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The Physiology of Milk Ejection and its Role in Dairy Production

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One of the most significant findings of the work that has been carried out on identical twins at Ruakura has been the very high heritability values recorded for both butterfat yield and milk production of dairy cattle. It has also become apparent that very large differences exist in the genetic make-up of cows within any one herd—this difference being reflected in large repeatable production differences between animals placed in identical environmental conditions. Consequently it may be asked "What is the difference, in terms of physiological function, between high producing and low producing cattle?"—alternatively the question may be stated in the form, "What are the common factors, inherent in the animal itself, that limit its milk producing ability, and how best they may be overcome?"

It follows that if the overall process of milk production may be subdivided into various components, and an estimate is made of the likely importance of each component as a limiting factor in milk production, we may be in a position to better understand the reasons for the variability of production of animals cared for under uniform conditions.

The mechanism of milk production within the cow may be readily split into four major dependent processes. Briefly stated these are:

1. The successful anatomical development of the mammary gland.
2. The maintenance of the milk secretory cells within the gland itself.
3. The maintenance of an adequate flow of milk precursors to those secretory cells.
4. The successful removal of milk once formed.

In this paper I desire to briefly review our knowledge of the mechanism of successful milk ejection, to present some experimental results related to the problem, and to discuss the role of milk ejection as a limiting factor in milk production.

Until a matter of 20 years ago the prevalent concept regarding milk formation, postulated that the act of milking resulted in the rapid formation of milk within the gland. This idea was, no doubt, based upon the phenomenon of milk-ejection, a process whereby the udder enlarges and becomes turgid—signs which might be taken as evidence of active secretion. Such a notion is now generally discounted, although there is still belief by some overseas scientists that 15% or so of the total yield is actually formed at the time of milking (Usuelli and Piana 1952).

With the realization that the reflex secretion of milk could not explain the rapid increase in udder pressure observed at milking, a number of hypotheses were put forward in an endeavour to explain the phenomenon. As far back as 1910, Ott and Scott had demonstrated that the injection of an extract of the posterior lobe of the pituitary gland of a lactating goat, caused the discharge of milk from the mammary gland. Gaines realised the significance of this observation and distinguished between milk synthesis and milk ejection. Pursuing this idea, he suggested that milk ejection was brought about by a reflex contraction of smooth muscle within the mammary gland; his views however, found little support. Some 16 years later

Krzanwek and Bruggemann surmised that the contraction of "basket cells" around the alveoli was the primary cause, while Hammond (1936) postulated that the pressure rise was due to an erection of the udder and nipple and caused by an accumulation of blood in these tissues.

Gradually two schools of thought emerged. The American workers favoured the view that milk ejection was activated by stimulation of the teats causing a release of a pituitary factor into the blood, the mammary glands being the target organ, while Hammond believed that the ejection of milk was brought about by a nervous reflex causing an engorgement of mammary tissue with the blood.

Using a cow in which the afferent nerve fibres to one half of the udder had been severed, Ely and Peterson (1941) found that milk ejection could be evoked in both halves by milking, or by posterior pituitary extracts, or conversely, inhibited in both halves by either adrenalin or fright. On the basis of these results these workers suggested that milk ejection involved a neuro-hormonal arc. They believed that palpation of the teat and possibly other external stimuli, were sources of sensory impulses reaching the central nervous system, which in turn, stimulated the posterior lobe to secrete oxytocin into the blood, this factor causing the observed increase in intra-glandular pressure. In a similar manner they suggested that fright stimulated the secretion of adrenalin by the medulla of the adrenals, thus causing an inhibition of milk ejection.

Important supporting evidence for this theory was provided by Gomez (1939), and later Cross and Harris (1952), who found that animals lacking a functional posterior lobe of the pituitary were unable to successfully nurse their young. About the same time the presence of a milk ejecting principle in the blood of a cow stimulated to milk "let-down," was demonstrated independently by Petersen and Ludwick (1942) and Peeters et al (1947).

At the annual conference of the New Zealand Dairy Science Association in 1948, Whittlestone reported that McFarlane, in an unpublished communication, had clearly demostrated the existence of a network of myoepithelial cells surrounding the alveoli and ductules, entities which might well be responsible for the physical act of milk ejection. On this basis Whittlestone rejected the hypothesis of Hammond that milk ejection was due to an erectile tissue mechanism, for McFarlane's sections showed no evidence of the blood vessels necessary for this hypothesis.

In 1949 Richardson clearly identified these myoepithelial cells, so confirming McFarlane's communication. Linzell (1952) later published a paper re-affirming the conclusion postulated by Richardson regarding the identity, contractibility, and participation of these myoepithelial cells in the milk ejection reflex.

Thus four important links in the chain of events leading to milk ejection have been established.

Briefly summarised these are:

1. Posterior pituitary extracts are capable of eliciting a milk ejection response in both the normal and perfused gland. Moreover, the posterior lobe of the pituitary appears essential if milk ejection is to be stimulated.
2. The blood of a cow stimulated to let-down contains a substance capable of evoking milk ejection in a perfused udder.
3. The complete denervation of the mammary gland prevents the milk ejection response from being initiated.

4. The mammary gland contains myoepithelial cells so placed that their contraction would cause the ejection of milk from the alveoli. Posterior pituitary extracts actually cause a contraction of these muscular myoepithelial elements.

A problem arises in the response of the mammary gland to substances other than posterior lobe factors however, for milk ejection is stimulated by acetyl choline, while inhibition of milk ejection is produced by adrenalin. Such response point to the possibility of the normal milk ejection reflex being modified in its action by the involuntary nervous control of the mammary gland. Unfortunately, there is not time to discuss the problem in detail here, however, I should like to summarise the conclusions I believe, hold in regard to the nature of the autonomic nerve supply of the mammary gland.

1. The mammary gland has an extensive nerve supply of sympathetic nature. This supply is vascoconstrictor in action (St. Clair 1940) (Peeters at al 1949, 1951, Linzell 1950).
2. The evidence available indicates the absence of a parasympathetic supply (ibid).

From these conclusions, one might envisage inhibitions of ejection being brought about by stimuli directed from the hypothalamus to the mammary gland, without the adrenal medulla as an intermediary factor. It seems most unlikely, however, that milk ejection may be brought about by the activity of the autonomic nervous system.

One is thus left with the conclusion that the neuro-endocrine theory provides the most suitable explanation of the phenomenon of milk ejection.

Of late years it has become increasingly apparent that the milk ejection mechanism may fail to operate at an optimium level. The experience of medical practitioners, and of dairymen, has indicated that lactation may be impeded, or even fail, because of the absence of a suitable milk ejection response. This observation immediately leads one to query the extent to which the sub-optimal functioning of the milk ejection reflex may limit the milk yield of dairy cattle.

An important approach in deriving an answer to this problem is to find some way of measuring quantitatively the milk ejection factor. Whittlestone (1952) made a very valuable contribution to the problem when he demonstrated that the lactating sow offered scope as an assay animal. It is his basic technique that I have used in milk ejection studies, and at this stage, I desire to outline some of the results of this work to you.

In the summer of 1951 when this study was commenced approximately 13 sows were available for use. These consisted of animals of three breeds—Berkshires, Tamworths, and Large Whites. Pitocin was used as the source of the milk ejection factor. All injections were administered intravenously, the sow being held in a crush bail. The time for which milk might be expressed from the gland after injection was used as the criteria of ejection response. The time period between consecutive injections was 5 minutes, and the time lapse between injection schedules on the one sow was never less than 48 hours.

A relationship between the milk ejection response, as measured by duration of milk ejection and the amount of Pitocin administered was known to exist. In order to investigate this relationship, an experiment was set up involving a latin square design in which 4 sows, 4 doses, and 4 repeats were incorporated, this being repeated with different sows on 4 occasions. On each occasion a linear relationship was found to exist between the milk ejection response and the log of the dose of Pitocin administered.

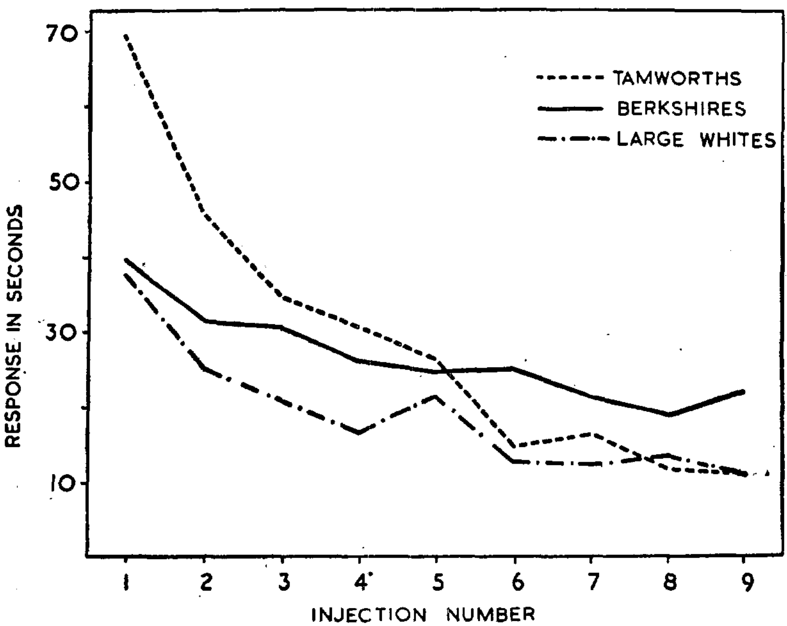
With this relationship as a basis, a 4 point assay technique was proposed and tested. Two doses of a standard preparation of pituitary powder were taken such that one was exactly double the others in potency, likewise 2 doses of the unknown were prepared such that one was double the other in potency, these 4 doses then being assigned at random to a 4 x 4 latin square, so that the 4 doses were administered 4 times, thus making a total of 16 injections into the one sow.

The responses were analysed according to the method published by Emmens (1951).

Table I presents the result of 7 such assays.

TABLE I

Assay No	Potency I.U.		% Error
	True	Estimated	
1	1.0	0.95	4.5
2	1.0	0.88	12.0
3	1.0	1.01	1.0
4	0.69	0.71	2.9
5	0.83	0.85	2.4
6	0.60	0.56	6.7
7	0.66	0.70	6.1



This early work demonstrated that consecutive standardised doses of pitocin elicited a successively diminishing ejection response. Figure I presents the average response of the three breeds of sow used plotted against injection number. The initial difference in response between the Tamworths and Berkshires is highly significant and is an interesting point for speculation, for no difference in the natural suckling time of piglets of different breeds could be detected.

This variation in sensitivity indicates that a difference in the output of the milk ejection factor must exist between breeds of sows as a result of the suckling stimulus. A similar situation may possibly exist between breeds and even strains of dairy cattle. It is interesting to note that the sow ceases to let down her milk in spite of the continued suckling of her piglets—even though the piglets have removed an amount of milk of the order of only 1½ ozs., leaving something like 2½ ozs. still in the gland. We may conclude, I believe, that in the sow at least the amount of milk removed by the piglets is largely determined by the milk ejection mechanism. Experience with the machine milking of pigs at Ruakura has likewise indicated that the amount of milk removed is proportional to the amount of Pitocin administered.

It soon became apparent that a within sow variation existed in the ejection response to standard doses of Pitocin from day to day. In seeking to explain this, it appeared that the amount of milk in the gland, and the rate at which it was removed influenced the duration of ejection.

An attempt was made to derive data on the problem using the indirect method of influencing the volume of milk in the gland. Removal of milk was undertaken in two ways, namely bulk removal using a large dose of Pitocin, and gradual removal with a series of small doses. In a further experiment, the intra-alveolar volume was increased by the intraduct injection of large volumes of physiological saline. Thus, in all, 3 types of experiment were attempted. It may be noted here that it was already known that a parallel pattern of behaviour existed between any 2 glands on the one sow when subject to varying doses of Pitocin. Therefore, it seemed reasonable to conclude that if a treatment applied to one gland only caused a disruption of this parallel behaviour, the disruption could be attributed to the treatment applied.

The results of each type of experiment indicated that the volume of milk within the gland, and further, the rate at which it was removed, influenced the duration of milk ejection. It appeared then, that in the sow at least, the cessation of milk ejection was brought about not only by the enzymatic inactivation of the milk ejection factor, but also by a reduction in the volume or pressure of milk within the gland.

As with dairy cattle, milk production in the sow varies with the stage of lactation. If the intra-alveolar pressure is influencing the duration of milk ejection, as these results have indicated, and if milk production and intra-mammary pressure are related as is commonly believed, there should be a trend in the ejection response to standard doses of Pitocin throughout lactation. An analysis of the large number of responses recorded in this work has indicated, however, the absence of any well defined trend in the ejection response. This observation is similar to that recorded by Whittlestone, and is of particular interest in regard to the nature of the progressive lactational involution of the mammary gland. This result is in harmony with the view that the nature of the involution process must be such as to maintain a resonably constant intra-alveolar pressure throughout lactation.

Thus we arrive back at the problem posed in the introductory paragraphs—namely to what extent does the rapid evanescence of milk ejection limit the yield of milk from lactating animals?

The evidence related to this problem may be conveniently classified under 5 headings.

1. Observations on the lactating sow.
2. Variation in the production level of dairy cattle associated with milking technique.

3. The milking of dairy cattle with the aid of pitocin.
4. Frequency of milking.
5. Associated effects of the milking stimulus.

It has already been mentioned that the lactating sow apparently limits the amount of milk removed at each suckling by means of the milk ejection mechanism. Here then is evidence of milk ejection apparently providing a major limiting factor to the milk yield of at least one species of mammal.

Some four years ago No. I Dairy at Ruakura ceased hand stripping with the result that in the first year of non-stripping one particular strain of pedigree Jersey within the herd dropped an estimated 50 lb. in production as compared with the grade animals in the same herd. This drop was attributed to non-stripping, and presumably resulted from the incomplete removal of milk from the udders of this particular strain of cattle. Evidence of this nature is likewise provided by Dairy Board Consulting Officers. From such sources have come reports of cows producing at a low level in one herd, yet when transferred to another shed, differences in production are encountered which can hardly be explained by feeding conditions.

A number of workers have increased the milk and fat yield of animals over comparatively short periods by removing residual milk with the aid of Pitocin. (Adams and Allen 1948, Johansson 1949, Elliot 1953). Likewise 3 times a day milking as compared to twice a day milking is known to increase production. In cases such as this, the increase in production is usually attributed to a general reduction in the intra-alveolar pressure, which in turn has lead to an increased rate of secretion. The possibility exists, however, of this stimulus of milking being of greater importance than merely causing the onset of milk ejection. Recently it has been demonstrated that oxytocin, which is probably the most important milk ejection principle released in response to the milking stimulus, actually causes the release of ACTH and TSH from the anterior pituitary, both these factors being of importance in the maintenance of successful lactation (Fraja and Martini 1953) (Libretti and Martini 1953). Reinforcement of the idea that factors other than milk removal are involved in successful milking is provided by some recent work at Ruakura, the results of which suggests that the rate of milk secretion **per se** is increased by the administration of Pitocin. If this is the case, the increase in production associated with more frequent milking may be due not only to an increased secretion brought about by a reduction in the mammary pressure, but also by a general increase in secretion rate initiated by the more frequent release of posterior pituitary factors.

Further evidence suggesting a relation between the milking stimulus and augmentation of lactation is provided by anthropologists. These reports (Deansly and Parkes 1950) indicate that it may be a widespread and relatively common practice amongst native tribes for both elderly women and virgin girls to be brought into lacation by physiological and nervous stimuli. Moreover the induction of lactation by psychic mechanisms in modern women has been reported by medical practitioners in recent years (Foss and Short 1950).

At this stage I believe it is useful to bring into the discussion some other Ruakura results. At No. 2. Dairy the production differences between 2 herds of cattle subject to widely varying planes of nutrition has been comparatively small. At No. 4 Dairy identical twins have been subjected to very high and very low planes of nutrition throughout their lactation period, yet the difference in production between the two groups was of the order of only 120 lb. fat per cow. If the genetic differences between herds are of the order of 10%, as Bonnier and Robertson claim, and if nutrition differences commonly account for only 100 lb. or so of fat, how then can large between herd production differences be explained? Variation in the milk ejection response as a result of varying milking technique may be a possible explanation.

Such then is the state of knowledge concerning the physiology of milking. It is obvious that we have but a bare understanding of the mechanisms involved, and we have little factual knowledge as to the importance of the milking stimulus in terms of the production of the national herd.

What indication there are, point to the milk ejection mechanism being more important than has hitherto been believed.

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Discussion

Dr. WHITTLESTONE: I would like to congratulate Mr. Brumby on his plan of attack on the problem of the inheritance of the mechanisms involved in efficient milk ejection. A speaker earlier in this Conference stated that if the chemist could tell the plant breeder what to breed for, the latter would then be able to produce a suitable plant. In the case of the sow and her milk ejecting characteristics we have an astonishingly complex problem. It seems probable that the hormone responsible for milk ejection is actually secreted within the brain, stored in the posterior pituitary, and released as a result of the stimulus of milking. Hence, the efficiency of milk ejection depends on the effectiveness of the reflex, the level of activity of the cerebral secretory cells, and the sensitivity of the target organ, in this case the udder. To study the inheritance of these mechanisms involves the solution of many difficult problems, and I think Mr. Brumby is to be commended for addressing himself to a task which many of us have regarded with trepidation.

Professor CAMPBELL: The importance of a careful thorough milking technique has been emphasised by many, but we actually have little exact information on which to assess the importance of this factor in farm practice. If, through the type of work Mr. Brumby has outlined, more exact information can be obtained about the relation of milking efficiency to productivity, a very worthwhile contribution to our knowledge of dairy husbandry will have been made.

One means by which poor milking may be detrimentally affect milk secretion not touched on by Mr. Brumby may possibly be the so-called 'milk stasis' effect. It has been suggested that the presence of a quantity of milk left in the udder following a milking may, of itself, depress secretion. Could Mr. Brumby comment on this possibility?

Mr. BRUMBY: Quite recently we have been considering the variations of milk and fat secretion rate as a function of the length of the secretion interval. By interposing a 12-hour interval between those of varying length we have been able to obtain some measure of this 'milk stasis' effect. Briefly, we have found that the milk yield in a 12-hour interval is depressed according to the length of the preceding interval, the greater this interval, the greater is the depression. Fat yield, however, appears to be increased by a larger preceding interval.

Another interesting observation that has come out of this work is the influence of the milk ejection function upon the rate of milk secretion. In view of the marked responses we have obtained with growth hormone, it seems feasible, in view of the structure and blood supply of the pituitary, that the milk ejection hormone may actually cause a release of the lactogenic hormones from the anterior lobe of the pituitary, these augmenting the secretion rate of milk.

Mr. THOMPSON: Can Mr. Brumby indicate the relative importance of under-feeding dairy cattle at varying stages of lactation?

Mr. BRUMBY: As far as I'm aware, there has been no systematic study of the problem. General experience indicates, however, that cattle underfed immediately following calving tend to recover to a greater extent than those underfed in later stages of lactation.

Professor CAMPBELL: Using twins underfed for a 6-week period immediately following calving, we have observed a reduction in the peak yield and total yield, in spite of a high level of nutrition throughout the remainder of the lactation period. Thus it would seem that even immediately after calving underfeeding has persistent detrimental effects.