

## Studies on Cystic Ovarian Disease in Dairy Cattle

### II. Therapeutic Efficacy of an Intramuscular Injection of Corticosteroids

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### 乳牛の卵胞嚢腫に関する研究

#### II. 合成副腎皮質ホルモンの筋肉内注射による治療成績

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#### Introduction

Adrenal hyper activities lead to an eventual inhibition of gonadotropic secretion and thereby glucocorticoids may alter the secretion of gonadotropic hormone (BALDWIN, *et al* 1974).

Previous paper (NAKAO, *et al* 1975) reported that cows with cystic ovarian disease (COD) had apparently declined adrenocortical response to ACTH administered intramuscularly, which could be resulted from the excess release of ACTH from the pituitary. Differences in the response to ACTH among cows having different patterns of estrous behavior were also described.

SHORT (1961) suggested that there would be two ways in the treatment of COD in cattle, one was to establish a functional corpus luteum in the ovary by giving lutenizing hormone or rupturing the cysts and the other was to inhibit pituitary activities by administering progestational compounds.

Since corticosteroids are known to reduce the release of ACTH and LH from the pituitary (ARIMURA, *et al* 1969, BALDWIN, *et al* 1974), it is of interest to administer corticosteroid preparations for the treatment of COD.

The purposes of this study were to examine therapeutic efficacy of synthetic corticosteroids given intramuscularly and to study the relationship between the prognosis and estrous behavior in cows with COD.

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### Materials and Methods

Out of 112 cows with COD which had been examined for serum concentrations of 11-hydroxycorticosteroids and sex steroids, serum protein pattern and adrenocortical function, and reported (NAKAO, *et al* 1975), 109 cows were offered for the trials soon after blood sampling.

Betamethasone (Betsolan, Glaxo) 10-40 mg was injected intramuscularly to 92 cows and dexamethasone (Corson P, Takeda Chemical Industries, Ltd.) 10-20 mg to 8 cows. The other 9 cows were treated with chorionic gonadotropic hormones (Gonatropin, Teikoku Hormone Mfg. Co. Ltd.) 10,000 MU. All the cystic ovaries were ruptured except those remained unruptured at the time of treatment. Ten days after treatment, ovaries were examined by rectal palpation. Animals, where corpus luteum formation was observed, were kept under observation until the next estrus when artificial insemination was performed. For the animals, whose cystic ovaries remained unchanged or where new cysts reappeared, treatment was repeated several times more.

Only the animals which conceived following treatment were considered as recovered cases.

### Results

#### 1. Results of treatment.

Results of the treatment of 100 cows having COD with corticosteroids and the treatment of 9 such cows with chorionic gonadotropic hormones are summarized in Table 1. An average of 1.9 intramuscular injections of betamethasone 10-40 mg or dexamethasone 10-20 mg resulted in a 74 % pregnancy rate within  $71.1 \pm 46.4$  days after the first treatment in the case of the 100 cows with COD. Confidence limits of this pregnancy rate were between 79.5 % and 66.9 % at the 5 % level.

#### 2. Relationship between prognosis and estrous behavior.

Pregnancy rates and days to conception differed among the groups and subgroups which were earlier divided according to estrous behavior. The highest pregnancy rate and the shortest period up to conception was observed in anestrus cows. When anestrus cows were divided into two groups based on breeding histories, one having been anestrus since the last calving and the other having shown estrus several times and then turned to anestrus, pregnancy rate in cows of the former group was significantly higher than that of the latter group ( $P \leq 0.05$ ). Pregnancy rate in cows with anestrus since calving was also significantly higher ( $P \leq 0.05$ ) than either cows with continuous or intense estrus or cows with irregular or regular estrus. The pregnancy rate in cows with continuous or intense estrus was lower than in anestrus cows and higher than in irregular or regular estrous cows. Eighty percent of the 25 cows with continuous estrus conceived, while only 40 % of the 5 cows showing true nymphomania became pregnant.

**Table I.** Results of treatment of cystic ovarian disease in cows with corticosteroids.

Group Subgroup	No. of cows treated	No. of cows conceived	Pregnancy rates (%)	Confidence* <sup>1</sup> limits of pregnancy rates	Ave. No.* <sup>2</sup> of treatment	Ave. No.* <sup>3</sup> of A. I.	Ave. days to conception
Group I							
True nymphomania	5	2	40.0	81.1- 8.7	2.0	1.5	63.5
Continuous estrus	25	20	80.0	91.8-61.6	2.1±1.2	1.9±1.3	76.6±52.3
Total	30	22	73.3	86.1-57.1	2.0±1.2	1.9±1.2	75.4±50.6
Group II							
Irregular estrus	23(3)* <sup>4</sup>	16(1)	69.6	84.9-49.8	2.1±0.9	2.2±1.2	83.3±38.8
Regular estrus	14(2)	9(2)	64.6	84.7-38.4	1.6±0.7	2.3±1.7	90.4±79.0
First estrus postpartum	5	2	40.0	81.1- 8.7	2.0	1.0	62.0
Total	42(5)	27(3)	64.3	76.4-49.2	1.9±0.9	2.1±1.4	84.1±53.7
Group III							
Anestrus since calving	21(2)	21(2)	100.0	100.0-86.7	1.6±0.7	5.7±0.7	57.0±27.4
Anestrus after estrus	16(2)	10(1)	62.5	82.3-39.3	2.0±1.2	1.3±0.7	56.5±40.9
Total	37(4)	31(3)	83.8	92.7-71.7	1.7±0.9	1.5±0.7	56.8±31.6
Grand total	109(9)	80(6)	73.4	79.5-66.9	1.9±1.0	1.8±1.1	71.1±46.4

\*<sup>1</sup>.  $P < 0.05$ \*<sup>2</sup>. Total number of treatment / number of cows conceived.\*<sup>3</sup>. Total number of insemination / number of cows conceived.\*<sup>4</sup>. Figures in parenthesis show the number of cows treated with chorionic gonadotropic hormones.

The lowest pregnancy rate and the longest period up to conception was observed in cows showing irregular or regular estrus.

### 3. Relationship between prognosis and the time of treatment during the lactation period.

At the time of treatment, longer the interval after calving, less cows conceived and required extra treatments. A significant correlation was observed between the intervals after calving taken as days after the last calving and the recovery expressed as a number i.e. pregnancies as one and failures as two ( $r=0.24$ ,  $P \leq 0.05$ ), and also between days after calving at the time of treatment and the number of treatments per head ( $r=0.22$ ,  $P \leq 0.05$ ).

The average number of days after calving in cows which conceived and those which failed to conceive were,  $133.4 \pm 88.9$  and  $276.2 \pm 470.8$  days, respectively. Animals were divided into two groups on the basis of the time of conception after parturition in normal cows, one of which comprised those treated within 90 days and the other, those treated later than 90th day postpartum. Ninety-one point nine percent out of 37 cows treated within 90 days after calving conceived, while only 63.9% out of 72 cows treated later than 90th day postpartum conceived. There was a significant difference in pregnancy rates between these two groups ( $P \leq 0.05$ ).

### Discussion

Published data on the treatment of COD in dairy cattle has been summarized by SHJERVEN (1971). According to his review, recovery rate (number of cows conceived/number of cows treated) are reported as between 37 and 91 % (75 % in average) for the treatment by intramuscular injection of chorionic gonadotropic hormones, between 44 and 80 % (72 % in average) by intramuscular or intravenous injection of pituitary gonadotropic hormones and between 45 and 90 % (70 % in average) by intrafollicular injection of gonadotropic hormones. Since corticosteroids have not been used so widely as gonadotropic hormones for the treatment of COD in dairy cattle, only a small amount of data has been available regarding the therapeutic efficacy of these preparations. ONO, *et al* (1968) reported the treatment of COD by intramuscular injection of 10-20 mg dexamethasone. The treatment resulted in 81.5 % efficiency rate (number of cows inseminated / number of cows treated) after an average of 38.4 days. SCHJERVN (1971) also obtained favourable results using 2.5 mg flumethasone or 20 mg betamethasone. Of 21 cows treated 12 (57 %) conceived after a single injection of corticosteroids and finally 16 (76 %) conceived following several injections.

Efficacy of the treatment with corticosteroids was confirmed during the present study. A 74 % pregnancy was obtained after an average of 71 days following intramuscular injections of 10-40 mg betamethasone or 10-20 mg dexamethasone. This data compares well with data of the treatment with chorionic gonadotropic hormones.

It is of value to notice that there were considerable differences in prognosis, described as pregnancy rate and interval from treatment to conception, among groups classified according to estrous behavior. The highest pregnancy rate in association with the shortest period up to conception was observed in cows showing anestrus (Group III). In this group, cows showing anestrus since calving had significantly higher ( $P \leq 0.05$ ) pregnancy rate than cows which turned to anestrus after several times of estrus. This could be partly due to the differences in intervals after calving at the time of treatment between these subgroups. In cows showing anestrus since calving, the average number of days from calving to diagnosis was significantly shorter ( $P \leq 0.01$ ) than those in cows showing anestrus after estrus. In cows exhibiting true nymphomania and in those showing irregular or regular estrus, pregnancy rates were markedly lower than in anestrus cows. Longer intervals from treatment to conception were observed in cows with irregular or regular estrous cycles as compared to those with continuous estrus. These findings indicate a close relationship between estrous behavior and prognosis of COD. This was consistent with the observations of ROMANIUK (1972) on the relationship between estrous behavior and prognosis of COD. Pregnancy rates were reported as being 19.3 % in 31 cows exhibiting nymphomania, 74.0 % in 127 cows showing anestrus since calving, 71.2 % in 94 cows showing anestrus after insemination, and 64.2 %

in cows with irregular estrous cycles. KUDLÁČ, *et al* (1970) also demonstrated the differences in pregnancy rates among cows having different patterns of estrous behavior as a result of treatment with a combination of 3,000 IU chorionic gonadotropic hormone and 125 mg progesterone. Pregnancy rates were given as follows; 90.0 % in cows showing anestrus, 75.0 % in cows with continuous estrus, and 70.5 % in cows with irregular estrus. The former suggested that the relationship between estrous behavior and prognosis might be due to different extents of irreparable degeneration in the pituitary and uterus.

In the previous study (NAKAO. *et al* 1975), it appeared that there was an important relationship between estrous behavior and adrenocortical function as well as serum concentrations of progesterone and estrogens. The author, therefore, is of the opinion that adrenocortical function and sex steroids are closely related with prognosis of COD and this brings about the differences in prognosis among cows having different patterns of estrous behavior.

It was found that cows treated up to 90th day after calving recovered more readily than those treated later than this period in this study. And the average days from calving to treatment were 133 days in 80 successfully treated cows and 267 days in 29 unsuccessfully treated cows. Similar results were reported by ROBERTS (1955), SPRIGGS (1968), SCHJERVEN (1971) and ROMANIUK (1972). Subsequently it was thought that the earlier the treatment was conducted, higher pregnancy rate would be obtained. The cause of these findings have not been well studied, although SHORT (1961) explained that since the granulosa cells underwent degeneration in the cystic follicles and thus insufficient granulosa cells were responsible to disturb establishing functional corpus luteum, the earliest treatment after cyst formation would result in the best recovery rate.

### Conclusions

1. An average of 1.9 intramuscular injections of betamethasone 10-40 mg or dexamethasone 10-20 mg resulted in a 74 % pregnancy rate within  $71.1 \pm 46.4$  days after the initial treatment in 100 cows with COD. Therefore corticosteroids can be recommended for the treatment of COD.

2. Pregnancy rates and the intervals from the first treatment to conception differed among the groups and subgroups. Recovery rates and their confidence limits ( $P \leq 0.05$ ), and the mean intervals from treatment to conception in each group are as follows; 83.3 %, 92.7 - 71.7, and  $56.8 \pm 31.6$  days in cows showing anestrus, 73.3 %, 86.1 - 57.1, and  $75.4 \pm 50.6$  days in cows exhibiting continuous or intense estrus, and 64.3 %, 76.4 - 49.2, and  $84.1 \pm 53.7$  days in cows showing irregular estrus. Among subgroups the highest pregnancy rate (100 %) was obtained after an average of  $57.0 \pm 27.4$  days in cows showing anestrus since calving.

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## 摘 要

先に副腎皮質機能検査と血中性ステロイド濃度並びに血清蛋白分画の測定を行った112頭の卵胞嚢腫牛のうち、100頭に合成副腎皮質ホルモン10~40 mgを、また9頭にはHCG 10,000 MUを筋肉内注射し、卵巣の変化を観察した。その結果、合成副腎皮質ホルモンを平均1.9回筋注した100頭のうち、74頭は治療開始後平均71日で受胎したことから、本剤はHCG同様に卵胞嚢腫の治療に有効であることがわかった。さらに、その予後を治癒率(受胎頭数/治療頭数)および受胎までの日数で表わし、卵胞嚢腫の外部徴候別に比較してみると、無発情型が83.2%、51日と最も良好で、思牡狂および持続性発情型が73.3%、75日とこれにつき、不規則発情型では64.3%、84日と最も不良であった。このことから、卵胞嚢腫牛の予後と外部徴候の間には密接な関係があることが明らかにされた。