RESPONSES OF SHEEP TO THYROXINE IMPLANTATION

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IT IS NOW THREE YEARS since the first report was made to this Society of the response in wool growth which could be obtained by implanting thyroxine pellets in sheep (Hart, 1955). As may be expected, a considerable amount of experimental work has been completed at Lincoln since then by means of laboratory pen trials, involving relatively small numbers of animals, and field trials on commercial farms where larger numbers of animals were available.

Results with respect to wool from some of these trials have already been published elsewhere and it must be admitted that they have so far been encouraging (Hart, 1957; Coop, 1958). With this point in view, and knowing that a process is being dealt with which involves the administration of fairly substantial amounts of exogenous hormone to the animal, thus in all probability bringing about disturbances in the animal's natural hormone status for an unknown period of the year, it became imperative that some preliminary information should be obtained on the effect, if any, of this treatment on the other productive functions of sheep. Of these, the ones considered of prime importance were longevity, reproduction and lactation. To some extent associated with these were the questions of dose rates, possible differential breed responses, and the accepted fact that the two-tooth ewe, being not yet physiologically or endocrinologically mature, would doubtless respond differently from the mature ewe. Concurrently with this and always liable to complicate the issue, was the problem which most experimenters with hormones meet sooner or later, namely, the constantly changing hormone status of the individual animal from season to season and week to week, which results in wide ranges of responses occurring within groups and complicating the interpretation of results.

Experimental

All animals used in these trials were randomized into their groups on an age basis, and identified, in the case of studs, by individual ear-tags, with flocks by paint branding of groups, or numbers. The groups were then run as one mob from tupping

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onwards and subjected to the management which was normal for that particular district and class of stock.

At lambing, daily records were kept of all births, and each day's drop was shedded off from the ewes yet to lamb, thus making sure accurate records were kept.

Lactation records were obtained by individually tagging twin-bearing ewes and their lambs and implanting alternate ewes in order of lambing thus preserving an even distribution for date of lambing. The lambs were then weighed at stated periods throughout lactation, being run as one mob continually until weaning.

Fleece records were obtained in the manner previously described (Hart, 1957), each fleece being identified by either group brand or individual number, then weighed and sampled. In some cases the fleeces were graded in the shed; otherwise grading was carried out on the samples subsequently, when measurements for length and count assessments were also made in the laboratory.

Results

Longevity

It will be appreciated that no definite evidence can yet be reported on this point as repeated annual doses from the two-tooth stage onwards throughout the life of the animal will be necessary before worthwhile conclusions may be drawn. Nevertheless, it can be stated that in pen trials some five-year-old ewes have had three successful annual treatments of thyroxine with no increase in mortality from that of their controls. Also, the College stud ewes which are due this season for their fourth successive treatment, have yet to show any discernible ill effects. The lifetime studies commenced two years ago with the College stud flocks as the material.

Reproduction

The thyroxine implants used in these experiments, in addition to other effects, usually bring about a loss of liveweight following implantation. It was in fact this liveweight loss which was first used as a measure of the extent to which the dose was biologically active (Hart, 1954).

The loss following implantation (60 to 90 mg) can be expected to commence about five days afterwards and continues until between the 14th and 21st day when it usually reaches its maximum. From this point onwards, mature sheep gradually

recover the lost weight during the ensuing months. In pen trials where food intake has been controlled, the recovery has taken place without any alteration in the rationing which is kept at a constant level so that the control animals neither gain nor lose liveweight.

Two-tooths take much longer to recover and appear to require some additional feeding when given the doses of 60 to 90 mg used for adult ewes.

Study of the liveweight reponses of ewes to autumn thyroxine implantation for increased wool growth suggested that it might be artificially inducing in the animal similar types of weight changes to those which take place when ewes are made to follow the well-known practice of flushing. Wallace (1951) showed that where ewes were mated whilst they were gaining weight through additional feeding—*i.e.*, flushing—increased lambing percentages would result.

The first experiment to investigate this possibility was carried out in the autumn of 1955 with a group of five-year-old Border Leicester halfbred cross ewes. Fifty of these ewes were implanted with 90 to 100 mg of thyroxine about fourteen days prior to putting the rams out on the first of March. The resulting lambing increase of 32% over the controls was both significant and spectacular.

Attempts to reproduce this result during the 1956 breeding season with the College fat lamb flock and a special slaughter flock were also successful. In this latter trial designed to show the effect of thyroxine on egg production, 140 ewes were randomized into two groups, one being implanted with 90 mg of thyroxine, the other retained as controls. Fertile raddled rams were run with the ewes, as one mob, from the tenth day of implantation onwards. Records were kept twice daily as the ewes came into oestrus and were served by the ram. All mated ewes were slaughtered within five days of the end of oestrus and a careful study of their reproductive organs made, involving the recovery and assessment of liberated ova and counting of corpora lutea. The ewes were fed so that the controls neither gained nor lost weight throughout the experiment. The increased ovulation rate is shown in Table 1 and, although substantial, just fails to reach 5% significance with these numbers.

The field trial results for 1955 and 1956 are shown in Table 2, the increases being statistically significant for the first two trials only.

TABLE 1: OVULATION RESPONSE

Treatment	No. of Ewes Tupped and Slaughtered	No. of Ova	Potential Lambing (%)
Control	65	80	123.1
90 mg thyroxine implant	69	95	137.6

TABLE 2: FERTILITY

Experiment	Treatment	Ewes to Ram	No. Lambs Born	Per Cent.
1955	Controls	50	52	104.0
Farm trial crossbred B/L ewes, 5-year-old ewes	90 mg thyroxine implant 100 mg thyroxine implant	50	69	138.0
1956	Controls	262	297	113.3
College fat lamb flock, mixed ewes	90 mg thyroxine implant	182	220	120.8
	60 mg thyroxine implant	187	247	132.8
1956	Controls	46	58	126.0
Stud-Romney breeder, 4-tooth and older	90 mg thyroxine implant	54	72	133.2

Table 3 shows the fertility results from a 1957 complete farm field trial, where all ewes on the farm were included, approximately two-thirds of the flock being treated and one third left as controls, there being an equal number of two-tooths in each group. The differences beween treated and control ewes are significant for all ages, but this is not so if two-tooths only are considered.

LACTATION

There is ample evidence that under certain conditions lactation in cattle and goats can be affected by substances capable of acting on the thyroid gland (Blaxter *et al.*, 1949). Reports

TABLE 3: FERTILITY (ALL AGES)

Treatment	No. of Ewes Lambing	No. of Lambs Born	Lambs/ Ewes (%)	Ewes Barren (%)
Control	335	395	117.9	3.7
60 mg thyroxine (M.A. ewes) 30 mg thyroxine (two-tooth ewes)	546	717	131.3	5.0
	TWO-TOOTHS			
Control	96	104	108.3	6.9
30 mg thyroxine	87	98	112.6	6.9

as to the effect of these substances on lactation in sheep are difficult to find and it appeared that little work had been done on this aspect, although recently Singh *et al.* (1956) were able to show that Shropshire ewes with high thyroid activity tended to produce faster gaining twin lambs to three weeks of age than ewes with low thyroid activity.

College measurements commenced at the 1955 lambing with a mob of Corriedale ewes at Ashley Dene. A number of the in-lamb ewes were implanted with 90 mg of thyroxine on 29 June, 1955, approximately 8 weeks prior to their lambing; of the remainder of the mob when it came to lambing, each second ewe to lamb having twins was implanted with 90 mg of thyroxine between 2 and 3 weeks after lambing. The final numbers of lambs in the groups were as follows:

Control	14 lambs
July implants	8 lambs
September implants	10 lambs

Figure 1 shows the average group lamb weights in days throughout lactation; both treated groups have grown at a greater rate than the control, the differences between the treated groups and the control group being significant.

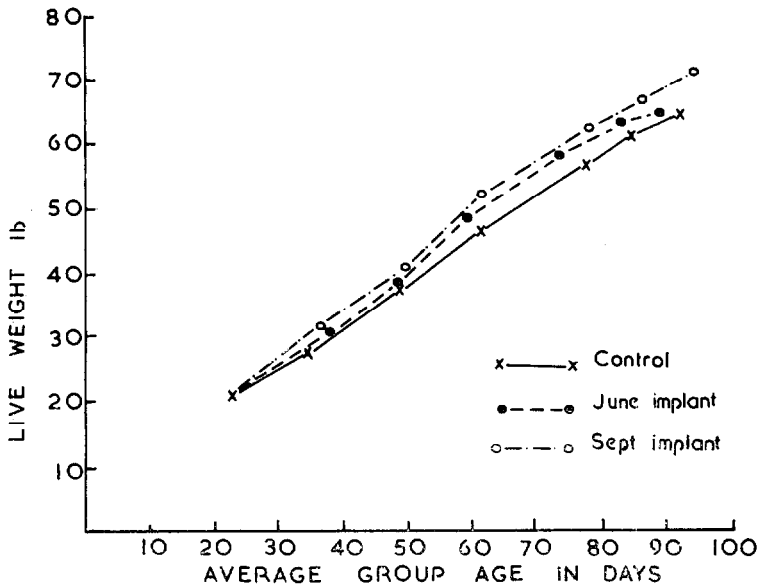

Fig. 1: Effect of thyroxine on lactation (twins only).

As the result of this increased growth of twins suckled on mature ewes it was decided to record measurements on the growth rate of twin lambs suckled on two-tooth ewes.

Purebred stud Romney two-tooth ewes were used for this trial and divided into two groups, one of which was implanted with 90 mg of thyroxine just prior to mating. At the subsequent lambing, birth weights and weaning weights were obtained for the lambs. The average daily gain from birth to weaning for twins from two-tooths was as follows:

22 lambs suckling control ewes gained 0.5 lb per day.

14 lambs suckling thyroxine treated ewes gained 0.6 lb per day.

The difference of a tenth of a pound per day in favour of the thyroxine treated group is significant.

Bearing in mind the strong correlation which exists between milk production and twin lamb growth, it appears that both the mature and two-tooth ewes' ability to lactate has been stimulated by the thyroxine implants.

Wool Production

The effect of thyroxine implants in increasing the weight of the fleece, as well as improving the grade of the wool produced on mature sheep, has been well demonstrated (Hart, 1957; Coop, 1958). All that remains now is to determine the optimum dose for mature ewes and also for the two-tooths, although in the light of present knowledge it appears doubtful if the use of thyroxine for wool stimulation purposes only on two-tooths may be justified. Preliminary figures from some of the 1957 trials show no wool response in two-tooths from 30 and 40 mg implants but a possible slight increase in lambing percentage compared with 60 and 90 mg implants which give some increase in wool weight and quality but indicate a possible lowering of lambing percentage.

Regarding mature ewes, Tables 4 and 5 show the results for fleece weight and quality from the complete 1957 farm trial. The increase has fallen to 5% with the lower dose of 60 mg of thyroxine which was used in the trial this year. However, the

Table 4: Fleece Weights

Treatment	No. of Ewes	Ave. Fleece Weight	Increase (lb) (%)
Control	369	10.0	
60 mg thyroxine (M.A. ewes) 30 mg thyroxine (Two-tooth ewes)	599	10.5	0.5

TABLE 5: COUNT, GRADE

Treatment	No. of Ewes	Ave. Count	Ave. Grade
Control	369	7.9	9.7
60 mg thyroxine (M.A. ewes) / 30 mg thyroxine (Two-tooth ewes)	599	7.9	9.9

writer believes that the optimum dose for mature sheep will be somewhere between the 60 and 80 mg mark, depending slightly on breed and condition of sheep.

It is interesting at this point to analyse the 1957 complete farm trial results. Preliminary calculations indicate that the farmer concerned has:

(1) Produced one extra bale of wool
(2) Improved the quality of all wool from treated sheep
(3) Gained 72 extra lambs

at the cost of approximately 2s.0d. per treated sheep for materials, and 2½ to 3 hours' work in implanting the flock.

Discussion

Four responses—liveweight loss, reproduction, lactation and wool growth—resulting from the implantation of thyroxine have been reported which are certainly of physiological and academic importance. It may be early yet to decide the economic application or value of these responses, for a considerable amount of research still needs to be done before a full understanding of the functions and interactions of this hormone is possible. For example, it was only in January, 1958, that it was learnt that all the new batch of the hormone produced for use in 1957 was of a more crystalline nature than that used in the trials reported in this paper and all previous work. This means that the crystalline material was not as easily leached out into the body tissues, and resulted in little or no liveweight loss, no increased fertility and a probable reduction in the magnitude of the wool response. Thus it appears that the value and interpretation of most of the 1957 results must be limited.

It is apparent, therefore, after over five years of experimental work, that this whole subject is an extremely complicated one and the physiological reactions of the sheep which result from the functioning thyroid gland and its secretions may be far

more complex than has hitherto been believed, and that in spite of the title to this paper no claim is made to a full and complete knowledge of all sheep responses to thyroxine.

Acknowledgments

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DISCUSSION ON SYMPOSIUM

Q: : *I was interested in Dr. Ferguson's finding that the maintenance requirement in sheep was related to the unit power of body weight rather than to some fractional power. Were the sheep of the same age and breed, with weight differences being due to nutrition or were there differences in age and size of skeleton?*

Dr. Ferguson referred to a 'family of curves' of diminishing increments of wool growth for individual sheep fed increasing amounts of feed. Does he also get a similar family of curves from different levels of protein in the ration?

DR. FERGUSON: : Our data were obtained from adult sheep of two different breeds. The main variation in body weight was due to differences in frame size rather than to differences in age or condition. The data were insufficient to define closely the power of body weight which is proportional to maintenance requirements for sheep in pens and our conclusion that unit power is correct is only tentative.

The protein percentage of the ration does not appear to affect the efficiency of wool growth until levels somewhere between 15 and 20 per cent. crude protein are reached. Further work is being carried out on this question.

Q: : *Were there any differences in the wool growth of lambs from the control and thyroxine treated ewes? Were there any differences in the skin of the lambs which might affect tanning?*

DR. ROSS: : No measurements were made on either wool growth or the skin of the lambs.

Q: : *Did I understand Dr. Ferguson to say that he had information on thyroxine responses in different breeds? Would there be a difference in the response of Merino and Romney sheep?*

DR. FERGUSON: : No direct comparisons have been made between different breeds in Australia. Differences in feed intake and environmental temperature make it difficult to compare results on the Merino in Australia with results on the Romney and Corriedale in New Zealand.

Q: : *Was the thyroxine used in Dr. Ross' trial of the lower activity type?*

DR. ROSS: : The thyroxine used was of the "high" activity type.

MR. HART: : Only the thyroxine used in the 1957 trials was of the low activity type.

Q: : *In the model relating feed intake and body weight change set up by Dr. Ferguson the implication is that a unit of body weight gain is equivalent to a unit of body weight loss. What was the nature of the association between body weight change and wool response in the trial reported by Dr. Ross?*

DR. FERGUSON: : The apparently linear relation between feed intake and body weight change does imply that the storage of feed energy as body tissue prior to its expenditure for maintenance does not involve any wastage. However, such a conclusion assumes that the energy content of body weight gain or loss is similar and that the maintenance energy requirement of sheep fed on sub-maintenance intakes is not reduced.

The relation between feed intake and body weight change is not likely to remain linear as sheep are kept on the different intakes long enough for them to differ appreciably in body composition which would induce both in alteration in the energy content of body weight change and an alteration in maintenance requirements.

DR. ROSS: : The results showed only a trend suggesting that those sheep which lost the most weight following the thyroxine implantation gave the best wool growth response.

DR. L. R. WALLACE: : Dr. Ferguson has shown that when thyroxine has been administered there is an increased level of food intake and increased wool production. This has to be taken into account in interpreting the results reported by Dr. Ross and Mr. Hart where their sheep were run together. Competition for pasture between treated and control animals may have resulted so that the effects on wool growth may have been quite different had the thyroxine treated and control animals been grazing on separate areas.

MR. LEWIS: : The competition effect referred to might apply under conditions of limited feed supply but in the present trial where feed was plentiful it was doubtful if this effect did in fact operate.

DR. L. R. WALLACE: : The body weight curves for the control animals do not appear to justify your assumption.

MR. LEWIS: : The feed was plentiful but for a short period in May the sheep did not appear to eat much of the feed.

DR. FERGUSON: : In a field trial to examine the commercial possibilities of thyroxine treatment either the wool growth data should be adjusted for body weight and intake differences or conditions established so that these differences do not invalidate the comparison between the groups. While a difference in the stocking rate between treated and control groups may ensure that each group obtains the same total amount of feed, it will not prevent a difference in body weight developing between the groups if *ad lib.* grazing is available. To prevent body weight differences developing between the groups some form of restricted grazing is necessary.

DR. D. S. FLUX: : There is evidence that competitive effects can occur between animals in the presence of adequate pasture. The relation between thyroid activity and lactational performance as measured by weight increase of lambs by Singh *et al.* referred to by Mr. Hart does not presuppose a causal connection between the former to the latter.

Q: : *In the farm trial described by Mr. Hart could not the results have been affected by the greater proportion of two-tooth ewes in the control group? In this trial was there a separate comparison made of the mature ewes?*

MR. HART: : It was not possible to make a separate comparison for wool growth but it could be expected that the higher proportion of two-tooths in the control group would tend to raise the mature ewe average, rather than lower it.

Q: : *The effect of thyroxine on lactation was measured by Mr. Hart in terms of lamb growth rate. In what way were the curves shown significantly different?*

MR. HART: : Analysis of variance of the differences between the points for similar stages of lactation showed them to be significant.

Q: : *Dr. Ross indicated that in the ewes treated with thyroxine those which showed the greatest loss in body weight also gave the best response in terms of wool. Was there any relationship between this responsiveness and initial level of production?*

DR. ROSS: : There was no significant relationship between wool production for the pre-implantation period and response to thyroxine as assessed by production of oven-dry wool per square centimetre.

Q: : *Did wool breaks occur in any of the sheep treated with thyroxine? Massey sheep treated with larger amounts of thyroxine than those reported in this symposium showed distinct breaks in their wool 28 days after implantation.*

MR. HART: : All our observations on "break" show a reduction in the amount occurring in the wool of thyroxine treated sheep.

DR. ROSS: : There was no sign of any break following thyroxine implantation. The 'lambing break' which occurred 5 to 6 months after implantation was less severe in the thyroxine treated group.

Q: : *Would Dr. Ferguson comment on differences between administration of thyroxine by infection as against implantation?*

DR. FERGUSON: : Lambourne found that 90 mg implants and injections of 1 mg once weekly gave equivalent responses in Merino ewes.

Q: : *Goitre is relatively common in New Zealand and the incidence of enlarged thyroid glands in lambs at birth is relatively high. It has been accepted on not very convincing grounds that the only economic loss in*

this connection is the death of a proportion of such lambs at birth. Could there be a more subtle loss in terms of wool and lamb growth rates and would thyroxine be effective in this moderately hypothyroid condition? Do the speakers know of any results on the effect of a hypothyroid state on wool growth?

DR. FERGUSON: : Thyroidectomy of new born lambs suppresses secondary wool follicle development. When sufficient thyroid tissue is left to maintain normal body growth, follicle development may still be subnormal. However, if the thyroxine deficiency is corrected within three months the full quota of follicles will still develop. The wool growth of thyroidectomized lambs is also depressed but not as a consequence of the effct on the number of follicles.

It is possible that there is a sufficient degree of hypothyroidism in goitre regions to affect wool growth but I do not know of any experimental work to determine whether this is so.

Q: : *In the second year of the trials at Invermay we have implanted 60 mg thyroxine 12 days before mating with a resultant 8 per cent. loss in lambing in the treated ewes which were four-tooths. Has Mr. Hart any results on four-tooths versus two-tooths showing any effect of thyroxine on lambing percentage?*

MR. HART: : No, a four-tooth ewe for our purposes has been regarded as an aged ewe; hence we have no comparisons of this nature.

Q: : *Have the investigations considered the after-effects of thyroxine administration in relation to the damping-down of the animal's own thyroid activity?*

DR. FERGUSON: : After thyroidectomy in sheep it takes several weeks for the hypothyroid state to develop and I think this period would allow ample time for the animal's own thyroid to re-establish function.

DR. R. L. W. AVERILL: : We have made radioactive iodine uptake determinations in control and treated ewes six months after implantation of 60 mg of thyroxine but could detect no difference.

Q: : *Did I understand Dr. Ross to say that thyroxine had delayed conception? In goitrogenic animals we found that gestation length was extended.*

DR. ROSS: : Yes, there was a delay in the rate of successful matings in the treated group of ewes. As no mating data were recorded this delay is based on the assumption that the treatment did not affect the length of the gestation period.

DR. FERGUSON: : We did not find any effect of thyroxine treatment on the gestation period when treatment was started after conception.

Q: : *Could Mr. Hart provide information on the time of mating, mean lambing date, and gestation length for the treated and control ewes?*

MR. HART: : The rams were joined with the ewes on March 17, 1956; the mean lambing date for the controls was September 2 and for the treated ewes September 1. We did not obtain mating dates for individual ewes, so cannot give their gestation periods.

Q: : *Has Mr. Hart given 90 mg thyroxine to two-tooth ewes?*

MR. HART: : Yes.

Q: : *Are we to understand that the principal reason for this difference between the two groups of two-tooth ewes was the greater amount of feed given to Mr. Hart's ewes*?

MR. HART: : Not necessarily; there was also an initial liveweight difference of approximately 20 lb in favour of the stud two-tooths. I think the difference between the two groups is the result of a combination between superior growth and better feeding at time of implanting, and in their subsequent management.

Q: : *Were the stud and Invermay two-tooth ewes implanted at the same time*?

MR. HART: : No, the stud two-tooths were implanted on March 6, 1956, and the Invermay two-tooths on March 23, 1956.

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