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Physiology of Reproduction in Relation to Nutrition

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In the infantile animal the reproductive organs gradually develop but do not begin to function as organs of reproduction until the age of puberty, although their internal secretions begin before this time. In the female the cause for their functioning lies outside the ovary itself, for immature ovaries transplanted into adults begin to function immediately, whereas adult ovaries transplanted into immature animals do not function until the age of puberty is reached (Foa, 1901). It is now generally recognized that the functioning of the ovary depends on gonadotrophic hormones coming from the anterior-pituitary gland (Smith & Engle, 1927; Zondek & Aschheim, 1927), the two main hormones being the follicle-stimulating hormone (F.S.H.) and the luteinizing hormone (L.H.). The anterior-pituitary gland also produces growth hormones (Evans, Meyer & Simpson, 1933). Normally the onset of puberty occurs as the adult weight is approached and the rate of growth declines. Injection of gonadotrophic hormones into the infantile animal immediately causes functioning of the ovary and the onset of puberty, and so one must suppose that the time of onset of puberty depends on a change in the balance of output between the gonadotrophic and the growth hormones of the anterior-pituitary gland. With animals that have a breeding season (such as the sheep) the age and size of the animal when puberty begins vary according to the time of year at which it is born, for in such species the gonadotrophic hormone output of the anterior-pituitary gland is seasonal and is dependent on the ratio of hours of darkness to hours of daylight. Thus a definite age and size are not necessarily associated with puberty.

How far then is the age of puberty affected by the plane of nutrition on which the animal is reared? Experiments by Prentice, Basket & Robertson (1930) (Table 1) on fowls have shown that increased rate of growth due to good nutrition lowers the age

Table 1. *Food supply in relation to maturity in White Wyandotte pullets*

Ration	Age when first egg laid (days)	Average body-weight when first egg laid (g.)
Basal	186	1715
Basal and minerals	146	1726
Basal and milk	137	1830

of puberty, but that the body-weight at which puberty occurs is higher than normal. Conversely, poor nutrition leads to delay in the age of puberty, but puberty takes place at a lower body-weight than normal. This latter in the mammal where the extra strain of pregnancy and lactation falls on the mother, herself underweight, may lead to disastrous results, as both cow keepers and gynaecologists are aware. On the other hand, where good nutrition increases the rate of growth and the body-weight and lowers the age of puberty, there is the danger with the mammal (in which the process of egg production only, without pregnancy, places no particular burden on the individual) that the somatic tissues will develop to such an extent that the competition between them and the reproductive organs (embryo and mammary gland) when pregnancy eventually occurs will act unfavourably on reproduction and lactation (see theory of partition of nutrients, Hammond, 1943). It is a common belief among cattle breeders that well-grown heifers kept from breeding until late in life become 'shy breeders' and poor milkers, although there are no exact experiments on this point. Asdell, Bogart & Sperling (1941) found that rats bred for the first time late in life averaged only 4·9 young as compared with 6·2 for those bred at the normal time, and McKenzie (1928) found the same to be true for pigs.

There is some possibility (Bonsma, 1948) that the degeneration in size and in fertility of successive generations of European cattle bred under the hot conditions of the tropics is due to the effects of high air temperatures causing increased body temperature and inhibition of the development of the anterior-pituitary gland in the young animal. Since these effects of high temperatures can in part be alleviated by good feeding, i.e. while the calf is obtaining plenty of milk from the mother, high air temperatures may exert their effect on reproduction through their effect on general nutrition. Another much more specific action of nutrition on the anterior-pituitary gland has been described by Madsen, Hall & Converse (1942), who found that calves reared on vitamin A-deficient rations developed cysts in the anterior-pituitary gland and that as a consequence fertility was affected.

Just as the anterior-pituitary gland produces two main hormones affecting the ovaries (F.S.H. and L.H.), so the ovary itself produces two main hormones affecting the preparation of the female tract for attachment of the egg—oestrogens produced from the developing follicles, and progesterone from the corpus luteum. The supply of these from the ovary is also supplemented by their production from the placenta in the later stages of pregnancy. A proper balance between these two hormones is necessary not only for fertility but also for the maintenance of pregnancy.

Fertility is controlled in the adult at three main stages in the reproductive process: (1) by the number of ova shed, (2) by the number of these ova that become fertilized and (3) by the number of these fertilized ova that develop normally to the time of birth.

(1) The effect of nutrition on the number of eggs shed is well recognized in agricultural practice, although the mode of action of nutrition, whether on the ovaries directly, or indirectly through action on the anterior-pituitary gland or other glands of internal secretion, is still obscure in many cases.

Severe malnutrition causes breakdown and coalescence of the Graafian follicles in the ovaries, so that multiovular follicles are produced (Loeb, 1917). Malnutrition too in sheep, whether caused by lack of energy or protein in the feed (Roux, 1936; Miller, Hart & Cole, 1942) or by a deficiency of trace elements such as cobalt which act on general nutrition (Dunlop, 1944), causes delay in the onset of the breeding season and reduction also in the number of lambs born. There is, however, but little evidence at present to show whether the general lowering of body nutrition has a direct effect on the ovary itself or on the output of gonadotrophic hormones from the anterior-pituitary gland. What available evidence there is at present suggests that the former is true rather than the latter, for injection of the F.S.H. is ineffective in causing follicular growth and ovulation in sheep on a very low plane of nutrition. Where, however, the deficiency is one of vitamins rather than one of energy and protein—e.g. in vitamin B-deficiency in rats which causes cessation of oestrus—there is evidence that ovulation can be induced by injections of the anterior-pituitary hormone (Marrian & Parkes, 1929). With poultry, which make far greater actual demands on protein and energy for egg production, it is well known that the number of eggs laid is directly proportional to the intake of these nutrients. There is also a suggestion that the same is true of sheep where 'flushing' or an increased plane of nutrition before mating is well known to increase the number of eggs shed (Marshall, 1908) and the proportion of twins born, in spite of the fact that, according to Kelley (1937), this extra feeding does not speed up the onset of the breeding season, as it might be expected to do if its action were on the anterior-pituitary gland. Just as injection of gonadotrophic substances increases the number of eggs shed, so ingestion of plant gonadotrophins in the feed was found by Bodenheimer & Sulman (1946) to cause increase of litter size in the vole (*Microtus agrestis*) and to be responsible for the periodic appearance of voles in exceptional numbers; this explanation was also suggested by Heape (1931) to account for the rapid multiplication of lemmings in certain years. In areas deficient in phosphate (Du Toit & Bisschop, 1929) the ripening of follicles in the ovaries of cattle is frequently delayed, especially during lactation when an extra drain on the phosphate reserves of the body occurs; in such areas cattle and horses do not breed during suckling, and so produce young only in alternate years.

(2) The effect of nutrition on the number of eggs fertilized is largely a question of the effect of feeding on the production and vitality of spermatozoa. It is necessary for the spermatozoa to be very numerous in the semen, for although only one sperm is required to fertilize an ovum, the chances that any one sperm will be at the right place at the right time are small.

Something more than mere numbers of sperm are, however, required since, owing to the time elapsing between insemination and ovulation, the sperm often have to live for many hours (and in some species days) in the female tract before ovulation, and the possibility of fertilization, occurs. After production in the testes the sperm are stored in the epididymis and mature there. In this position they lose but little energy for they are immobile, and they retain their fertilizing capacity here for some 4–6 weeks. After ejaculation, however, and mixture with the secretions of the accessory glands, the sperm become mobile and the drain on their energy reserves begins, so that the viability test becomes a measure of their state of nutrition.

As an example of the effects of nutrition on male fertility may be quoted the observation of Laptev (1940), who found that though succulent or green feeds increase the volume of the semen, i.e. the output of the accessory glands such as the vesiculae seminalis in bulls, they do not increase the number of spermatozoa or their viability. On the other hand, both Smirnov-Ougryumov (1937) and Larsen & Sørensen (1944) found that the number and viability of the sperm in bull's semen is in direct proportion to the amount of protein in the ration.

As with production of ova there is some, but rather conflicting, evidence to suggest that sperm production may be affected by glands of internal secretion. For example, Reineke (1946) claims that the feeding of iodinated casein increased sperm production in bulls of low fertility, and it may be that thyroid and iodine deficiencies may be the cause of some sterility, although as yet little direct evidence has been forthcoming. We do not know, however, whether thyroxin acts directly on the testes or is effective through its action in speeding up body metabolism generally.

(3) The effects of nutrition on the number of the fertilized ova which develop normally to the time of birth may be brought about in two main ways, either by direct action on the development of the embryo itself, through the general level of body nutrition, or by indirect action in affecting the supply of those hormones which control the attachment of the embryo to the uterus and so maintain its nutrition. As an example of the direct action of nutrition on the embryo Wallace (1948) found that submaintenance feeding of ewes in the last 2 months of pregnancy caused such retarded development in the lamb at birth that many of the lambs were born at full term in an immature condition and so died at or shortly after birth.

An example of the indirect action of nutrition, by way of the hormones necessary for pregnancy, is the subsequent heavy lactation of rabbits that have become pregnant shortly after parturition. This leads successively to failure in production of the gonadotrophic hormone of the anterior pituitary, non-production of progesterone from the corpus luteum, atrophy of the maternal placenta and, finally, death and absorption of the young (Hammond, 1925). This foetal atrophy is particularly marked where the plane of nutrition of the mother is low. Absorption of embryos in this way is also caused by lack of vitamin E in the diet (Evans & Bishop, 1923) in rodents, but there is no evidence that this is so in cattle.

Another very striking example of the effect of feeding-stuffs in causing disturbances in fertility and especially on the birth of viable young through action on internal secretions is that observed in the subterranean clover pasture areas of Western Australia. Owing to the presence of large quantities of oestrogens in the herbage, the amount of which varies from time to time, dystocia, and often continued sterility in the ewe, is caused (Gorrie, 1946). The full details of the action of these oestrogens in the clover on the ovary and on the developing young have not yet been worked out, but when they are, they may throw light on other at present inexplicable causes of abortion, retention of embryos and sterility.

The effect of over-fatness of the mother on the development of the fertilized ovum is still a matter on which there is some doubt, as few direct experiments have been made. Eckles (1920) showed that over-fat cows at parturition had rather smaller young than those which were in thriving but lean condition, and many stockmen blame over-fatness as a cause of sterility, but whether this is effective through the action of fat in absorbing oestrogens or blocking the production of progesterone is not known. It should be remarked, however, that over-fatness may be the result, as well as the cause, of infertility.

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Spermatogenesis and Nutrition

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Before one can appreciate the significance of experimental data on the effects of nutrition on separate organs of the body it is necessary to have a clear perspective of the metabolic processes involved and of their magnitude in relation to the general economy of the body as a whole. This is perhaps more necessary with the testis than with other organs, because, for psychological reasons, this organ may be accorded an importance in the mind of man far in excess of its actual physiological significance. In addition, one should have an understanding of the methods used in measurement of sperm production and testis activity and know how these measurements are related to the physiological functions which they are supposed to assess. In this paper I deal primarily with these aspects and not with the experimental or clinical data, because I think that they are fundamental and often neglected.