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GALACTOKINETIC RESPONSES TO OXYTOCIN AND OTHER SOLUTIONS IN THE COW

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SOMMAIRE

Chez la Vache, l'éjection provoquée par l'injection intraveineuse de différentes solutions, est appréciée par la mesure du lait résiduel évacué de la glande mammaire. Les solutions injectées sont détaillées sur le tableau 2. L expérience porte sur 24 animaux de race *Frisonne*.

Le schéma expérimental permet de juger de l'efficacité de chaque injection, après des intervalles de traite de 8 heures et de 16 heures.

L'analyse des résultats montre :

1° que l'importance de l'éjection est la même pour la gamme des doses d'ocytocine injectée ;

2° que les injections intraveineuses de solutions de chlorure de sodium à différentes concentrations, ainsi que de placebo provoquent une éjection de lait dont l'importance est d'environ 60 p. 100 de celle obtenue après injection d'ocytocine ;

3° que l'injection répétée d'ocytocine semble inhiber l'éjection naturelle.

Les auteurs suggèrent, en conclusion, que le lait résiduel pourrait être extrait par des doses d'ocytocine plus faibles que celles généralement utilisées.

INTRODUCTION

Reviewing the reports of investigations into the galactokinetic dose response to oxytocin in domestic animals, MORAG and FOX (1966) concluded that the quantitative dose response had not yet been adequately described. The investigation of the minimal effective dose necessary for complete udder evacuation in the cow is important in view of the galactopoeitic role of oxytocin demonstrated in that animal (MORAG, 1967). It is no less important, because so many experimental designs in secretion rate studies have been based on the oxytocin removal of residual milk. MORAG and FOX (*loc. cit.*) went on to describe an experiment in which a double injection of 2.5 i. u. oxytocin was needed to satisfactorily remove residual milk in the ewe. The same authors further reported that by a weak milk ejection was elicited by intravenous injections of isotonic saline.

The following experiments were carried out in order to examine the dose response to oxytocin and to various concentrations of saline in terms of the ejection of residual milk in dairy cow, and to test for any interaction between the galactokinetic properties of exogenous oxytocin and the length of the milking interval (and/or the amount of residual milk).

MATERIALS AND METHODS

The amount of residual milk ejected in response to different levels of oxytocin injection and other solutions were estimated in 24 *Friesan* heifers. The animals, all in the second month of lactation, were ranked according to previous milk yield. Pairs of animals in the rank order were divided at random to provide two matched yield groups each of 12 animals, which are hereafter referred to as Experiment 1 and Experiment 2, respectively. Each group was subdivided into 2 blocks on the basis of previous yield and in each block animals were randomly to the treatment sequences of a 6 × 6 Latin square. The two group received the treatments concurrently and in all respects other than in the treatments defined in tables 3 and 4 as main plots, they were subject to the same milking, feeding and management procedures. Details of the animals are given in table 1. The experiments were carried out using a split-plot Latin square design for which the main plot treatments were as defined in table 2. The sub-plots were two milking intervals — a 16 h night and an 8 h day. The total length of the experiments was 6 days.

$$6 \text{ periods} \times (16 \text{ h} + 8 \text{ h}) = 144 \text{ h} = 6 \text{ days}$$

Semi-permanent nylon cannulae were inserted in the external jugular veins of the heifers 4 days prior the experiment. They were held in place with a plaster bandage. The cow were housed in a byre and were held in the stalls by a neck chain above the plaster bandage. They remained in the stalls throughout the experiment.

Milking was carried out using a Gascoigne bucket plant (pulsation rate of 60/mn at the ratio of 3 : 1 and a vacuum of 37 cm Hg). At milking time the bucket was placed close to the cow by the first operator (cowman) and connected to the vacuum line. The udder was then whashed in warm disinfectant and wiped dry with a disposable paper towel, and the cups were applied immediately. Fore-milking was not practiced. When the flow of milk (as seen through an observation glass) had ceased the cups were removed and the milking lid was fitted to a second bucket. The milk so far obtained was referred to as the *naturally ejected* fraction. A second operator (injector) approached the cow, placed his left hand on the neck and through a piercible rubber cap on the cannula administered a 2 ml injection (In Experiment 1 oxytocin and in Experiment 2 other solutions- 0,5 p.100 chlorbutol was included as a treatment in Experiment 2 as it is the normal preservative for the oxytocin in this series). Immediately following this injection 1 ml of citrated normal saline was flushed through the cannula to ensure that all the intended dose contained in Injection 1 had entered the blood (the dead volume of the cannula was 1 ml). For the dummy injection in Experiment 2 (treatment A) the needle of an empty syringe was inserted into the cannula and in this case no flush was given. On the water treatment (E) no citrated flush was given but an additional ml of water was injected. The cups were then replaced by the cowman and when the flow had again ceased they were removed and the buckets changed. The injector then gave the second injection and flush and the cowman replaced the cups, removing them only when the flow had ceased. The responses to the two injections were referred to as *Residues 1 and 2*. There was no feeding immediately prior to, or during milking. There were no time lapses between cup removal, the injection and cup replacement, and the planned milking intervals of 8 and 16 h never varied for any cow by more than 2 minutes. After the third removal the tests were dipped in 5 p. 100 solution of Iosan C. Both the cowman and the injector had worked regularly with the heifers for one month previously. The heifers were accustomed to the presence of the injector and to the handling of their neck for two weeks prior to the experiments. The animals shewed no signs of distress at his approach, or indeed at the introduction of the various solutions into their blood.

The inclusion of a control treatment amongst a series of levels of oxytocin would tend to increase greatly the error term, which because the exprimental design is a Latin square, cannot thus be divided up between the treatments. In order to avoid this situation the series of oxytocin treatments in Experiment 1 does not contain a control (saline) treatment as did the treatments reported by MORAG

TABLE I

Details of experimental animals. All animals were Friesan *heifers in the second month of lactation*
Description détaillée des animaux expérimentaux
(génisses = jeunes vaches Frissonnes *au 2e mois de production de lait)*

Cow number	Mean daily milk yield over previous week, *g.*
EXPERIMENT 1	
High yielding block	
1	14 925
2	17 950
3	14 375
4	16 225
5	14 700
6	15 325
Low yielding block	
11	13 450
12	12 650
13	11 500
14	13 900
15	12 850
16	12 075
EXPERIMENT 2	
High yielding block	
21	14 050
22	17 375
23	15 825
24	14 675
25	14 975
26	14 800
Low yielding block	
31	12 075
32	13 625
33	12 775
34	12 100
35	13 925
36	13 400

All animals were Friesan heifers in the second month of lactation.

TABLE 2

Experimental design. All injections were administered in 2 ml volume
Détails de l'expérience. Toutes les injections ont été administrés en doses de 2 ml

Cow number	Latin square Periods					
	1	2	3	4	5	6
1, 11, and 21, 31	A	C	B	E	F	D
2, 12, — 22, 32	B	D	C	F	A	E
3, 13, — 23, 33	C	E	D	A	B	F
4, 14, — 24, 34	D	F	E	B	C	B
5, 15, — 25, 35	E	A	F	C	D	B
6, 16, — 26, 36	F	B	A	D	E	C

Treatments (Main plots)

Experiment 1	Injection 1	Injection 2
A	4.0 i. u. oxytocin	5.0 i. u. oxytocin
B	2.0 i. u. oxytocin	5.0 i. u. oxytocin
C	16.0 i. u. oxytocin	5.0 i. u. oxytocin
D	0.5 i. u. oxytocin	5.0 i. u. oxytocin
E	1.0 i. u. oxytocin	5.0 i. u. oxytocin
F	8.0 i. u. oxytocin	5.0 i. u. oxytocin
Experiment 2	**Injection 1**	**Injection 2**
A	Dummy injection	7.5 i. u. oxytocin
B	30 p. 100 saline	7.5 i. u. oxytocin
C	0.5 p. 100 chlorbutol	7.5 i. u. oxytocin
D	15 p. 100 saline	7.5 i. u. oxytocin
E	Pyrogen-free water	7.5 i. u. oxytocin
F	0.9 p. 100 saline	7.5 i. u. oxytocin

All injections were administered in 2 ml volume.

and Fox (1966). During preliminary trials on 8 cows a third oxytocin injection of 5 i. u. was given following administration of (5 + 5), (5 + 7·5), (2·5 + 5) and (2·5 + 7·5) i. u. respectively and yielded less than 10 ml of milk even when the cows were hand stripped. It was for this reason that only one clearing injection was given in the present experiments (see treatments in table 2).

7 kg of hay and 3 1/2 kg of a standard dairy nut were offered daily in two equal meals given after milking to each cow. Water was laid on at each stall. The animals were bedded on wheat straw and cleaned out daily. The byre was brightly illuminated throughout the experiment by day and night. The cows were milked at 0 800 and 1 600 h.

Milk yields were weighed to the nearest 5 g.

The treatment injections were of an oxytocin extract. This extract (made by Armour Pharmaceuticals Ltd.) is obtained from whole pig pituaries by a process involving the solvent fractionation of the anterior pituitary principle, 0.5 p. 100 cholorbutol is added as a preservative. The principle is then diluted to the required strength. The vasopressin content in the batch was 1 i. u. vasopressin to 98 i. u. of oxytocin. Contamination with pituitary solutions other than vasopressin was not measurable. The required treatment concentrations were especially prepared in 2 ml aliquots by the manufacturer. All oxytocin injections were flushed through the cannulae with 2 ml of physiological saline. Stringent antiseptic measures were taken with the cannulae and syringes throught the trial.

TREATMENT OF RESULTS

The yields and secretion rates of milk and fat for the totals and fractions were analysed separately as for a split-plot design, according to the following model :

$$\begin{aligned} Y_{ijklm} = {} & \mu + B_i + C_{ij} + P_k + (BP)_{ik} + T_l + (BT)_{il} + \varepsilon_{ijkl} \\ & + I_m + (IB)_{mi} + (IC)_{mij} + (IP)_{mk} + (IBP)_{mik} + (IT)_{ml} \\ & + (IBT)_{mil} + \gamma_{ijklm} \end{aligned}$$

When :

μ = mean yield or rate of a cow in an interval (sub-plot)

B_i = the effect due to the ith yield block $i = 1,2$

C_{ij} = — — jth cow in the ith yield block $j = 1,2,...6$

P_k = — — kth period $k = 1,2,...6$

$(BP)_{ik}$ = — — ith yield block in the kth period treatment

T_l = — — lth treatment $l = 1,2,...6$

$(BT)_{il}$ = — — ith yield block in the lth treatment interval

I_m = — — mth interval $m = 1,2$

$(IB)_{mi}$ = — — mth interval in ith yield block.

$(IC)_{mij}$ = — — mth interval in the jth cow in the ith yield block.

$(IC)_{mk}$ = — — mth interval in the kth period.

$(ICB)_{mik}$ = — — mth interval in the kth period in the ith yield block.

$(IT)_{ml}$ = — — mth interval in the lth treatment.

$(IBT)_{mil}$ = — — mth interval in the lth treatment in the ith yield block.

The means for yields and secretion rates of milk and fat with the appropriated sandard errors are given in tables 3 and 4 (Experiment 1) and 5 and 6 (Experiment 2).

The analysis carried out on rates (g/h, see Table 3 and 5) enables sub-plot i. e. interval comparisons to be tested with a standard error derived from the mean

TABLE 3

Quantities of total and residual milk obtained in response to intravenous injections of oxytocin Results given in g/h of the milking interval. (Experiment 1)

Quantités totales et résiduelles de lait obtenues à la suite d'injections intraveineuses d'oxytocine. Résultats donnés en g/h d'intervalle entre les traites (Expérience 1)

Milk	Total			Residual			Residue 1			Residue 2		
	Sub-plots			Sub-plots			Sub-plots			Sub-plots		
	8 h	17 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.
Main plots												
0.5 i. u. oxytocin ..	437	620	579	80.2	69.7	75.0	61.4	54.5	57.9	18.8	15.2	17.0
1.0 i. u. oxytocin ..	524	612	568	73.9	75.8	74.9	51.9	61.6	56.7	22.0	14.2	18.1
2.0 i. u. oxytocin ..	539	627	583	73.7	73.2	72.9	59.6	63.6	61.6	13.1	9.6	11.3
4.0 i. u. oxytocin ..	541	607	574	78.0	76.2	77.1	63.1	67.5	65.3	15.0	8.6	11.8
8.0 i. u. oxytocin ..	560	626	593	85.6	75.4	80.5	56.5	64.3	60.4	28.1	11.1	20.1
16.0 i. u. oxytocin ..	564	615	590	78.2	81.8	80.0	61.5	73.2	67.3	16.7	8.6	12.7
X S. P.	544	618		78.1	75.4		59.0	64.1		19.1	11.2	
Period means { 1 to 3)	541	598	595	58.8	67.9	72.7	46.2	54.2	57.4	12.6	13.7	16.3
Period means { 4 to 6)	60	578	573	84.6	78.6	96.7	64.2	63,7	83.5	20.4	14.8	13.2
S. E. Main plots	13.3			8.86			7.33			4.63		
S. E. Sub-plots	5.10			3.19			2.30			2.61		

TABLE 4

Quantities of total and residual milk obtained in response to intravenous injections of oxytocin
Results given in g for each milking interval (Experiment 1)

Quantités totales et résiduelles de lait obtenues à la suite d'injections intraveineuses d'ocytocine
(Expérience 1). Résultats donnés en g d'intervalle entre les traites

Milk	Total			Residual			Residue 1			Residue 2		
	Sub-plots			Sub-plots			Sub-plots			Sub-plots		
	9 h	16 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.
Main plots												
0.5 i. u. oxytocin ..	4 296	9 928	14 224	642	1 116	1 758	491	872	1 362	151	243	394
1.0 i. u. oxytocin ..	4 195	9 798	13 793	591	1 213	1 804	410	986	1 400	176	228	404
2.0 i. u. oxytocin ..	4 309	10 024	14 334	582	1 171	1 753	477	1 017	1 497	105	154	259
4.0 i. u. oxytocin ..	4 326	9 708	14 034	625	1 219	1 844	505	1 081	1 586	120	138	258
8.0 i. u. oxytocin ..	4 476	10 013	14 490	685	1 207	1 892	452	1 029	1 482	132	178	410
16.0 i. u. oxytocin ..	4 515	9 841	14 158	624	1 309	1 933	492	1 170	1 662	134	148	272
$\bar{X}$ S. P.....	4 353	9 844	14 648	625	1 206	1 802	472	1 026	1 454	153	180	348
Period means 1 to 3.	13 588	14 518	14 012	1 442	1 622	2 278	1 144	1 310	1 982	298	312	296
Period means 4 to 6.	14 674	13 986		2 008	1 830		1 502	1 502		415	328	
S. E. Main plots	322			199			180			86		
S. E. Sub-plots	66.54			35.39			32.78			23.81		

TABLE 5

Quantities of total and residual milk obtained in response to intravenous injections of various solutions Results given in g/h of the milking interval. (Experiment 2)

Quantités totales et résiduelles de lait obtenues à la suite d'injections intraveineuses de diverses solutions (Expérience 2) Résultats donnés en g/h d'intervalle entre les traites.

Milk	Total			Residual			Residue 1			Residue 2		
	Sub-plots			Sub-plots			Sub-plots			Sub-plots		
	8 h	16 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.
Main plots												
Dummy injection....	545	602	574	40.4	42.1	41.3	8.4	4.5	6.4	32.0	37.6	34.8
Pyrogen-free water ..	554	587	571	56.8	48.0	52.4	36.9	25.1	31.0	19.8	22.9	21.4
0.9 p. 100 saline....	575	611	575	50.3	67.4	58.8	31.8	45.3	38.6	18.4	18.4	20.7
15 p. 100 saline.....	580	614	580	58.2	73.0	65.6	30.5	49.8	40.2	27.7	23.0	25.5
30 p. 100 saline.....	570	602	570	46.9	44.3	46.6	34.1	20.1	27.1	12.8	24.1	18.5
0.5 p. 100 chlorbutol	567	587	567	76.1	47.6	61.9	56.8	29.1	42.9	19.4	18.5	19.0
$\bar{X}$ S. P.....	565	600		54.8	53.7		33.7	29.0		21.7	24.7	
Period means 1 to 3 .	553	583	586	53.1	45.8	46.8	30.4	21.7	23.9	22.7	24.1	23.0
Period means 4 to 6..	564	582	568	51.8	56.6	71.4	29.8	32.2	48.2	22.0	24.4	23.2
S. E. Main plots	12.50			9.85			12.40			5.66		
S. E. Sub-plots	7.83			5.96			5.62			2.34		

TABLE 6

Quantities of total and residual milk obtained in response to intravenous injections of various solutions
Results given in g for each milking interval (Experiment 2)

Quantités totales et résiduelles de lait obtenues à la suite d'injections intraveineuses de diverses solutions. Résultats donnés en g d'intervalle entre chaque traite (Expérience 2)

Milk	Total			Residual			Residue 1			Residue 2		
	Sub-plots			Sub-plots			Sub-plots			Sub-plots		
	8 h	16 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.	8 h	16 h	$\bar{X}$ M. P.
Main plots												
Dummy injection....	4 359	9 635	13 993	324	674	996	67	72	140	256	602	858
Pyrogen-free water ..	4 434	9 405	13 839	454	7 768	1 220	296	402	698	159	366	525
0.9 p. 100 saline....	4 310	9 775	14 085	402	1 078	1 480	255	724	979	148	354	502
15 p. 100 saline.....	4 368	9 825	14 193	466	1 168	1 634	244	797	1 041	222	372	594
30 p. 100 saline.....	4 312	9 625	13 938	375	708	1 084	273	322	596	103	387	490
0.5 p. 100 chlorbutol	4 376	9 390	13 766	609	762	1 370	454	466	920	155	296	451
$\bar{X}$ S. P.....	4 360	9 610		438	860		264	464		174	312	
Period means 1 to 3 .	13 670	14 132	14 372	134	1 080	1 168	584	478	582	550	602	586
Period means 4 to 6 .	13 668	14 128	13 838	1 070	1 422	1 814	642	858	1 226	537	563	588
S. E. Main plots	289			364			306			248		
S. E. Sub-plots	92.410			79.29			72.82			34.02		

square of error *b* which is of an appropriate order of magnitude ; whilst the analysis carried out on the yields (g, see table 4 and 6) make any consideration of the size of the fractionated portions of milk in the diferent intervals more easy. It is noted that in certain of the analyses error *b*) was larger than error *a*). In a split-plot design error *b*) is characteristically smaller than error *a*) (SNEDECOR, 1956). It is suggested that in this case the increase in size of error *b*) occurred as a result of a negative correlation between periods, and that in future, in order to avoid such a situation, discard intervals should be inserted between the treatment intervals.

It is noted that the means of Residue 1 measured the actual response to treatment injection, whilst value of Residue 2 was a measure of the galactokinesis due to the treatment *plus* 5 i. u. in Experiment 1 and the treatment *plus* 7.5 i. u. of oxytocin in Experiment 2.

The results of Experiment 1 shew that there was no significant difference in galactokinetic response over the treated dose range of 0.5 to 16 i. u. In Experiment 2, the salines, water and chlorbutol were found to have some 60 p. 100 of the galactokinetic activity exhibited by the oxytocin.

DISCUSSION

Experiment 1

The apparent linear trend between the oxytocin dose and the quantities of residual milk ejected (Residue 1) was non-significant. The values of Residue 2, as could be expected, appeared to confirm this slight and non-significant trend. The values for Residual and Total milks, however, showed no treatment differences, and thus indicated that the administration of a second clearing injection completely removed any slight main plot trend. The lack of any significant difference in treatment responses and the subsequent removal by the second injection of any slight trends suggests that double injections of very small doses could be effective for the removal of residual milk. In recent secretion rate studies carried out by SCHMIDT (1961), TUCKER, REECE and MATHER (1961) and LINNERUD (1964) single injections of 10 i u. were used; whilst ELLIOTT (1959) used double injections of 10 i. u. each in her later experiments. The present data suggest that those workers who used single doses may not have removed all the residual milk (the mean response to the second injection was 332 g per day), whilst ELLIOTT probably effectively removed all the residua but used a dosage far in excess to that required. The definition of a minimal effective dose is particularly important in view of the evidence of galactopoeitic action by oxytocin demonstrated by DENAMUR (1953), in the goat, and by DENAMUR and MARTINET (1961), and MORAG and FOX (1966) in the ewe.

A given dose of oxytocin proved more efficient ($P < 0.001$) when the amount of milk in the gland was greater (see mean values for Residue 1 in two milking intervals). This increase in effectivness of the hormone with an increase in milk volume is similar to that observed by MARTINET (1967). He found that the contractions of mammary strips of guinea pig and rat, measured *in vitro*, became more pronounced with an increase in milk volume.

The period means for Residual milk shew a significant increase from the first day to the last ; these values expressed as percentages of Total milk were 10.6, 11.2, 12.3, 13.7, 13.8, and 16.2 p. 100. This apparent inhibition of natural ejection and the increase in the relative size of the residual fraction with the administration of exogenous oxytocin and the removal of the residual fraction is in accordance with the observations of SHAW (1942) and of DODD (1966), the reasons for which are quite obscure. MORAG and FOX (1966) reported a similar phenomenon in ewes, but in that case the increase of the inhibition with treatment was far steeper. In a similar way the period values for Residue 1 shew a significant increase over the 6 days. This could be due to the same obscure and unexplained phenomenon.

Experiment 2

The treatment responses as expressed by the values of Residue 1 would suggest that a definite ejection was produced whenever one of the examined solutions was introduced into the blood. Comparing this response to that obtained in the heifers in Experiment 1, the ejection appears to be some 60 p. 100 of that produced in response to the injections of the hormone. (The mean amount of milk ejected by the first injection in Experiment 1 was 1 498 g whilst the mean of the five treatments in which *liquid* was introduced into the blood in Experiment 2 was 846 g (i. e. excluding the dummy injection treatment A). This response was much larger than the response to isotonic saline reported in the ewe by MORAG and FOX (1966), where the amount of residual milk ejected in response to isotonic saline was only 30 p. 100 of the amount ejected in response to oxytocin. The standard errors for Residue 1 and 2 are much larger in Experiment 2 than in Experiment 1 ; this is because the inclusion of a control treatment has tended to « explode » the error term. One is unable to calculate an error wich would apply only to the other five treatments because of the Latin square design. (See Materials and Methods.) The present data do not suggest that there is any relationship between the concentration of the saline solutions and their galactokinetic activity. Indeed, the response to the water treatment suggests that the ionized radicals of the other solutions are not, in fact, the activators of the ejection. It may be that the liquids have a direct galactokinetic effect on the myoepithelial target tissue and do not act indirectly through the elicitation of an oxytocin release from the pituitary. This hypothesis could possibly be tested by comparing the degree of response to carotid arterial as opposed to jugular venous administration. It is noted that ANDERSSON (1951), HOLLAND, CROSS and SAWYER (1959), and ANDREOLI and CHIAUDANO (1961), have described milk ejection in goat, in rabbit, and in woman respectively, in response to hypertonic saline solutions. Evidence of anti-diuretic activity stimulated by *hypertonic* solutions has been reported by many authors, but the solution were injected into the carotid artery.

It is difficult to see the responses to the dummy injection (Residue 1 — treatment A) as the result of a further ejection. It is suggested that this amount of milk — the quantity of which in absolute terms was similar in both intervals — represents a part of the naturally ejected fraction, which is not removed by the milking routine. It is stressed in the connection that neither machine nor hand stripping were carried out.

The rate of milk secretion and the changes in the quantity of residual milk

In both experiments the rate of milk secretion was higher during the 16 h than during the 8 h interval. These estimates correspond to the actual amount secreted during the intervals as residual milk was removed at the beginning and at the end of every interval. It could be argued that the difference in secretion rate was due to a preceding interval effect (the 8h interval always coming after the 16 h interval and *vice-versa*), but from the quantitative estimates of this effect published by ELLIOTT (1959) and SCHMIDT (1961) is would seem that this effect would not account for the significant increase of 12 p. 100 in Experiment 1 and of 6 p. 100 in Experiment 2 in the rate of milk secretion. There has been no previous communication which has reported an actual secretion rate which was higher during the 16 h than during the 8 h interval in the cow.

In both experiments the amount of residual milk after an interval of 16 h was twice the amount after an interval of 8 h. This confirms the general model proposed by TURNER (1955), in the cow and by SEMJAN (1962), in the sheep, but does not lend support to the model presented by ELLIOTT (1959) in which she described a constant level of residual milk after intervals of 8 to 16 h.

The effectiveness of the small doses of oxytocin in Experiment 1 and the relatively strong ejection demonstrated by the various liquids in Experiment 2 indicate the necessity of further work in which even lower doses of oxytocin are tested both as first and second (clearing) doses, and in which *successive* doses of the various liquids are tested (i. e. as first and second doses) for their galactokinetic activity.

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SUMMARY

The galactokinetic dose responses to intravenous administration of oxytocin (0.5-16.0 i. u.) to various strengths of saline, to water and to 0.5 p. 100 chlorbutol were measured in terms of ejection of residual milk in the cow. A split-plot Latin square design was used and each injection was tested after an 8 h and 16 h interval.

The trial was carried out using 24 *Friesan* heifers. No significant differences in galactokinetic activity were found to exist aver the tested range of oxytocin. Saline, water and chlorbutol solutions were found to have some 60 p. 100 of the galactokinetic activity shown by oxytocin.

The administration of oxytocin inhibited natural milk ejection. It was suggested that residual milk could be effectively removed by doses smaller than those generally used.

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