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## Effect of nutrition on androgenic activity and spermatogenesis in mammals

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To define the nutrient requirements essential to the male organism for its normal reproductive function is by no means a simple matter. It is a problem of many aspects because the processes involved are subject to fluctuations even within a single species, according to climate, environmental conditions, food habits, and the age of sexual maturation. A further complication arises from the effects of so-called 'nervous', 'stress' or 'conditioning' factors which can alter the normal requirements of an individual for a specific nutrient by influencing the absorption of food, storage and utilization of metabolites in the tissues, and their excretion to such an extent that the result is 'malnutrition' in spite of adequate food composition (Ershoff, 1948). It must also be kept in mind that failures of reproduction brought about by 'malnutrition' may be aggravated by congenital anatomical as well as genetic factors. However, by far the greatest difficulty encountered in the appraisal of reproductive disorders due to 'malnutrition' is to distinguish between primary effects due to the lack of a specific dietary component such as a vitamin, a trace element, or an essential amino acid, and secondary effects arising from diminished appetite, inadequate food intake and, finally, inanition, all of which are sequelae of deficient diets. This is one of the reasons why pair-feeding is such an essential and important prerequisite for all experimental investigations on the relationship between nutrition and reproduction.

The literature on the subject of nutritionally conditioned reproductive failures in the male is vast and abounds in observations on testicular atrophy, gynaecomastia, diminished libido and impotence, associated with such conditions as diabetes, hepatic cirrhosis, atrophic glossitis, gingivitis, seborrhea, keratosis of the eyelids and others; in this category belongs also the important study of Evans & Burr (1927) on degenerative and atrophic changes in the testes and male sterility, associated with deficiency of vitamins A and E. Together, these and similar studies represent an imposing total of valuable data which have been comprehensively reviewed from time to time, in particular by Biskind (1946), Hertz (1946), Samuels (1948), Russell (1948), Mason (1949), Ferrando (1953), Meites (1953), Roche (1957), and more recently by Lutwak-Mann (1958).

Earlier investigators have relied chiefly upon observations concerning the libido and upon the examination of spermatozoa as their criteria, and were not specially concerned about the endocrine activity of the testes and the function of the accessory organs. Even in the recent postwar surveys on the effect of malnutrition on human reproduction, carried out by several teams of investigators on ex-prisoners of war and ex-inmates of concentration camps, this limited outlook tended to prevail. Yet, endocrinologists have long been aware of the fundamental fact that regression changes in the male accessory glands, which occur as a result of diminished endocrine activity of the testes, often precede the decline in the gametogenic function of the testes, and that the accessory organs respond frequently more readily than the spermatogenic tissue to both the restriction and the restoration of an adequate supply of food. Nearly 30 years ago Moore & Samuels (1931) demonstrated that a few weeks on a diet deficient in vitamin B, or a diet containing vitamin B but quantitatively inadequate, invariably led in rats to a rapid involution of secondary sex glands which, they found, could be remedied effectively by the administration of either testicular hormone or anterior-pituitary extracts. They concluded that the primary lesion caused by inadequate feeding was located in the pituitary gland, and recognized that the effects of underfeeding on the sexual apparatus resemble those which ensue after hypophysectomy. Similar conditions, referred to as 'pseudohypophysectomy', were reported in experiments carried out by Mulinos & Pomerantz (1941), Pazos & Huggins (1945) and other groups of investigators. In respect of male reproductive performance, the pathological picture of vitamin B deficiency is quite different from that resulting from lack of vitamin E, which affects primarily the gametogenic, and not the androgenic, function of the male gonad. It has to be remembered, however, that much of what is known about the 'antisterility' properties of tocopherol is derived from experiments on rats, and does not apply necessarily to other species. With regard to farm animals in particular, as pointed out explicitly by Blaxter & Brown (1952), there is little to indicate that avitaminosis E is linked specifically with gonadal function as such, or with reproduction. Caution is similarly required in other attempts to apply to man or farm animals knowledge gained from studies on nutritionally conditioned reproductive dysfunctions in the rat. Even as regards the generally recognized importance of proteins and amino acids for normal testicular function, studies on different species point to different requirements. On the whole, however, there can be little doubt that, at least so far as proteins are concerned, these rank high in general importance as nutritional factors essential for reproduction in the male. Lysine, tryptophan, tyrosine or arginine may be of unequal importance to a laboratory rodent, a farm animal or man, but nevertheless their general usefulness can hardly be doubted, particularly for the young, sexually maturing male (Leatham, 1958).

Our own interest in the relationship between nutrition and reproduction in the male has centred during recent years mainly on the effect of underfeeding on the onset of spermatogenesis and androgenic activity in the young maturing male (Mann & Rowson, 1957; Davies, Mann & Rowson, 1957). Most of our experiments were carried out with monozygous male twin calves. One animal of each pair of twin

bull calves was kept for periods of several months on a defective diet, while the control was maintained at a normal level of nutrition. The effects of underfeeding were assessed by analysis of semen collected at regular intervals by the electric ejaculation method. The appearance of the spermatozoa and their density in the electro-ejaculates served as an indicator of the gametogenic function of the testes and determinations of fructose and citric acid in the seminal plasma provided criteria for assessing the secretory function of the male accessory organs, which in turn reflects the androgenic activity in the living animal. Restriction of food intake had a marked delaying effect on the onset of secretion of fructose and citric acid, and a smaller delaying influence on the appearance of spermatozoa. These alterations in the composition of semen agreed well with histological changes in the accessory organs and testes. It was also found that the delaying effect of underfeeding on the output of fructose and citric acid in semen could be prevented or reversed by injections of chorionic gonadotrophin. From this finding we concluded that the delay in the onset of androgenic activity observed in young bull calves reaching maturity is due to the absence of adequate stimulation of the testes by the pituitary gonadotrophin, rather than to an inherent inability of the testes to produce androgens.

A problem on which L. E. A. Rowson and I are at present engaged, concerns the question whether in male twin calves the response of the male accessory organs to gonadotrophin or testosterone is the same in underfed as in normally fed animals. We are trying to solve this problem by treating twin calves, well-fed and underfed, with small doses of hormones and then studying the response of their accessory organs by analysis of semen. As yet, this problem has never been dealt with by means of quantitative chemical methods, and data so far available (Goldsmith & Nigrelli, 1950; Kline & Dorfman, 1951; Grayhack & Scott, 1952; Meites, 1953) are derived exclusively from anatomical observations. There is some evidence that the 'responsiveness' of male accessory organs to hormonal treatment decreases markedly as a result of defective nutrition, particularly if the animals are given a diet deficient in riboflavin or folic acid.

Unbalanced diets of one kind or another, and overfeeding, like underfeeding, can all lead to serious disturbances in male reproductive functions. Rats maintained from the age of 4 weeks onwards on a high-fat diet have underdeveloped accessory organs. In farm animals overfattening has an adverse effect on male fertility, and animal breeders are well aware of this danger. In man certain forms of obesity are commonly associated with sterility. Gynaecomastia occurs frequently in men who, after a period of undernourishment, have reverted to a normal, or excessively high, level of nutrition. This observation has been made repeatedly after the war on the male population of liberated countries and also on ex-prisoners of war undergoing rehabilitation. The precise mechanism underlying this phenomenon is by no means clear but it is believed to involve some definite nutritionally conditioned changes in the enzymic rate of inactivation of oestrogens and androgens by the liver. A great deal more remains to be done before we shall arrive at the mechanisms concerning the various fundamental problems of hormone-nutrition interrelationships in reproduction. The immediate and perhaps most formidable task is to

discover the possible points of interaction between specific food constituents (particularly vitamins) on the one hand, and the pituitary and gonadal hormones on the other, so as to be in a position to decide in each instance whether a given deficiency is the outcome of (1) a failure in hormone production or release by the endocrine organ, (2) a loss of responsiveness on the part of the target organs, or (3) an increased or decreased rate of hormone metabolism and destruction in the animal tissues.

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*Afternoon Session*

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**Nutrition and reproduction in insects**

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The reproductive activity of the male insect is little affected by nutrition; but all kinds of nutritional factors may influence the production of eggs in the female. These statements can best be illustrated by specific examples.

Females of the blowfly *Lucilia* require at least one meal of protein before eggs are laid, whereas it is not necessary for the fertility of the males (Evans, 1935; Mackerras, 1933). The housefly *Musca* needs both sugar and protein as well as water; it lays no