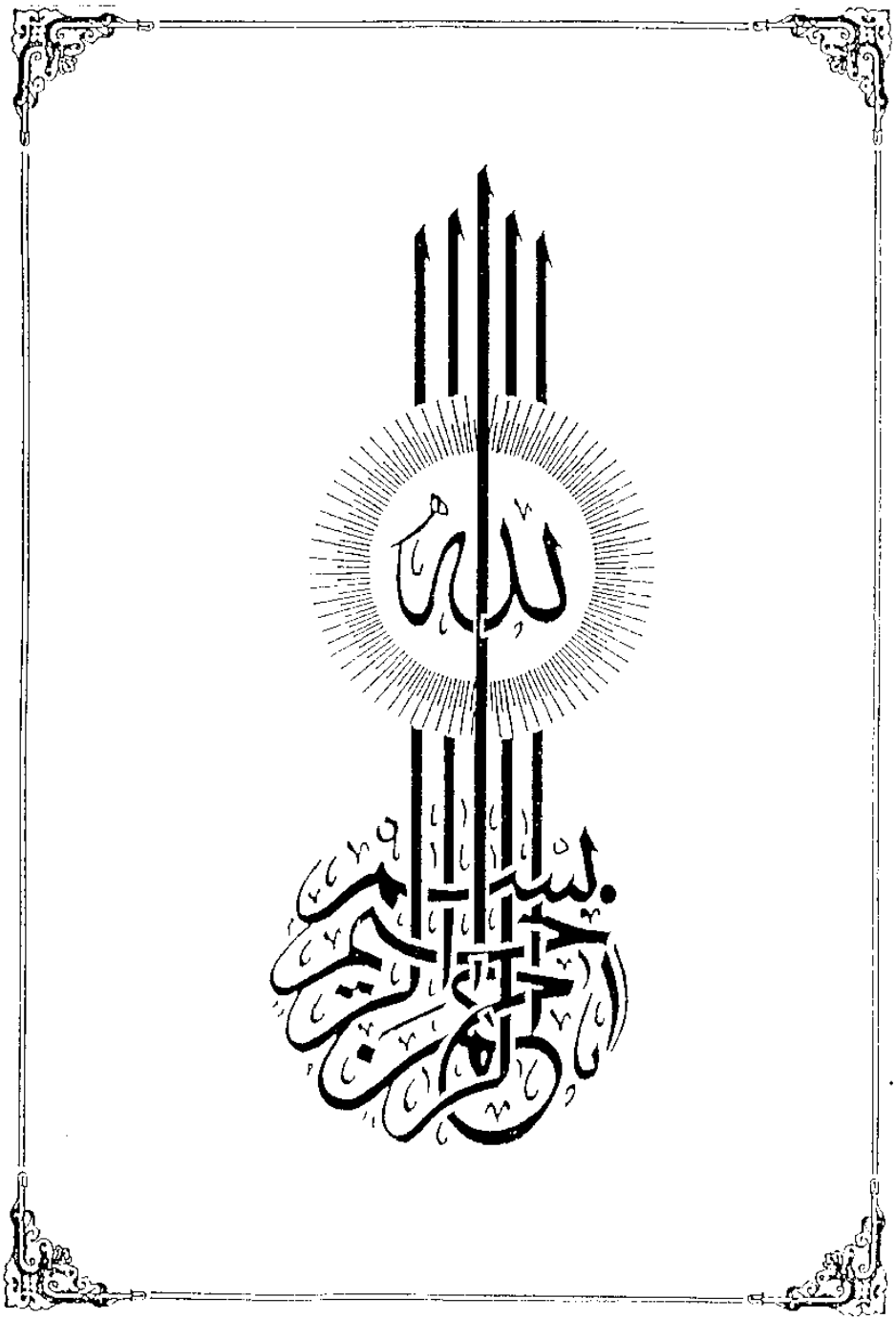

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REPRODUCTION

REPRODUCTION

The ability to reproduce new living individuals is a basic characteristic of all plants and animals. Early biologists understood correctly how the higher animals reproduce, but for centuries it was believed that many forms of life arose from non living materials by spontaneous generation. These erroneous ideas were gradually abandoned after Francesco Redi showed in 1866, that maggots and flies are produced from meat only if living flies have laid eggs on such material.

All reliable evidences indicate that new life comes only from pre-existing life (omne uivum ex vivo); this is the process of biogenesis, or reproduction.

Two distinct types of reproduction are present, asexual reproduction involving only one "parent with no special reproductive structures, it occurs in plants and many lower animals. It takes a lot of forms, binary fission, multiple fission, budding and fragmentation.

Most animals increase by a process in which new individuals develop from sex cells from two parents, male and female, join together to produce a new individual, typically this is sexual reproduction.

The germ cells are produced in organs known as gonads, the sperm in testes, and the ova in ovaries.

After birth, the gonads remain quiescent until adolescence, when they are activated by gonadotropins from the anterior pituitary. Hormones secreted by the gonads at this time cause the appearance of features typically of the adult male or female.

In males, the gonads remain more or less active from puberty onward. In human females, ovarian function regress after a period of time, and sexual cycles cease (the menopause).

In both sexes, the gonads have a dual function: the production of germ cells (gametogenesis) and the secretion of sex hormones. The secretory and gametogenic functions of the gonads are both dependant upon the secretion of the anterior pituitary gonadotropins, F.S.H. and L.H.

The sex hormones feed back through the hypothalamus to inhibit gonadotropins secretion. In males gonadotropins secretion is non cyclic, but in post pubertal females sequential secretion of gonadotropins is necessary for the occurrence of menstruation, pregnancy and lactation.

The testes are made up of loops of convoluted tubules, along the walls of which the spermatozoa are formed from the primitive germ cells (spermatogenesis). Both ends of each loop drain into a network of ducts in the epididymis. From there, spermatozoa pass into the vas deferens. They enter through the ejaculatory ducts into the urethra in the body of prostate at the time of ejaculation. Between the tubules in the testes are nests of cells containing lipid granules, the interstitial cells of leydig, which secrete testosterone into the blood stream.

The reproductive system of the female, unlike that of the male, shows regular cyclic changes that teleologically may be regarded as periodic preparations for fertilization and pregnancy.

Certain requirements must be met to achieve pregnancy. The male must produce satisfactory number of normal motile spermatozoa, he must have patent conduits and potency to ejaculate spermatozoa into the vagina. The spermatozoa must reach the cervix, pass through the cervical mucus, and ascend through the uterus and

oviduct at an appropriate time to encounter an ovum. The spermatozoa must be capable of penetrating and fertilizing the ovum. The female must release an ovum that has access to a patent oviduct. The fertilized ovum must move into the uterus and find an endometrium prepared for implantation. The embryo must implant, develop normally, and produce the glycoprotein gonadotropin (human chorionic gonadotropin) to rescue the corpus luteum.

This is a series of complex events requiring the integrity of several systems. A moderate or sporadic defect in any one can cause infertility. A severe, consistent defect results in sterility (Tracy et al., 1968).

Causes of infertility are numerous, both male and female are responsible for this problem, the male factors constitute 40% of causes. As regard the female, the ovulation factors constitutes 20%, tubal or pelvic factors constitutes 20%, cervical and uterine factors 10%, vaginal factors < 5%, immunologic factors < 5%, nutritional and metabolic factors 5% (David et al., 1984).

ANATOMY OF THE CERVIX

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The cervix (term taken from latin, means neck) is the inferior portion of the uterus. It is barrel shaped, measuring 2.5-3.5 cm. from above downwards. Half of it projects into the vagina (vaginal cervix or portio-vaginalis) while half is above the vaginal attachment (supra-vaginal cervix). The vaginal part is covered with squamous epithelium continuous with that of the vagina. The supra-vaginal part is surrounded by pelvic fascia except on its posterior aspect where it is covered with the peritoneum of the pouch of douglas (Jeffcoat, 1975).

The endocervical canal is fusiform in shape, about 3 cm. long, and is flattened from front to back. When the cervix in its normal position, the anterior lip occupies a position lower in the vagina than the posterior, as a result of which, the external os and both lips are in contact with the posterior vaginal wall.

The endocervical canal is quite variable in length (average is 25 m.m.) and is encroached upon by cervical folds, the plica palmatae. In cross-section the cervical canal represents a complex branching structure *the arbor vitae uteri*.

It is connected with the corpus by a fibromuscular junction usually referred to as internal os. So the internal os marks the junction between the muscular corpus and the fibrous cervix (Alex Ferenczy, 1974).

Several ligaments hold the cervix in position including the Utero-sacral ligaments and lateral ligaments. The utero-sacral ligaments consists mainly of fibrous tissue, they extend from the supravaginal portion of the cervix and vagina to the second, third and fourth sacral vertebrae. The lateral ligaments (transverse-cervical ligaments, cardinal ligaments or ligament of Mackenrodt) lie at the base of the broad ligament, where fascial ligaments contain connective tissue and smooth muscle. They

form an inverted-U, which is attached medially to the anterior, superior and posterior marginal walls of the supra-vaginal cervix, and laterally and below, to the white line and fascia of the levator anti muscle (Prichard et al., 1985).

Cervical Mucosa

The cervical mucosa is an intricate system of clefts, grooves, and crypts grouped together. It is called *Plicae Palmate* or *Arbor vitae uteri*, it resembles the trunk and branches of a tree.

The basic subunit of cervical epithelium is the villus, which is ovoid in shape and 1-2 mm in diameter. The cervical crypts lie within the cervical villi. The endocervical canal contains approximately 100 secretory units that secrete the cervical mucus into the lumen of the canal (Odeblad, 1966).

The cervical crypts are made of columnar cells. In scanning electron microscopy, the cells appear polygonal of uniform size and closely packed, with a cobble-stone semblance. The columnar cells are of two types: non-ciliated secretory cells and kino-ciliated cells. In general, secretory cells have a dome-shaped surface covered with micro-villi, and their cytoplasm contain numerous secretory granules (Hafez, 1972).

The ciliated cells are covered with kino-cilia, which beats rhythmically toward the vagina. Ciliated cells are frequently seen in endocervical columnar epithelium,, but rarely on ectocervical columnar epithelium. Ciliated cells particularly prominent at the utero-cervical junction. Occasionally, areas of columnar epithelium do not show the typical villi or crypts, giving rise to a relatively smooth surface.

The endocervical columnar epithelium does not undergo overt cyclic cytologic changes throughout the menstrual cycle. However, there are cyclic changes in the

ultra-structural characteristics of cells, e.g., variations, degree of development of secretory organelles.

Three types of epithelium of characteristics histologic appearance are recognized in the cervix:

1. Original (sometimes called native epithelium), either squamous or columnar.
2. Metaplastic squamous epithelium.
3. Atypical epithelium, including some with neoplastic potential.

The transition from the columnar epithelium of the endocervix to the stratified squamous epithelium of the portio externa is usually abrupt. The columnar epithelium may extend out-side the external os onto the vaginal portion of the cervix, which is a common feature of the cervix of the neonates and the pregnant women known as physiologic erosion. The stratified squamous epithelium of the portio-externa is made of several layers, basal, para-basal, intermediate and superficial. The basal layer consists of a single row of cells an-d rests on their basement-membrane. The superficial and intermediate layers of the epithelium contain a large amount of glycogen, which serves an important function in maintaining the acidic pH of the vaginal contents. The glycogen released by the glycolytic bacterial flora of the vagina form lactic acid.

The superficial cells are desquamated into the vaginal lumen but retain their nuclei, this is unlike the desquamating cells of heavily cornified epithelium such as thick skin.

The squamous epithelium of the cervix differentiates under hormonal influences, with the more mature superficial cells exfoliating into the vagina and being replaced by the metabolically active basal cell layer.

The rapidly regenerative nature of the basal cells is reflected in its ultrastructure and is characterized by a high nucleus- Cytoplasm ratio, prominent nucleoli, a convoluted nuclear membrane, and an abundance of ribosomes and mitochondria.

The cervical stroma, which is made of collagenous connective tissue with elastic tissue and smooth muscle fibres, becomes very vascular during pregnancy (Hafez, 1979).

Cervical Connective Tissue

The uterine cervix from fertile non-pregnant women contains 80% water. The dominating molecule in the dry material is collagen (85% of dry weight), of which 70% is type I (typical cross striated collagen) and 30% is type III (reticular fibers). The ground substance contain elastin and proteo-glycans. Dermatan-sulphate proteoglycan is the quantitatively dominating glycosaminoglycan, 15% heparin-sulphate and 15% hyaluronic acid are also found (Hafez, 1980).

PHYSIOLOGY OF THE CERVIX

PHYSIOLOGY OF THE CERVIX AND CERVICAL MUCUS STUDY

The cervical mucus is a mixture of secretions and transudation of the mucus-producing elements of the cervical canal to which contributions from upper part of the genital tract also may be added to an unknown extent. Mucus is being produced continuously, varying in quality and quantity depending upon other factors such as neuro-muscular impulses. There seem to be qualitative differences between the secretion of different glands and different areas of the cervix which is called by Odeblad as "mosaic pattern" (Odeblad, 1968).

During the pre-ovulatory phase of the cycle or under estrogen administration the cervical secretions are profuse, watery, clear and alkaline. But during the post-ovulatory phase or under administration of progestational agents it is reduced in volume, scanty, thick, opaque, less alkaline or acidic and containing an increased number of leucocytes and unfavorable for sperm penetration (Davajan and Kunitak, 1969).

Cervical mucus, once secreted by the cervical crypts, which are at right angles to the cervical canal, is released perpendicularly to the axis of that channel. Probably as a result of the force of gravity, the filaments flow dow parallel to the axis. The cervical canal thus acts as a capillary tube where the main filaments have a parallel arrangement.

Once the column of cervical mucus flows out of the external os, it is suspended within the vaginal fluid, accumulating in the vaginal fornix. There, the cervical mucus is freed from the capillary biophysical constrains encountered in the canal. After intercourse, spermatozoa enter into the cervical mucus, where they are protected from the acidic pH of the vagina and are transported rapidly between the micelles of mucus within the vaginal pool.