INTRODUCTION

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The inability of individuals to produce offspring may arise in several ways, such as failure of gametogenesis or abnormalities in mating behaviour. The production of young by marsupial and eutherian mammals involves internal fertilization and viviparity. Thus, failure to give birth to young may also occur in these animals when spermatozoa and ova fail to reach the internal site of fertilization, or when embryos die during the period of development within the female genital tract. The latter cause is of particular significance in monotocous species, such as man. The females may become pregnant, yet if the newly created embryo dies within the period of an oestrous or menstrual cycle, the young are not found, and consequently it might never be known that the female had conceived.

Although Hammond (1914) called attention to the incidence of embryonic mortality in pigs, the widespread incidence of embryonic death in mammals was first described by Robinson in the Sir John Struthers Lecture of the Royal College of Surgeons of Edinburgh, published in the Edinburgh Medical Journal in 1921. The terms of the will of Sir John Struthers established these lectures in anatomy and embryology, and specifically stipulated that

the lecturer should not discuss problems in pathology. Robinson cleverly evaded this restriction by emphasizing that although the death of a particular embryo certainly involves pathological processes within itself, embryonic death was so widespread in mammals that it should be accepted as a normal phenomenon within individual mothers. This same conclusion was also reached independently by Corner, who published his findings in the American Journal of Anatomy in (1923).

The extent of embryonic death in normally fertile animals is now known to be substantial. Table(1) lists various studies which have been made on cattle, pigs and sheep. Only one relevant study has been made on women (Hertig, 1960), and the results suggest that a high incidence of early embryonic death may occur in normally fertile patients. In 'repeat breeder' animals the incidence of embryonic death is much higher. Data on cattle and pigs are summarized in Table(2).

A full analysis of this subject could be an arduous task since it is readily apparent that many disturbances may affect the embryo. Corner (1923) classified the causes of embryonic death in three categories: defects of zygosis; defects of the zygote; and faulty maternal milieu.

Table (1)

INCIDENCE OF EMBRYONIC MORTALITY IN NORMALLY FERTILE CATTLE, PIGS, AND SHEEP

Species	Day examined	Embryonic mortality (%)	Reference
Cow	33	14.9	Bearden, Hansel & Bratton (1956)
Cow	90	16	Kidder, Black, Wiltbank, Ulberg & Casida (1954)
Cow	150	19.9	Hawk, Tyler & Casida (1955)
Cow	100	20.6	Erb & Holtz (1958)
Cow	27	21.0	Laing (1949)
Pig	55	23	Reddy, Moyer & Lasley (1958)
Pig	25	30-43	Baker, Self, Chapman, Grummer & Casida (1956) Baker, Chapman, Grummer & Casida (1958)
Pig	25	33.0	Day, Anderson, Emmerson, Hazel & Melander (1959)
Pig	25	34.0	Lerner, Mayer & Lasley (1957).
Pig	25-40	34.8	Perry & Rowlands (1962)
Pig	28	39.0	King & Young (1957)
Pig	term*	40.0	Perry (1954)
Pig	term	41.0	Lasley (1957)
Pig	term	44.0	Casida (1953)
Pig	70	50.0	Baker, Self, Chapman, Grummer & Casida (1956)
Sheep	40	30.0	Hulet, Voigtlander, pope & Casida (1956)

* 75 % of the embryos died by the 25th day.

TABLE (2)

INCIDENCE OF EMBRYONIC MORTALITY IN 'REPEAT BREEDER'

CATTLE AND PIGS

Species	Day examined	Embryonic mortality (%)	Reference
Cow	34	39.2	Tanabe & Casida (1949)
Cow	27	44.0	Laing (1949)
Cow	34	51.7	Hawk, Wiltbank, Kidder & Casida (1955)
Cow	30	54.1	Tanabe & Almquist (1953)
Cow	34	59.4	Casida (1953)
Pig-gilt	25	51.3)	Warnick, Grummer &
Pig-cow	25	100.0)	Casida (1949)

A more detailed classification of these causes, based on Corner's primary categories, was given by Boyd & Hamilton (1952). Other useful information is given by Brambell (1948) on wild mammals; Casida (1956) on domestic mammals and in recent symposia edited by Benirschke (1967), and by Lamming & Amoroso (1967).

Subfertility and pregnancy wastage combine to provide an index of reproductive efficiency. There is no sharp boundary between these two categories but, for present purposes, subfertility refers to failure of fertilization, whereas pregnancy wastage embraces loss of conceptuses in terms of both abortion and perinatal mortality.

One may first isolate the problem of the causes of assumed failure of fertilization, accepting for the time being that, clinically, one cannot distinguish this from preimplantation or early post-implantation losses. In this context it is useful to distinguish two categories of aetiological factors-determining or decisive factors, which by themselves virtually preclude conception, and contributory or conditioning factors which reduce fertility but do not totally prevent conception.

In this thesis,the discussion will be restricted to pregnancy loss by spontaneous abortion. It is probable that uterine factors have a more critical role to play here than in failure of fertilization and that they operate either by interfering with mechanisms of implantation or through failure to accommodate the growing products of conception.

In introducing the causes of animal pregnancy wastage it is convenient to distinguish three categories:

Errors within the extra-uterine environment. Within this category one includes such possibilities as acute febrile illnesses, pyelitis or appendicitis for example; chronic disorders-such as severe hypertension, endocrine disorders-such as hypothyroidism, but including also inadequate luteal activity; nutritional disorders-such as foliate deficiency; and even psychosomatic disturbances.

Errors within the contents of the uterus. This refers mainly to problems of abnormal embryogenesis. In more than 60 % of spontaneous abortuses one can demonstrate an anomaly of the products of conception, and the earlier the abortion occurs, the more pronounced is its association with malformation (Hertig & Sheldon, 1943). At least 30 % of all first trimester abortions show a gross chromosomal anomaly, and this is usually associated with defective embryogenesis (Kerr & Rashad, 1966).

It is, of course, certain that some of these abnormalities of the conceptus are themselves secondary to uterine or extra-uterine factors, but the major cause of abnormal embryogenesis in first trimester abortions is more likely to be errors in cell division of fusion occurring at or around the time of fertilization.

Errors within the cervix. In these cases, the diagnosis usually rests on the failure to demonstrate an adequate number of motile spermatozoa in cervical secretions soon after coitus (Sims - Huhner test). The term'cervical hostility' is frequently used, implying that in these cases there is some active resistance on the part of the cervix or its secreetions to sperm entry and migration.

A part from seminal or coital faults, the cervix may be responsible for inadequate sperm migration by reason of structural or functional faults.

The common domesticated species are the horse, cow, sheep, pig, dog and cat. They present very different reproductive patterns as regards season of breeding, occurrence of oestrous cycles, relationship between parturition, lactation and time of fertile mating, expected level of fertility and numbers of offspring born.

For economic reasons, in the farm species, attempts are made to keep a short interval between parturition and subsequent pregnancy, and there is a commonly acceptable parturition-conception interval for each species. Although differing from the definition of infertility laid down a marked delay in achieving pregnancy is rightly regarded as infertility by livestock owners. Parturition and the puerperium are periods when the uterus is exposed to a variety of assaults which can affect the parturition-conception interval markedly, either through dalay in subsequent ovarian function or in reduced fertility following service.

Transformation of the fibroblasts of the endometrium into decidual cells with the formation of the implantation chamber is a rare example of morphogenesis in the adult mammal (Krehbiel, 1937; Finn, 1971). The preparation of the endometrium for the reaction is under strict endocrine control, which can however be mimicked by exogenous hormones in ovariectomized animals (Psychoyos, 1967a; DeFeo, 1967; Marcus & Shelesnyak, 1970). In rodents, a stimulus is required to initiate the reaction in the sensitized uterus.

It is quite possible that the administration of B-sitosterol would upset the supply of ovarian

hormones either at the level of the corpora lutea or the hypothalamic/ pituitary system. The effect on decidualization might, therefore be complicated by hormone interference.

To investigate this, the effect of B-sitosterol on the progress of implantation has been evaluated in rats treated with B-sitosterol hormone on a schedule which has previously been shown to affect the uterus and endocrine glands in response to the in vivo injection of B-sitosterol (Diab, 1983; Moshiera, 1985 and Wafaa, 1987).