
VOLUME 62 2002

HORMONES IN RELATION TO ANIMAL PRODUCTION

John Hammond*

WHEN FEEDING STUFFS are digested and the nutrients are absorbed into the blood stream there is competition for them from the different parts and tissues of the body. During foetal development 'organizer substances' are produced which determine the order of development of the various parts and tissues of the body, that is, they give priority of nutrition to each in orderly succession. Thus with the tissues, brain and nerve are given first priority, bone second, muscle third, and fat last. In the growing animal therefore when the plane of nutrition is reduced the various tissues suffer in the reverse order; the last tissues to be developed are the first to suffer. As the animal grows up, the function of these 'organizer substances' is taken over very largely by hormones, chemical substances produced in certain glands which secrete into the blood stream. These hormones act specifically on certain cells or tissues in the body to stimulate their growth or function so that they are given a temporary priority of nutrients from the blood stream.

In animal production, where we are interested in directing the nutrients given to the animal mainly towards the formation of some particular product, such as reproduction, milk or wool, these hormones are all-important therefore in increasing the efficiency of production. Since the hormones act by directing the use of nutrients rather than their supply, the effects produced by any given dose of hormone will depend on the nutritive level of the animal.

The Hormones

Of all the glands of internal secretion, the pituitary gland is the most important, for not only is it closely connected with the nervous system and therefore is capable of response to environmental conditions and stimuli, but it also acts as a regulator by its action on other glands of internal secretion. For example, the anterior pituitary responds to daylight hours in some species such as the sheep by increasing or decreasing the output of gonadotrophic hormone and so the output of secondary hormones from the ovary; also by changes in the amount of thyrotrophic hormone secretion the amount of thyroxine pro-

Emeritus Reader in Animal Physiology, School of Agriculture, Cambridge University, England.

duced by the thyroid gland varies with the time of year. Regulation of hormone action is also produced in other ways. In an autocatalytic chemical reaction when the product accumulates the rate of its production slows down. Likewise, for example, where large quantities of oestrogen are circulating in the blood, as in the caponization of fowls by implantation of stilboestrol, the formation of gonadotrophic hormone by the anterior pituitary is prevented and so the sex organs fail to function.

Now let us consider the main hormones connected with the various animal products so far as they are at present known.

Reproduction

The primary hormones concerned in reproduction are the two gonadotrophic hormones F.S.H. and L.H. from the anterior pituitary which act on the ovary to produce follicles and corpora lutea respectively. These in turn produce oestrogens and progesterone respectively, and lead to the production of the symptoms of heat and secretion of the uterine fluids necessary for pregnancy respectively. While oestrogens and progesterone are simple chemical compounds and can now be produced cheaply by synthetic means, F.S.H. and L.H. have a protein structure and syntheses have not yet been possible. Cheaper sources of these two latter hormones can be obtained respectively from the blood serum of pregnant mares (P.M.S.) between 45 and 90 days and pregnant women's urine (P.U.)

The balance between F.S.H. and L.H. production by the anterior pituitary varies between the different species of farm animals in a graded series—mare, sow, ewe and cow. F.S.H. is high in the mare and L.H. high in the cow, and this accounts not only for their different reproduction patterns, but also for the types of sterility they are most prone to. For example, in the mare oestrus is prolonged owing to the low L.H., and so injection of L.H. at the time of mating, causing ovulation, increases the chances of fertilization. On the other hand, in the cow, and to a lesser degree in the sheep, L.H. is high, and so ovulation is often caused before there is time to develop the signs of oestrus and so 'silent heats' (ovulation without oestrus) are frequent under conditions when the activity of the anterior pituitary is low.

F.S.H.

Not only is P.M.S. cheaper than the F.S.H. from the anterior pituitary but it is not easily destroyed by the body, so that one injection will remain active for about four days as compared with only about twelve hours for F.S.H. from the anterior pituitary. The same thing probably applies to the different forms of P.M.S., the purified substance being more easily destroyed than the freeze-dried and this again than the raw frozen serum. F.S.H. is injected subcutaneously so as to have as prolonged an effect as possible.

For cattle, P.M.S. has been used to overcome the anoestrum in heifers and young cows during the late winter; about 2,000 to 3,000 i.u. is required. It should not be injected in 'silent heat' cows unless the corpus luteum is first squeezed out, otherwise the only result will be to form cysts. It is useless when heifers are in a very low state of nutrition when follicles with antra are not present in the ovaries. In beef breeds, about 2,000 i.u. injected some four days before the expected heat period will on the average give twin ovulations, although calves born as a result will vary from 1 to 3. When heat cannot be easily detected, as in cows suckling calves, the corpus luteum can be squeezed out and the P.M.S. injected at the same time. Cows producing twins or more need to be fed well for about six weeks before parturition to ensure strong calves at birth.

Research has not proceeded far enough yet to exploit the use of P.M.S. for the purposes of egg transplantation in cattle (this will be considered below under sheep), but when perfected will reduce the cost of beef production by enabling the Jersey cow not needed to breed replacements to produce an Aberdeen Angus calf. Up to 25 fertilized eggs and perhaps more can be obtained at a time from a cow; but to be of use in practice they need to be inserted in the uterus by methods similar to those used in A.B. However, if the eggs are inserted 5 days after oestrus when the mucosa is under the influence of progesterone, infection is caused, and if inserted in the oestrous stage they will not survive. Possibly insertion in conjunction with hormone injection may be the solution.

Young bulls unwilling to serve may often be induced to start by injections of 5,000 i.u. P.M.S. one to two days before they are tried. Although sperm production can be prevented by removal of the anterior pituitary this acts by way of general nutrition of the testes, and so far no hormone has been found to increase sperm production.

For sheep, P.M.S. has been successfully used to increase the lambing percentage, which is one of the chief factors in lowering the cost of fat lamb production. A raddled vasectomized ram is run with the ewes and 12 to 13 days after oestrus they are injected with P.M.S., 400 to 600 i.u. according to activity, and turned in with the fertile ram. By this means the lambing percentage can be increased by about 40 in low fertility breeds to about 20 in high fertility ones. As with cattle when multiple pregnancies are high, the ewes should be well fed before lambing if strong lambs are required at birth. No immunity is set up by these hormone injections and flocks can be treated successfully in successive years.

When required, the onset of the breeding season can be speeded up; ewe lambs not forward enough to be bred from in their first autumn can be made to breed in the spring and a certain number of ewes can be made to breed twice a year by the use of P.M.S. in conjunction with injections of progesterone. In all sheep at the beginning of the breeding season, there is a 'silent heat', ovulation occurs without oestrus; the progesterone from the corpus luteum probably develops the uterus so that at the following ovulation the substances necessary to develop the fertilized egg are produced. To produce this artificially, daily injection of 25 mg synthetic progesterone are given for about six days and this is followed one day after the last one by an injection of about 750 i.u. P.M.S. and the ewes are turned in with the ram; service should occur within about four days.

Within the breeding season when larger doses of P.M.S. are given, a larger number of eggs are shed and up to about 30 at a time can be fertilized. All but the maximum number of young normally produced by the ewe, however, atrophy at an early stage. That this is not due to any defect in the eggs themselves is shown by the fact that, if the fertilized eggs are transplanted two at a time into other ewes at the same reproductive stage, they will develop normally. By this means, genetically good ewes have been made to produce twelve lambs in a season. In the writer's opinion, the number of fertilized eggs which can survive depends on the amount of a not yet discovered 'special growth hormone' or substance present in the uterus, just as the number of eggs ripening in the ovary depends on the amount of F.S.H. in the blood stream. Fertilized sheep eggs will survive in a rabbit's uterus for about five days and can then be transplanted back to a ewe and developed normally; this may be useful in reducing the cost of importing pedigree stock.

L.H.

As mentioned above, the use of L.H., given intravenously for quick action, speeds up ovulation and can be given to 'long heat' mares just after service, or after insemination when the sperm may be lacking in vigour, to increase the chances of fertilization. Since the sow is rather like the mare in its hormone balance, it is possible that the conception rate in A.B. might be improved by injection after insemination early in heat.

Milk Production

During pregnancy the ovarian hormones, oestrogen and progesterone, are supplemented by supplies of these hormones from the placenta. It is the raised output and balance between these hormones which acting possibly by way of a lactogenic hormone in the anterior pituitary stimulates the development and secretion of the mammary tissue.

In the cow where the natural hormone balance is on the L.H. side, implantation of stilboestrol tablets (without an excipient) at high dosage levels (sixty 30 mg tablets) will bring a heifer or even a steer into milk within about six weeks. The amount of milk produced by such implantations depends not only on the state of nutrition during this period but also on the extent of the previously developed duct and alveolar system. For example, steers and freemartins, where the duct development is limited, yield but small quantities of milk after treatment. The hormones concerned in duct development have not yet been discovered, although there is some indication from species like the rabbit that oestrogens are concerned. In any attempt to increase yields materially by hormone treatment, it will be necessary to attack this problem. Swett's finding in U.S.A. that the amount of duct tissue in the calf at four months old is related to the adult yield, falls in line with this. While on the development of secretion there is evidence that the oestrogen acts indirectly by way of lactogenic anterior pituitary hormones, increase in the size of the teats is probably due to direct action on the teat tissues.

The rate of milk secretion can be increased by thyroxine which speeds up the metabolism of cells generally throughout the body. When feed supplies are limited, there is little to be gained by its use for it also speeds up the metabolism of tissues other than the mammary gland. However, when feed supplies are not the main consideration, it has been found worth while to give it to ewes suckling fat lambs up to, at any rate, the tenth week of lactation. The rate of milk secretion has been materially increased by injections of growth hormone, particularly in the early stages of lactation. At the present cost of growth hormone, however, this is not a commercial proposition.

The 'let-down' of milk caused by oxytocin released from the anterior pituitary by nerve stimulus to the hypothalamus is necessary for the continuance of milk secretion at a high level. In the improvement of milk production in the primitive breeds of cattle, the first step necessary is to break the 'conditioned reflex' for let-down to the suckling calf only. Whether or not there is any connection between this 'suckling reflex' and the output of F.S.H. and L.H. by the anterior pituitary is still an open question. Between and within species there is an indication that the larger the number of times per day the young are suckled the less readily the female comes into heat during lactation.

Meat Production

The main hormone affecting growth is the growth hormone of the anterior pituitary gland; when injected into animals it increases the efficiency of nitrogen retention and results in increased growth of bone, muscle and skin. It is a protein substance and so will be difficult to synthesize; so far, no cheaper alternative forms to extracts of ox anterior pituitary have been discovered. The thyroid also affects growth but the addition effects are small and require to be carefully adjusted to internal production in the young growing animal; removal effects, however, are striking.

The most striking effects on growth, of sufficient size to warrant commercial application, are those obtained by implanting or feeding oestrogens. Synthetic progesterone and testosterone have also been used, either alone or in combination with oestrogens, but their effects are smaller and their present price too high. The synthetic oestrogens most commonly used are stilboestrol or hexoestrol, but the latter is probably better since, when given at the same dose, the side effects and the effects on man are less. Provided the hormone is fed or implanted in the base of the ear which is cut off from the carcass at slaughter, there is no danger in the meat for human consumption.

The dose given is most important: if doses beyond the optimum are given, not only is there no additional growth effect but harmful side effects (such as raised tail-head, growth of teats and udder, and prolapse of rectum or vagina) may be produced. As tested in Britain, the optimum doses given some 100 days before the expected slaughter of the animal, are for steers 10 mg per day incorporated in the concentrate feed, 60 mg implanted in the base of the ear for steers on winter feed, 45 and 35 mg respectively for steers and heifers on summer feed, and 12 mg for wethers and ewes.

The cost in materials is about 8d. for cattle, 1d. for sheep, plus labour costs, by the implantation method, and slightly higher for feeding. On the average of a large number of experiments in Britain, the expected increased gain in liveweight is about 0.5 lb per day for steers making normal gains of about 2 lb per day. In heifers it is rather less and in wethers and ewes about a 20% increase is obtained. Different lots of cattle and sheep vary somewhat in the gains made; reasons for these have not yet been determined.

The composition of the increase made is mainly bone, muscle, water in the connective tissue,and, to some extent, skin. It diverts nutrients in the blood stream to these tissues and not to fat so that it should not be given to animals such as young animals or those on a low plane of nutrition where the carcass is likely to be deficient in fat or otherwise they will be degraded. On the other hand, it is most useful under good feed conditions where for today's requirements the amount of fat required—especially kidney fat, is less than formerly. From the limited number of experiments done on pigs, there appears to be little or no increase in liveweight, but there is some indication that it reduces the amount of back fat on hog pigs, making them more like gilts. This effect on the tissues of mammals is quite different from that on birds where caponization by the implantation of hexoestrol increases the fat in the muscles.

There are two theories as to the mode of action. The first, that the oestrogen stimulates the adrenal to increase the output of androgenic substances, seems unlikely since greater effects on growth can be obtained by the implantation of oestrogens than by testosterone. Moreover, the amount of muscle is increased in parts other than the neck and there is no evidence for the darkening of muscle colour as would be expected if testosterone was the cause. The second theory, that oestrogens damp down the gonadotrophic activity of the anterior pituitary and so allow increased production of growth hormone, seems the more likely since the effects of oestrogen implantation are very similar to those of growth hormone injection. Against this, it could be argued that heifers, which have natural oestrogen secretion in their blood, are smaller and not larger than steers. The cause for this sex difference in size is, however, not due to hormones but to sex-linked organizer substances in the embryo, for in sheep no increase in the number of muscle cells occurs after the third month of foetal life and the difference in size between male and female is due, not to differences in size of cells, but to differences in the numbers of muscle cells determined during foetal life.

Wool and Hair Growth

Since much work has been done on this subject in New Zealand there is no need to detail this work here, but only to note a few results which have been independently obtained in Great Britain.

In poultry, the autumn moult can be prevented by increasing the daylight to dark ratio and moulting produced by decreasing it. The action is probably through the thyrotrophic hormone of the anterior pituitary.

In sheep, the direct effect of thyroxine is to increase fleece weight by increased length growth and not fibre thickness growth as is produced by a raised plane of nutrition. Preliminary experiments seem to show that injections of growth hormone soon after birth increase the number of secondary follicles developing; but whether this is merely a speeding up of their development or a permanent increase, is not known.

DISCUSSION

Q: : *What is going to be the effect of repeated superovulation upon the lifetime breeding performance of donor cows?*

A: : We do not know; it has not been tried in cattle. Palsson in Iceland has tried it for three successive years in ewes and the results in the last year were as good as in the first.

Q: : *Has Dr. Hammond any information on the origin of the additional eggs ovulated after hormone treatment, that is, do they come from the supply of ova for future ovulations or are they ova which would, in the absence of hormone treatment, have been lost in the formation of atretic follicles as the dominant follicle develops toward ovulation?*

A: : The hormone does not cause egg formation in the ovary, but only ripens those that are there. A new born calf has about 75,000 eggs in the ovary, many of which atrophy during its life. The hormone merely ripens those follicles which are in a fairly advanced stage of development at the time it is injected.

Q: : *Has Dr. Hammond any idea why so many of the artificially induced lactations in cattle have been of a disappointingly low level?*

A: : One reason why disappointing results have been obtained is that the heifer has not been 'steamed up', that is, given extra food after the tablets have been implanted. The effect of any given dose depends on the level of nutrition. We have, however, obtained 1,000 gal lactations in heifers in one winter. During wartime, in the vicinity of Cambridge, we obtained over 100 tons of milk from implanted heifers. There is much, however, we do not understand about the treatment—for example, why is it much more effective in heifers than in dry cows?

Q: : *Would Dr. Hammond comment on the effect of stilboestrol/hexoestrol treatment upon the dressing out percentage since in Australian results we found that, although the treatment caused increased gain in body weight, this was not matched by carcass weight which showed much smaller increases?*

A: : One reason for this is that the treatment also adds slightly to skin or hide weight; it is known that injections of growth hormone also do this. Reduction of the amount of fat in the carcass would also reduce carcass dressing out percentage.

Q: : *In the Gisborne area, pre-lambing shearing has led to apparently greater feed utilization and consequent occurrence of over-large lambs in ewes bearing only one lamb with an associated lamb mortality at parturition. Farmers, therefore, have been recommended to keep their ewes in good condition and to avoid overfeeding. Would Dr. Hammond comment on this recommendation?*

With reference to Swett's work on the palpation of the udder in young dairy stock, it was our experience at Edinburgh that at the age suggested for this method the total mammary tissue was restricted largely to interlobular connective tissue and palpation did not appear to give any indication of relative mammary development. Other workers too have failed to confirm Swett's results.

Would Dr. Hammond comment on the very wide variations found in practice in the ratio of length (crown to rump) to body weight in lambs found dead after birth. Lambs in which no gross evidence of prematurity is obvious have been observed to show wide variations which would suggest that death was not due to total foetal nutrition but rather to some abnormalities in the placenta or uterus.

A: : In the 'steaming up' of both ewes and cows before parturition we aim at getting the dam into a hard thriving condition and not a fat flabby one. This is an aid to parturition as well as lactation.

I visited Swett some years ago and found that in his calves I could feel distinct differences in the development of the udder tissues at four months of age. In older calves, however, this was not possible owing to the deposition of fat. This interlobular connective tissue provides the basis for the development of the mammary ducts; this is almost non-existent in male calves.

Length growth is much less affected by the plane of nutrition than is weight. I am certain that in Great Britain, at any rate, large numbers of lambs are lost owing to inadequate feeding of the dam before parturition. Possibly in New Zealand there may be other causes in addition.

In moving a special vote of thanks to Dr. John Hammond, Dr. C. P. McMeekan said:

'It is seldom that we in New Zealand are able to meet, in the flesh, the men who have written the textbooks on which we have all been trained.

'That you, Dr. Hammond, are prepared to come so far to give us your guidance and helpful criticism is a great stimulus to us all. For no man in the Commonwealth has such a breadth of knowledge on matters pertaining to animal production. Almost the whole of the work you dealt with in your address sprang from your own laboratory or from laboratories stimulated by you. This must be of considerable encouragement to us.

'We should remember, too, that none of us here have had to face the physical difficulties in our facilities that Dr. Hammond has had to face. This shows that it is not facilities which determine the quality of the work, but the calibre of the man himself.

'The development of the technique for transplanting fertilized ova is of special significance. I was present in Hammond's laboratory some 20 years ago, when the idea was first conceived. I saw the early failures, but they were never allowed to dampen the enthusiasm of the workers concerned because of Hammond's encouragement.

'Perhaps his greatest contribution has been his ability to train younger people. No man has believed more in the importance of staffing the countries of the world with men of scientific ability and leadership. Hammond has students in almost every country in the world—Bonsma in South Africa, Palsson in Iceland, Pincus in America, Verges in the Argentine, to mention but a few. There are at least four of his students here tonight.

'Dr. Hammond, on behalf of all members of this Society, I wish you a long and happy life, and ask you to convey our best wishes to the British Animal Production Society.'