HAMMOND MEMORIAL LECTURE*

The magic of Hammond

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John Hammond died 16 years ago, and there are many of the younger generation to whom he is just a name. He became a legend in his time and his influence was enormous. He drew students from all over the world and these came to occupy key positions in animal science in many countries (Pl. 1, Fig. 1). We are a dying generation, but many of us have produced our own postgraduate students to whom some of the Hammondian philosophy has been transmitted, and they in turn are now producing their students.

The title of this address was suggested by a remark made to me many years ago by Professor 'Bunny' Austin. At an SSF meeting, I forget when or where, a group of us were talking about postgraduate training, and I remarked on the seeming casualness of Hammond. Practically all my discussions with him took place on Sunday over tea at Luard Road, and it seemed that he always left the next day for Argentina or some such place. As for my programme, he never interfered; he merely advised, guided and encouraged. He was not interested in teaching techniques—other than carcass dissection which I soon learned to avoid like the plague. But he knew who had the techniques and he passed this on—his son, John, at the Strangeways for ovum culture, Idwal Rowlands at Tunbridge Wells for information about PMSG, Wishart and Fisher for statistics, Pike for histology and Gordon Pluck for animal techniques. The esteem in which Hammond was held by all his students was well known and this seeming casualness excited Bunny Austin to exclaim, "Well, what was the magic of Hammond?". I don't think I answered at the time and this is a belated attempt to do so, based upon an account of his tremendous influence on me personally, on my work, and on that of my students.

I first met Hammond in 1938 when he came to Australia to advise the Government of the day about increasing meat exports to the United Kingdom. He visited the University of Western Australia and gave two lectures to the senior students of Agriculture, one on growth and development of meat qualities and one on reproduction. The impact on me was immense. I recognized that I was in the presence of a great man and I made up my mind, then and there, that I would work with that man. Well, the war intervened and 9 years were to pass before I found myself, in July 1947, on H deck of RMS Orion working my passage to Tilbury Docks as an Acting Temporary Steward, 3rd class on probation. And if any postgraduate student thinks that he or she is at the bottom of the barrel, try signing on as an Acting Temporary Steward, 3rd Class on probation!

In the meantime, two important things had happened on the agricultural front in Western Australia. First of all, the increased interest in lamb production for the English market had resulted in a switch from the Merino, with its capacity to breed at any month of the year, to the Border Leicester × Merino ewe with a restricted breeding season which was not geared to our Mediterranean type climate. Out-of-season breeding became an issue. Secondly, infertility of ewes grazed on the predominantly subterranean clover pastures suddenly emerged as a serious

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problem. On my return to the University in late 1945, I joined the team headed by Professor Eric Underwood and Dr William Bennetts working on this problem and this altered my direction from nutrition, in which I had been interested, towards animal reproduction. My particular task was to develop a bioassay for plant oestrogens based on the Allan–Doisy test. This involved making clover extracts and fractionating and purifying them to provide a non-toxic fraction which contained the oestrogen, and then to assay it quantitatively in immature mice. After 18 months, I succeeded and this was my first taste of the joys of discovery. The uterine growth and vaginal smear patterns of immature mice injected with clover extract were identical to those of mice injected with oestradiol and it was possible to produce quite nice dose–response lines (Curnow, Robinson & Underwood, 1948). The technique also permitted distinction between oestrogen-rich and oestrogen-free plants and demonstration that the activity was in the leaves (Robinson, 1949). Here was definite proof that the problem material was an oestrogen and not a substance with some oestrogen-like activities.

This set me on course to study the other major problem—out-of-season breeding—which has been a lifetime interest and, of course, was my thesis topic at Cambridge. Hammond was an agricultural scientist. His philosophy was to apply science to agricultural problems and to study science, as such, only when basic scientific knowledge was inadequate for the solution of the particular problem. It was a philosophy of constant advance and retreat, attempting always to push current biological knowledge into use in practical situations. Only when an attempt failed due to inadequate basic knowledge was the basic subject studied in its own right. Essentially this is what I have attempted to do in the 30 years which have passed since I left Cambridge and went to California for the year of 1950. I had the chance of a job in this country but Hammond was insistent that I go to the States to, as he put it, “have an outcross and get some hybrid vigour”. In California, I came to know Harold Cole well and a passing remark of his was to prove important a couple of years later. I was trying to collect some ram semen and I needed oestrous teaser ewes during the anoestrous period. The current technique was to inject 5 mg stilboestrol to an anoestrous ewe and, despite the massive dose, I found it to be most unreliable and Cole remarked that it was difficult to induce oestrus in the sheep using oestrogen.

In Melbourne in 1951, I started work again on out-of-season breeding. It was known that the first ovulation of the breeding season was ‘silent’; an active corpus luteum preceding ovulation was needed if oestrus was to be exhibited. Crystalline progesterone was becoming available so the obvious thing was to inject the anoestrous ewe with progesterone before PMSG to see if the ovulation induced by this treatment would be accompanied by oestrus. Three groups tried this independently—Thibault’s in France (Dauzier & Wintenberger, 1952), Casida’s in Wisconsin (Dutt, 1952, 1953) and mine (a boy, a sheep dog and me!) in Melbourne (Robinson, 1952, 1954a)—and we all published almost simultaneously.

These early results showed our lack of knowledge of the physiology of oestrus. My French colleagues did not speculate upon the role of progesterone. The Wisconsin group speculated but in non-specific terms and did not pursue the matter. Hammond’s hypothesis was that progesterone from a declining corpus luteum slowed down the growth pattern of the developing follicle thereby ensuring that the cyclic ewe was under the influence of oestrogen longer than one just coming into the breeding season. This was a perfectly logical concept, but there was another. Did progesterone have a potentiating effect on the neural centres involved in oestrous behaviour? To investigate this, spayed ewes were injected with massive doses of oestrogen. Initially they exhibited oestrus but they rapidly became refractory. Progesterone for a few days not only removed the refractory state (Text-fig. 1) but also made the ewes so sensitive to oestrogen that only a few micrograms were needed to induce full behavioural oestrus (Text-fig. 2). It was concluded that alternate progesterone–oestrogen influences are necessary for regular cyclic oestrous behaviour in the ewe.

The full biological significance of the progesterone–oestrogen interaction has taken a long time to sink in. When it was first demonstrated, all the thinking was in terms of the effects of

Fig. 1. Sir John Hammond and some of his past postgraduate students at the First International Congress of Animal Production, Rome 1963. From left to right: L. R. Wallace (N.Z.), D. F. Dowling (Aust.), T. J. Robinson (Aust.), F. N. Bonsma (S. Afr.), P. Bhattacharya (India), Sir John Hammond, J. Edwards (U.K.), R. W. Pomeroy (U.K.), H. Pálsson (Iceland), C. P. McMeekan (N.Z.), D. M. Joubert (S. Afr.), A. A. El-Itriby (U.A.R.).

Fig. 2. Thirty-seven Merino ewes and their 171 Poll Merino lambs produced as a result of multiple ovulation and embryo transfer to recipients. Overall, 236 Poll Merinos were produced by 86 donors in 2 years in a practical field demonstration of the application of the embryo transfer technique to flock improvement (Moore & Shelton, 1962).

Fig. 3. John Hammond and young admirers, Sydney 1958.

Text-fig. 1. Oestrous responses of ovariectomized ewes injected regularly with 5 or 2 mg oestradiol benzoate (12 ewes/group). A refractory state rapidly developed following treatment at weekly intervals. It disappeared after a 3-week period of no treatment but reappeared immediately when ewes were injected 2 weeks later. Pretreatment with progesterone for 3 days removed this refractory state. (Modified from Robinson, 1954b.)

Text-fig. 2. Oestrous responses of ovariectomized ewes injected at intervals of 2 weeks with oestradiol benzoate (ODB) alone or preceded for 3 days by 75 mg progesterone. There were 6 ewes in each of Groups A and B; Group A results are illustrated in the first of each pair of columns. Progesterone treatment was essential for the regular induction of oestrus which could be induced by oestradiol doses as low as 20 µg. (Modified from Robinson, 1954b.)

progesterone *after* oestrogen. Events started with the developing follicle which produced oestrogen which developed the vagina, induced oestrus and conditioned the uterus to respond to progesterone for implantation. The fact that most polyoestrous animals are regularly subjected to progesterone influence *before* oestrogen had been overlooked. We now know that this influence is profoundly important. The evolutionary processes which have resulted in a series of pseudopregnancies (which we call oestrous cycles) constituting a breeding season have culminated in some species in a dependence upon one or more such cycles for the events which lead to the successful establishment of a pregnancy.

The progesterone-primed spayed ewe became, and is still, a standard experimental model. It has been used for studies ranging from animal behaviour to post-implantation mortality by a host of postgraduate students, 1952–1980 (D. R. Lindsay, T. F. Reardon, S. Salamon, W. M. Brander, J. N. Shelton, I. D. Killeen, M. J. Carrick, T. D. Quinlivan, P. J. Holst, J. F. Smith, I.

C. Fletcher, R. G. Sinclair, R. J. Scaramuzzi, W. R. Gibson, K. P. Croker, A. J. Allison, G. Evans, D. T. Pearce, A. L. Poulton), starting with Neil Moore. Our basic facilities were the sheep station, the open paddock and the sheep yards. The wool shed was our laboratory and operating theatre (Robinson & Smith, 1967). Our experimental animals were virtually unlimited numbers of sheep in a free grazing situation. At one stage we had a standardized flock of some 200 spayed ewes and access to 8000 breeding ewes. This situation ultimately led to the development of a system of controlled breeding of sheep and the demonstration of the feasibility of large-scale embryo transfer (Pl. 2, Fig. 2).

The first step was to quantify the progesterone–oestrogen relationship in behavioural and vaginal oestrus. Progesterone was found to have an inhibiting as well as a potentiating effect. If given with oestrogen, oestrus was suppressed. If given before oestrogen, the interval from progesterone influence to oestrogen was critical. The duration of progesterone influence was important (12 days > 6 > 3) (Text-fig. 3) as was the daily dose (optimum 10 mg/day) and the interval between doses (2 day maximum). If an optimum progesterone pretreatment of 12 days, at 10 mg per day, is given with oestrogen 24 h after the last injection the oestrous response is totally predictable. It is a superb bioassay—what other will result in a predictable 4-fold increase in response with a doubling of dose?

Text-fig. 3. Dose–response lines for behavioural and vaginal oestrus in ovariectomized ewes pretreated with progesterone for 3, 6 or 12 days. Duration of pretreatment had no demonstrable effect on vaginal smear but had a progressive effect on behavioural sensitivity, the median effective dose of oestradiol benzoate (ODB) being reduced from 19 to 16 to 13 µg with successive increases in duration of progesterone pretreatment. The ewe is so sensitive to oestrogen that increasing the dose to the 12-day progesterone primed ewe from 10 to 17 µg results in a 4-fold increase (20–80%) in the oestrous response. (From Robinson, Moore & Binet, 1956.)

The interactions between dose of progesterone, duration of treatment and dose of oestrogen provided a multidimensional model which was used to quantify ovarian production of oestrogen and progesterone. By the use of parallel studies in entire anoestrous ewes and standardized spayed ewes, it was estimated that the ovary of the pro-oestrous ewe produced the equivalent of a single injection of about 12 µg oestradiol, and the active corpus luteum some 6–10 mg

progesterone per day (Robinson, 1959), estimates which still hold some 25 years later, despite all modern assay technology.

The initial experiments using the spayed ewe model used quantal data for oestrous behaviour. The ewe was scored 1 or 0 depending upon whether or not she displayed oestrus. A later refinement was to measure the duration and intensity of oestrus (Lindsay, 1966a, b; Fletcher & Lindsay, 1971a, b; Lindsay & Fletcher, 1972). The question of whether the effect of progesterone was one of potentiation or removal of inhibition to oestrogen occupied Scaramuzzi, Lindsay & Shelton (1972) and has never yet been satisfactorily resolved. In the heifer, Carrick & Shelton (1969) presented evidence that the latter is the more important. The time of onset of oestrus, its duration and its intensity are all quantitatively related to the dose of oestrogen. (Robinson, 1955; Scaramuzzi *et al.*, 1971). All of these observations are particularly relevant to modern observations on endocrine levels in animals of high and low fertility and on time relationships between peak oestrogen, times of onset of oestrus, LH release and ovulation.

Another interesting observation, made independently by Reardon & Robinson (1961) (Text-fig. 4) and by Raeside & McDonald (1959) in New Zealand, was that there is a seasonal variation in sensitivity of the spayed ewe to oestrogen. The behavioural centres in the hypothalamus, freed from any influence of positive and negative feedback from the ovaries, show a seasonal rhythm in sensitivity to oestrogen and this rhythm coincides with the annual rhythm of ovarian activity.

Text-fig. 4. Seasonal variation in the induction of oestrus in the progesterone-primed ovariectomized ewe by a standard dose of oestrogen. The pattern (c), which closely follows that of the breeding season, can be related either to (a) daylight hours or (b) liveweight change. (Modified from Reardon & Robinson, 1961.)

All of this had its side-lights, some unexpected and amusing. In the late 1940s, crystalline progesterone was unobtainable, but testosterone, believed at that time to have some characteristics of progesterone, was available. Some anoestrous ewes were therefore primed with testosterone before injecting PMSG. Most came into oestrus but failed to ovulate, with grossly

abnormal ovaries (Robinson, 1950). Some 10 or 12 years later, David Lindsay and I decided to clarify this problem by testing whether testosterone would prime the spayed ewe to respond to oestrogen, as did progesterone. A day or two after the first testosterone injection I had a phone call from a near-distraught David telling me that the experiment had gone all wrong; the rams had gone through the fence and were mating all the ewes. I drove down to the University farms and sure enough, all the androgen-treated ewes were in full behavioural oestrus. Vaginal smears revealed dry vaginas full of spermatozoa. The central and peripheral components of oestrus had thus been dissected out; vaginal development and production of mucus were not necessary prerequisites for coitus. Current thinking is that androgen can be aromatized to oestrogen but, if so, only the neural receptor sites have this capacity; peripheral sites do not. Interestingly, further studies showed that oestrogen and androgen were additive in their effect on behaviour but antagonistic on the vaginal response (Lindsay & Robinson, 1961a, 1964).

All of these studies were aimed at a better understanding of oestrus and the factors which controlled it. Most work on the control of oestrus was of a trial-and-error nature, and was dictated by the drug companies, who had surplus products derived from the search for oral contraceptives and for which they were seeking markets. If successful control of oestrus and ovulation were to be achieved a much better understanding of fundamentals was needed. By the 1960s, considerable progress had been made. First of all, the progesterone–oestrogen interaction on oestrous behaviour and vaginal changes had been worked out in detail (see Robinson, 1959). Secondly, it had been shown that the behavioural and peripheral components of oestrus were not necessarily dependent (Lindsay & Robinson, 1961a, 1964). Thirdly, the myth of rams detecting ewes in oestrus had been exploded; oestrous ewes either find their mates or permit themselves to be found (Inkster, 1957; Lindsay & Robinson, 1961b). Fourthly, the intensity, time of onset, and duration of oestrus were shown to be related to duration of progesterone pretreatment and dose of oestrogen (Robinson, 1959; Scaramuzzi *et al.*, 1971). Fifthly, the seasonal variation in these responses had been demonstrated (Raeside & McDonald, 1959; Reardon & Robinson, 1961). Sixthly, age and learning effects on oestrous response of ewes had been demonstrated (Lindsay, 1966a, b). Finally, these studies taken in context with the limited data available on plasma levels of oestrogen and progesterone in ovarian vein blood had given a fairly accurate understanding of the endocrinological events surrounding the period of oestrus. For example, it was known that peak oestrogen preceded oestrus (Moore *et al.*, 1969) and that the animal at oestrus had little, if any, residual ovarian hormones in circulation.

The stage was set for the development of a practical method of control of the oestrous cycle in the ewe. The object was to develop an artificial corpus luteum that could be inserted or removed at will. The first prerequisite was a highly potent progestagen with an activity profile indistinguishable from that of progesterone. Unlike compounds which were readily available, it had to be short acting and we were not interested in oral activity. At the suggestion of Gregory Pincus, I approached G. D. Searle and told them what was needed and they began to supply experimental compounds for use in a programme of screening with the spayed ewe model. By building into an assay the variables of dose level of progestagen and interval to oestrogen, activity and longevity could both be assessed. The result was the demonstration by Shelton (1965) that a synthetic fluorinated progestagen, SC 9880, now known as Cronolone, had a biological profile in the spayed ewe indistinguishable from that of progesterone and was some 25 times more active (Table 1). Cross-checking for the ability to block ovulation in entire ewes gave a similar result (Shelton & Robinson, 1967).

The next step was the development of the intravaginal method of administration and this proved to be extremely difficult until, in 1964, a plastic sponge was proved suitable and the technique was tested in the field (Robinson, 1965). This was the year in which Hammond died so he never saw the implementation of controlled sheep and goat breeding. Some 2 years earlier my family and I had stayed with him in Cambridge and I had told him that I was working on the development of an artificial corpus luteum that could be put in and taken out of the vagina at

Table 1. The responses of spayed ewes to oestradiol benzoate given 2 days after priming for 12 days with SC-9880 (0.4 mg/day) or progesterone (10.0 mg/day) (taken from Shelton, Robinson & Holst, 1967)

Main effect	No. of ewes	
	Treated	In oestrus
Type of progestagen		
Progesterone	72	35
SC-9880	72	36
Dose of oestradiol benzoate (μ g)		
10.0	48	5
15.6	48	27
24.3	48	39
		<i>P</i> linear < 0.001
		<i>P</i> quadratic N.S.
Total	144	71

will. He loved that. His eyes lit up and he exclaimed "By Jove, I never would have thought of that!"

The basic intention behind this whole programme was the large-scale introduction of artificial insemination into the Australian Merino sheep industry. In 1958 this aim received a tremendous fillip when we were joined by Steven Salamon, a Hungarian who had been trained in sheep breeding and A.I. in the Soviet Union. He brought with him Eastern European technology which we set about evaluating and adapting to the Australian environment (Salamon & Robinson, 1962a, b; Salamon, 1976). When, however, attempts were made to combine this A.I. technology to our system of controlled ovulation and oestrus, disaster struck. Although oestrus and ovulation could be easily and reliably controlled, fertility was often low. Much of the trouble was due to over expectation. Australian sheep production is extensive and large scale. Miracles were expected by graziers who were not geared up to controlled breeding and A.I. programmes and, I suppose, we were over confident. Also, as others can testify (Gordon, 1972), the original commercial sponges were relatively ineffective; the progestagen was not dispersed evenly throughout and absorption was poor. As shown in many studies, inadequate progestagen before oestrus and ovulation has a deleterious effect on a number of factors associated with fertility, such as the incidence and duration of oestrus, the quantity of follicular oestrogen produced (Smith & Robinson, 1970), proportion of ova fertilized, embryonic development (Miller & Moore, 1976) and ewes which lamb (Robinson, Moore, Holst & Smith, 1967). But even with seemingly adequate progestagen there remained a basic problem so, back to fundamentals again.

The work of the previous 15 years had been directed towards the endocrinological and sociological factors controlling oestrus and ovulation and on the technology of artificial insemination. There was now a problem of infertility following what appeared to be a perfectly normal ovulation and oestrus. It was soon established that failure of fertilization was involved (Moore, Quinlivan, Robinson & Smith, 1967) due to insufficient spermatozoa reaching the oviducts (Text-fig. 5), and that the problem could be overcome by use of a dense inseminate containing a seemingly excessive number of spermatozoa (Quinlivan, 1970; Allison & Robinson, 1971). Dose of progestagen was important and the use of a high dose, well dispersed through a sponge, improved the situation over that obtained with a low dose concentrated in the centre (Allison & Robinson, 1970; Robinson, 1970). Also, although the evidence is not entirely conclusive, it seems that the use of a small dose of PMSG may improve the situation.

Text-fig. 5. Log mean numbers of spermatozoa recovered from the oviducts of ewes at intervals after insemination at a normal oestrus (Δ) or one synchronized with progestagen-impregnated intravaginal sponge ($\bullet$). Each point is the mean value for 60 sheep. (Modified from Quinlivan & Robinson, 1967.)

This is where we now stand. Controlled year-round breeding of sheep and goats is in commercial use internationally, despite the requirement for excessive sperm numbers. However, to improve the technique and gain further control over breeding activity more basic information about the factors which control the breeding season and the ovarian and oestrous cycles is needed. In short, sheep and goat breeding technology has been taken to the limit of current scientific knowledge.

So, reluctantly, for the past decade I have turned my back on the field, the sheep station, the shearing shed and the large scale experimentation of the 1950s and 1960s, and have returned to the animal house and the assay laboratory. Four questions have been posed: (1) What are the endocrinological requirements for the establishment of sperm reserves in the ewe? (2) What are the endocrinological events in the cyclic ewe treated with exogenous progestagens and oestrogen? (3) What are the endocrinological events following the use of equine serum gonadotrophin? (4) What is the reproductive potential of sheep, when kept in controlled light environments and what are the associated endocrinological events in the Merino and its crosses and in the British breeds: is the Merino different?

First of all, the efficiency of sperm storage and transport through the female reproductive tract is extremely sensitive to the endocrine state. Progesterone and oestrogen both are involved but a normal pattern of sperm transport has never been produced in spayed ewes treated with ovarian hormones, although quantitative effects of oestrogen and an interaction with progesterone priming are apparent (Allison & Robinson, 1972). Nor has it yet been possible to obtain a completely normal pattern of sperm transport in the ewe in which ovulation and oestrus have been controlled (Robinson, 1975).

The pharmacological control of ovulation and oestrus involves the use of exogenous hormones during dioestrus. Progestagen feedback has no effect on the function of a formed corpus luteum but it will inhibit the function of a developing gland (Woody, First & Pope, 1967; Smith & Robinson, 1969). This has allowed the period of progestagen treatment to be reduced from 16 to 12 days, with a pronounced beneficial effect on subsequent fertility. The effect of oestrogen with progestagen has also been investigated. Given daily from the day of oestrus the effect of oestrogen is dose dependent and is ambivalent. At a low dose, 5 μg oestradiol/day, it has no measurable effect. At a moderate dose it may be luteolytic or luteotrophic, with a cycle of normal length. At a high dose, 125 μg oestradiol/day, it may be luteolytic or have a luteotrophic effect so great that progesterone production outstrips the capacity of the normal luteolytic process (Text-fig. 6). There is therefore no apparent practical application for oestrogen with progestagen for control of the cycle.

Text-fig. 6. Effect of a high daily dose of oestradiol (125 µg/day) for 22 days on luteal function in the ewe. In 3 ewes (▲) the corpus luteum is suppressed while in the other 2 (○) it is stimulated to excessive and prolonged activity and oestrus does not occur. (From Croker, Robinson & Shelton, 1976.)

The measurement of endocrinological events following the use of PMSG in the breeding and non-breeding seasons produced fairly predictable results (Evans & Robinson, 1980a). However, the follicle stimulated to ovulate in the non-breeding season produces only about 60% of the oestrogen produced in the breeding season. This results in the combination of low oestrogen and low central sensitivity to oestrogen and explains why the progestagen-PMSG treated anoestrous ewe has a short oestrus of low intensity. Serum gonadotrophin also has a residual oestrogen stimulating effect independent of the number of follicles induced to ovulate, so that increasing the dose in anoestrus—as is done routinely in France—is necessary to alleviate the problem of an inadequate oestrous response.

The truly fundamental question is how is seasonality of reproduction in sheep controlled? Why do Merinos breed in early summer when the days are getting longer while the British breeds do so in autumn when the days are shortening and is there a unifying concept applicable to all breeds? Well, there has to be. Apart from anything else, crosses between Merinos and British breeds have breeding seasons intermediate between their parent breeds.

With these thoughts in mind, we embarked some 4 years ago on our current modest programme of interrelationships between photoperiodism, fertility and endocrinology using two, small, light controlled rooms backed up by a hormone assay laboratory. The first series of experiments involved a comparison between Merinos and some of their crosses (Evans & Robinson, 1980b). Interestingly, Merino ewes showed exactly the same response to a 6-monthly light cycle as did their crosses with highly seasonal British breeds. Pituitary activity of entire and spayed ewes and of rams, as measured by LH release to GnRH, all were influenced by the light/dark regimen and the curves were all of the same shape (Text-fig. 7). The secondary characters, dependent upon pituitary activity, i.e. testicular size, plasma testosterone, cyclic ovarian activity, followed a much smoother curve (Text-fig. 8) indicative of 'damped' responses. Furthermore, the time lags differed for the rams and ewes, the former being about 1 month shorter than the latter which, perhaps fortuitously, fits the pattern observed in wild ruminants.

The second series of experiments, involving direct comparisons between Merino and pure British breeds, is still in progress but to date the patterns of response between breeds appear essentially the same.

In the past, the sheep and goat have been erroneously referred to as short-day animals in which breeding activity is induced by shortening hours of daylight. This concept stems from the

Text-fig. 7. The pituitary response to GnRH of 4 entire rams and 6 ovariectomized ewes kept in an artificial light regimen of 6 months over a 2 year period. The data for the 4 consecutive periods are pooled and each point represents 16 GnRH treatments for rams and 24 for ewes. Time lag regression analysis showed a significant relationship with the shape of the light regimen, with different time lags for the rams and ewes. (Modified from Evans & Robinson, 1980b.)

Text-fig. 8. The (a) ovarian and (b) testicular response of 40 ewes and 4 rams kept in the artificial light regimen of Text-fig. 7. (Modified from Evans & Robinson, 1980b.)

well known fact that the breeding season of British and Northern European breeds commences in early autumn when the days are shortening. Also the first experimental demonstration of the photoperiodic effect by Yeates (1949) used Suffolk ewes on a shortening light regimen. But the concept ignores the fact that most of the sheep in the western world, the Merinos of Australia and South Africa, begin breeding each year when the days are getting longer. The key to this puzzle, the unifying concept, lies in the observation, which emanated from the Hammond school, that the centre of the breeding season is roughly the same for all breeds (Hafez, 1952). In the Merino, evolved in a relatively benign environment, this is manifested by a long breeding season but with a maximum percentage of ewes exhibiting oestrus with multiple ovulations associated with relatively high conception rates in the autumn months as compared with the spring (Dun, Ahmed & Marrant, 1960). In the sub-arctic breeds such as the Romanov, a short breeding season of intense activity and high fecundity is restricted to the autumn months. So we have

gone full circle. A diagram illustrating the concept of an inverse relationship between hours of daylight and pituitary/hypothalamic activity was published 30 years ago (Robinson, 1951). About a decade later, a modified version was published in which similar curves were presented but the time-lag from change in the photoperiodic regime to peak of sexual activity was 3 months rather than 6 (Robinson, 1959). The concept is that decreasing hours of daylight do not in themselves initiate sexual activity but that all breeds have an annual rhythm of reproductive activity geared to the annual rhythm of daylight and dark hours and which reaches a peak at about the same season of the year (Text-fig. 9).

Text-fig. 9. Schematic representation of the nature of cyclic reproductive activity of the sheep in relation to the annual rhythm of change in daylight hours. Sensitivity of the hypothalamic-pituitary axis to external and internal stimuli follows a curve similar to that of the light/dark ratio, but with a time lag of about 3 months. All breeds reach a peak at about the same season of the year and differences in the duration of breeding activity can be accounted for by differences in threshold needed to stimulate ovarian and testicular activity. (Redrawn from Robinson, 1959.)

There is a school of thought that claims that this seasonality is essentially due to ovarian-pituitary feedback systems (Karsch, Goodman & Legan, 1980), but this overlooks two important phenomena. Firstly, the spayed ewe shows an annual rhythm of sensitivity to oestrogen. Secondly, the sensitivity to GnRH of the LH releasing mechanism in spayed ewes is closely geared to an artificial light regimen (Text-fig. 7), as it is in the natural environment (Land, Carr & Thompson, 1979). So there are two known aspects of reproductive function, one directly involving the hypothalamus and the other the pituitary, which show seasonality in the absence of gonadal feedback activity.

As I see it, the primary phenomenon in seasonality of breeding is photoperiodic control of centres in the hypothalamus, modified to various degrees by nutritional status (Gibson & Robinson, 1971). The system operates rather like a servo-system with an inbuilt time-lag. The ovarian and testicular responses are secondary, and their feedback mechanisms have only a modifying effect. Overt manifestations of sexuality, such as oestrous and rutting behaviour and changes in the external genitalia, are tertiary.

So far I have dealt primarily with the contributions made in my own laboratory, by my own

students. But we are now into the third generation, and it is fascinating to see how the Hammond line of thought and action is being continued. I will mention just two related examples. In the 1940s in Western Australia, Underwood, Shier & Davenport (1944) observed a peak of lambing early in the lambing season suggestive of a peak of mating activity about 3 weeks after the introduction of rams to ewe flocks. This 'ram effect' has been looked at in a rather desultory fashion since then and some practical use has been made of it, but its underlying mechanism has not been examined until quite recently. In Western Australia, the introduction of rams to previously isolated ewes resulted in an immediate rise in plasma LH, within 10 min, followed by increased pulse frequency, with an amplitude similar to that of a normal pre-ovulatory period, followed by ovulation (Martin, Oldham & Lindsay, 1980). This 'ram effect' could be due to the sight, sound or smell of the ram, and Knight & Lynch (1980) in New Zealand found that a similar effect could be obtained by putting ewes into pens over which were draped rams' skins. Ewes sprayed with ram's urine showed only a slight response. They concluded that the stimulus for LH release and ovulation is a pheromone produced by the sebaceous glands of rams, and we may well see the introduction of an aerosol pack containing ram 'perfume' which can be simply sprayed on the ewe's muzzles to initiate breeding activity! John would have loved that! Simple, conclusive, practical.

To conclude, it has been a great joy to me to present this memorial address and I thank the Chairman and the Committee of the Society for the invitation. I hope I have been able to convey some idea of the magic of Hammond and the deep impact of his philosophy of science on me and on my students and, in turn, on their students. But no tribute to Hammond is complete without mention of his immense personal charm. Here lay the real magic. He had a charm that attracted people of all ages as is evident from a photograph taken in Sydney in 1958 of Hammond and our two daughters, aged 3 and 4 (Pl. 2, Fig. 3). You can see delight written all over them. Hammond stayed with us for a week or so and the girls adored him. They would hop onto his bed every morning and he would read them a story and, to this day, I can hear his voice droning on as I took up the morning cup of tea. Two years after this was taken he received his knighthood but the girls, then of Sunday school age, could never get this 'Sir' bit: to them he was 'Saint' John.

References

- Allison, A.J. & Robinson, T.J. (1970) The effect of dose-level of intravaginal progestagen on sperm transport, fertilization and lambing in the cyclic Merino ewe. *J. Reprod. Fert.* **22**, 515–531.
- Allison, A.J. & Robinson, T.J. (1971) Fertility of progestagen treated ewes in relation to the numbers and concentration of spermatozoa in the inseminate. *Aust. J. biol. Sci.* **24**, 1001–1008.
- Allison, A.J. & Robinson, T.J. (1972) The recovery of spermatozoa from the reproductive tract of the spayed ewe treated with progesterone and oestrogen. *J. Reprod. Fert.* **51**, 215–224.
- Carrick, M.J. & Shelton, J.N. (1969) Oestrogen-progesterone relationships in the induction of oestrus in spayed heifers. *J. Endocr.* **45**, 99–109.
- Crocker, K.P., Robinson, T.J. & Shelton, J.N. (1976) The level of progesterone in peripheral plasma of cyclic ewes treated with oestrogen alone or with progesterone. *Proc. 8th Int. Congr. Anim. Reprod. & A.I., Krakow* **3**, 123–126.
- Curnow, D.H., Robinson, T.J. & Underwood, E.J. (1948) Oestrogenic action of extracts of subterranean clover (*T. subterranean* L. var. Dwalganup). *Aust. J. exp. Biol. med. Sci.* **26**, 171–180.
- Dauzier, L. & Wintenberger, S. (1952) Déclanchement simultané de l'oestrus dans un lot de brebis avec possibilité de gestation ultérieure. *Annls Zootech.* **1**, 49–52.
- Dun, R.B., Ahmed, W. & Marrant, A.J. (1960) Annual reproductive rhythm in Merino sheep related to the choice of a mating time at Trangie, Central Western New South Wales. *Aust. J. agric. Res.* **11**, 805–826.
- Dutt, R.H. (1952) Induction of estrus and ovulation in anestrual ewes by use of progesterone and pregnant mare serum. *J. Anim. Sci.* **11**, 792, Abstr.
- Dutt, R.H. (1953) Induction of estrus and ovulation in anestrual ewes by use of progesterone and pregnant mare serum. *J. Anim. Sci.* **12**, 515–523.
- Evans, G. & Robinson, T.J. (1980a) The control of fertility in sheep: endocrine and ovarian responses to progestagen-PMSG treatment in the breeding season and in anoestrus. *J. agric. Sci., Camb.* **94**, 69–88.
- Evans, G. & Robinson, T.J. (1980b) Reproductive potential and endocrinological responses of sheep kept under controlled lighting. II. Pituitary and gonadal responses of ewes and rams to a six-monthly light cycle. *Anim. Reprod. Sci.* **3**, 39–56.

- Fletcher, I.C. & Lindsay, D.R. (1971a) Effect of oestrogen on oestrous behaviour and its variation with season in the ewe. *J. Endocr.* **50**, 685–696.
- Fletcher, I.C. & Lindsay, D.R. (1971b) Effect of rams on the duration of oestrous behaviour in ewes. *J. Reprod. Fert.* **25**, 253–259.
- Gibson, W.R. & Robinson, T.J. (1971) The seasonal nature of reproductive phenomena in the sheep. I. Variation in sensitivity to oestrogen. *J. Reprod. Fert.* **24**, 9–18.
- Gordon, I. (1972) Control of reproduction in sheep: towards programmed lamb production. *J. Dept. Agric. Fish., Eire* **68**, 3–51.
- Hafez, E.S.E. (1952) Studies on the breeding season and reproduction of the ewe. *J. agric. Sci., Camb.* **42**, 189–265.
- Inkster, I.J. (1957) The mating behaviour of sheep. *Sheepfarming Annual, N.Z.*, pp. 163–169.
- Karsch, F.J., Goodman, R.L. & Legan, S.J. (1980) Feedback basis of seasonal breeding: test of an hypothesis. *J. Reprod. Fert.* **58**, 521–535.
- Knight, T.W. & Lynch, P.R. (1980) Source of ram pheromones that stimulate ovulation in the ewe. *Anim. Reprod. Sci.* **3**, 133–136.
- Land, R.B., Carr, W.R. & Thompson, R. (1979) Genetic and environmental variation in the LH response of ovariectomized sheep to LH-RH. *J. Reprod. Fert.* **56**, 243–248.
- Lindsay, D.R. (1966a) Modification of behavioural oestrus in the ewe by social and hormonal factors. *Anim. Behav.* **14**, 73–83.
- Lindsay, D.R. (1966b) Mating behaviour of ewes and its effect on mating efficiency. *Anim. Behav.* **14**, 419–424.
- Lindsay, D.R. & Fletcher, I.C. (1972) Ram seeking activity associated with oestrous behaviour in ewes. *Anim. Behav.* **30**, 452–456.
- Lindsay, D.R. & Robinson, T.J. (1961a) The oestrus inducing activity of testosterone in the ewe. *Nature, Lond.* **192**, 761–762.
- Lindsay, D.R. & Robinson, T.J. (1961b) Studies on the efficiency of mating in the sheep. II. The effect of freedom of rams, paddock size and age of ewes. *J. agric. Sci., Camb.* **57**, 141–145.
- Lindsay, D.R. & Robinson, T.J. (1964) Oestrogenic and anti-oestrogenic activity of androgens in the ewe. *J. Reprod. Fert.* **7**, 267–274.
- Martin, G.B., Oldham, C.M. & Lindsay, D.R. (1980) Increased plasma LH levels in seasonally anovular Merino ewes following the introduction of rams. *Anim. Reprod. Sci.* **3**, 125–132.
- Miller, B.G. & Moore, N.W. (1976) Effects of progesterone and oestradiol on RNA and protein metabolism in the genital tract and on survival of embryos in the ovariectomized ewe. *Aust. J. biol. Sci.* **29**, 565–573.
- Moore, N.W. & Shelton, J.N. (1962) The application of the technique of egg transfer to sheep breeding. *Aust. J. agric. Res.* **13**, 718–724.
- Moore, N.W., Quinlivan, T.D., Robinson, T.J. & Smith, J.F. (1967) The fertilization of ova following natural mating or artificial insemination after withdrawal of SC-9880 impregnated intravaginal sponges from cyclic Merino ewes. In *The Control of the Ovarian Cycle in the Sheep*, pp. 169–176. Ed. T. J. Robinson. Sydney University Press.
- Moore, N.W., Barrett, S., Brown, J.B., Schindler, I., Smith, M.A. & Smyth, B. (1969) Oestrogen and progesterone content of ovarian vein blood of the ewe during the oestrous cycle. *J. Endocr.* **44**, 55–62.
- Quinlivan, T.D. (1970) The relationship between numbers of spermatozoa inseminated and fertilization rate of ova in ewes treated with fluoro-progestagen intravaginal sponges in summer and autumn. *J. Reprod. Fert.* **23**, 87–102.
- Quinlivan, T.D. & Robinson, T.J. (1967) The number of spermatozoa in the Fallopian tubes of ewes at intervals after artificial insemination following withdrawal of SC9880 impregnated intravaginal sponges. In *The Control of the Ovarian Cycle in the Sheep*, pp. 177–194. Ed. T. J. Robinson. Sydney University Press.
- Raeside, J.I. & McDonald, M.F. (1959) Seasonal changes in the oestrous response by the ovariectomized ewe to progesterone and oestrogen. *Nature, Lond.* **184**, 458–459.
- Reardon, T.F. & Robinson, T.J. (1961) Seasonal variation in the reactivity to oestrogen of the ovariectomized ewe. *Aust. J. agric. Res.* **12**, 320–326.
- Robinson, T.J. (1949) Oestrogenic potency of subterranean clover (*T. subterranean* L. var *Dwalganup*): the preparation and assay of extracts. *Aust. J. exp. Biol. med. Sci.* **27**, 297–305.
- Robinson, T.J. (1950) The control of fertility in sheep. Part 1. Hormonal therapy in the induction of pregnancy in the anoestrous ewe. *J. agric. Sci., Camb.* **40**, 275–307.
- Robinson, T.J. (1951) Reproduction in the ewe. *Biol. Rev.* **26**, 121–157.
- Robinson, T.J. (1952) Role of progesterone in the mating behaviour of the ewe. *Nature, Lond.* **170**, 373–374.
- Robinson, T.J. (1954a) The production of coincident oestrus and ovulation in the anoestrous ewe with progesterone and pregnant mare serum. *J. Endocr.* **10**, 117–123.
- Robinson, T.J. (1954b) The necessity for progesterone with oestrogen for the induction of recurrent estrus in the ovariectomized ewe. *Endocrinology* **55**, 403–408.
- Robinson, T.J. (1955) Quantitative studies on the hormonal induction of oestrus in spayed ewes. *J. Endocr.* **12**, 163–173.
- Robinson, T.J. (1959) The estrous cycle of the ewe and doe. In *Reproduction in Domestic Animals*, Vol. 1, pp. 291–333. Eds H. H. Cole & P. T. Cupps. Academic Press, New York.
- Robinson, T.J. (1965) Use of progestagen-impregnated sponges inserted intravaginally or subcutaneously for the control of the oestrous cycle in the sheep. *Nature, Lond.* **206**, 39–41.
- Robinson, T.J. (1970) Fertility following synchronization of oestrus in the sheep with intravaginal sponges. II. Effect of dose of progestagen and rate of absorption. *Aust. J. agric. Res.* **21**, 783–792.
- Robinson, T.J. (1975) Contraception and sperm transport in domestic animals. In *The Biology of Spermatozoa*, pp. 202–213. Eds E. S. E. Hafez & C. Thibault. Karger, Basle.

- Robinson, T.J. & Smith, J.F.** (1967) The time of ovulation after withdrawal of SC-9880-impregnated intravaginal sponges from cyclic Merino ewes. In *The Control of the Ovarian Cycle in the Sheep*, pp. 158–168. Ed. T. J. Robinson. Sydney University Press.
- Robinson, T.J., Moore, N.W. & Binet, F.E.** (1956) The effect of the duration of progesterone pretreatment on the response of the spayed ewe to oestrogen. *J. Endocr.* **14**, 1–7.
- Robinson, T.J., Moore, N.W., Holst, P.J. & Smith, J.F.** (1967) An evaluation of several progestagens administered in intravaginal sponges for the synchronization of oestrus in the entire cyclic Merino ewe. In *The Control of the Ovarian Cycle in the Sheep*, pp. 76–101. Ed. T. J. Robinson. Sydney University Press.
- Salamon, S.** (1976) *Artificial Insemination of Sheep*. Department of Animal Husbandry, University of Sydney.
- Salamon, S. & Robinson, T.J.** (1962a) Studies on the artificial insemination of Merino sheep. I. The effects of frequency and season of insemination, age of the ewe, rams, and milk diluents on lambing performance. *Aust. J. agric. Res.* **13**, 52–68.
- Salamon, S. & Robinson, T.J.** (1962b) Studies on the artificial insemination of Merino sheep. II. The effects of semen diluents and storage on lambing performance. *Aust. J. agric. Res.* **13**, 271–281.
- Scaramuzzi, R.J., Lindsay, D.R. & Shelton, J.N.** (1971) The effect of oestradiol benzoate on the duration of oestrous behaviour in the ovariectomized ewe. *J. Endocr.* **50**, 345–346.
- Scaramuzzi, R.J., Lindsay, D.R. & Shelton, J.N.** (1972) Effect of repeated oestrogen administration on oestrous behaviour in ovariectomized ewes. *J. Endocr.* **52**, 269–278.
- Shelton, J.N.** (1965) Identification of progestogens of high activity for the control of the oestrous cycle in the sheep. *Nature, Lond.* **206**, 156–158.
- Shelton, J.N. & Robinson, T.J.** (1967) The evaluation of several progestagen treatments in the entire cyclic ewe. In *The Control of the Ovarian Cycle in the Sheep*, pp. 39–47. Ed. T. J. Robinson. Sydney University Press.
- Shelton, J.N., Robinson, T.J. & Holst, P.J.** (1967) The evaluation of several progestagen treatments in the spayed ewe. In *The Control of the Ovarian Cycle in the Sheep*, pp. 14–38. Ed. T. J. Robinson. Sydney University Press.
- Smith, J.F. & Robinson, T.J.** (1969) Luteal function in the Merino ewe and the effect of exogenous progestagen. *J. Endocr.* **44**, 78–79.
- Smith, J.F. & Robinson, T.J.** (1970) The effect of exogenous progestagen on the levels of free oestrogen in the ovarian vein plasma of the ewe. *J. Endocr.* **48**, 485–496.
- Underwood, E.J., Shier, F.L. & Davenport, N.** (1944) Studies in sheep husbandry in W.A. V. The breeding season in Merino, Crossbred and British Breed ewes in the agricultural districts. *J. Agric. West. Aust.* **11**, 135–143.
- Woody, C.O., First, N.L. & Pope, A.L.** (1967) Effect of exogenous progesterone on estrous cycle length. *J. Anim. Sci.* **26**, 139–141.
- Yeates, N.T.M.** (1949) The breeding season of the sheep with particular reference to its modification by artificial means using light. *J. agric. Sci., Camb.* **39**, 1–43.