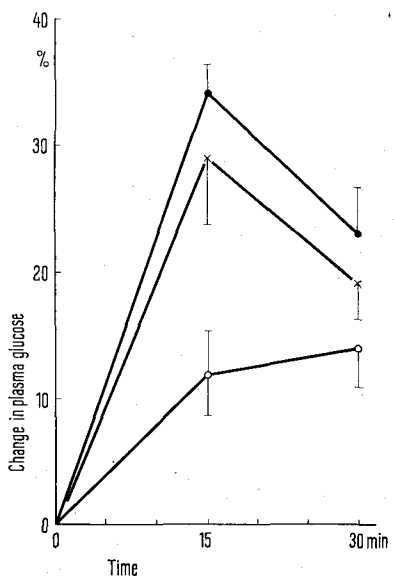
The chicks were bursectomized surgically[8] at one day of age, the bursal stalk being cauterized to prevent regeneration[9]. One half of the bursectomized group was injected with plasma prepared from normal, intact 3-week-old chickens. Blood was obtained by a frontal heart puncture technique, the syringe having previously been wetted with a solution of heparin in order to prevent coagulation. The sample was immediately centrifuged at 4 °C, the plasma collected and injected into the recipient bird. The whole procedure took about 15 min. Each donor bird was bled *once only*: the bursa is particularly sensitive to stresses, responding by regression[1] which might therefore have adversely affected the concentration of any humoral agent secreted by it. Each chick received 1.5 ml plasma intraperitoneally twice weekly beginning on the day following the operation. At 3 weeks of age the treated, bursectomized birds, the untreated bursectomized birds and normal intact birds were given L-adrenaline (300 mg/kg i.p.) and plasma glucose levels determined 0, 15 and 30 min after injection.



The percentage change in plasma glucose following stimulation with adrenaline (300 µg/kg i.p.). Each point is the mean of 10 observations; the standard errors are indicated. ●, treated, bursectomized; X, normal; ○, bursectomized.

The results are summarized in the Figure. It will be noted that whereas the untreated bursectomized birds showed a markedly reduced hyperglycaemia as compared with the normal, intact birds, the treated bursectomized birds showed not only a restored response but a slightly enhanced one.

These results are consistent with the hypothesis that a humoral factor was present in the plasma of the normal bird that was absent from the bursectomized bird and that this factor was responsible for enhancing the activity of the glycogenolytic mechanism.

It has been claimed, on the basis of the restoration of immunological activity by bursal implants[10] and extracts[11], that the bursa of Fabricius should be considered an endocrine gland. The findings described in this report support this view.

Résumé. Des poussins boursectomisés traités avec du plasma de poussins intacts ne subissent pas de perte de réponse glycémique à l'insuline, mesurée d'après les changements de niveaux du glucose dans le plasma sanguin. Il est suggéré que les résultats sont compatibles avec l'hypothèse selon laquelle la bourse de Fabricius est une glande endocrine.

B. M. Freeman

Houghton Poultry Research Station, Huntingdon, PE17 2DA, (England), 12 November 1971.

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Effects of 2-Br-α-Ergokryptine on Plasma Prolactin Level During Parturition and Onset of Lactation in Cows

The prolactin inhibitor 2-Br-α-ergokryptine was shown to have an inhibitory effect on lactation in rats[1], rabbits and pigs[2] by measuring the weight gain of litters as criterion for the milk production of treated mothers.

In a series of experiments concerning the effects of the ergot alkaloid 2-Br-α-ergokryptine-methane-sulfonate (CB 154) on plasma prolactin level and milk yield in cows, we could demonstrate a depression of prolactin to a very low basic level during lactation: contrary to the drastic decrease of prolactin, the milk yield remained unchanged or dropped only slightly (about 15%)[3]. We concluded that prolactin in the bovine is not a major factor for the maintenance of lactation (galactopoiesis). One preliminary observation reported in this first communication suggested that the inhibitory action of CB 154 may have a stronger effect on the onset of lactation. In the present paper we studied the effect of CB 154, administered around parturition, on prolactin level and milk yield in cows; these experiments were motivated by the fact that the most distinct prolactin elevation occurs shortly before parturition in cattle[4–6].

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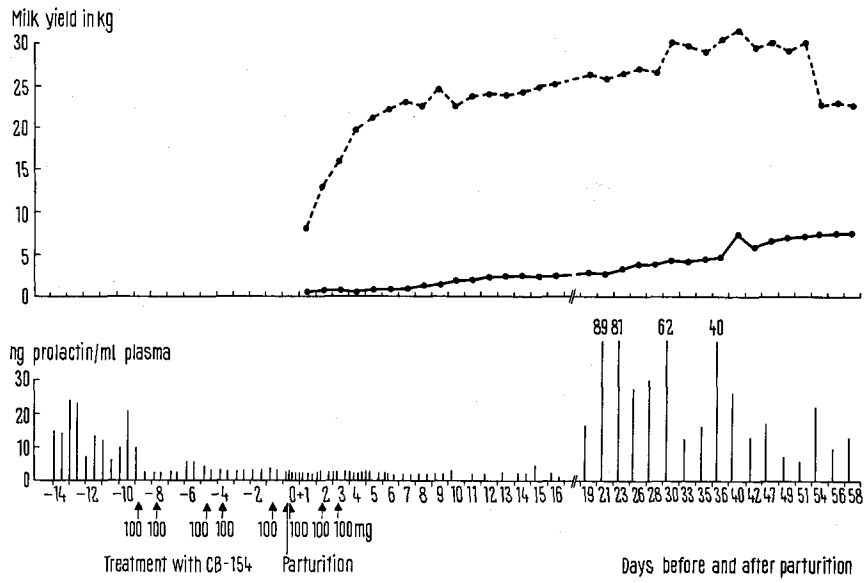

Fig. 1. Cow 'Kaliro'; treatment with CB-154 before and after parturition; effect on plasma prolactin and milk yield ●—●, milk yield after treatment (delivery Nov. 15, 1971); ○---○, Milk yield 1 year before without treatment (delivery Nov. 10, 1970)

Material and method. Animals. 3 pregnant cows, 5, 10 and 12 years old, were kept in an open stable; they were fed with hay, maize silage and concentrates. The experiments were begun 2–3 weeks before the expected time of parturition.

Blood sampling. Blood plasma was collected from the jugular vein by needle puncture into centrifuge tubes containing heparin ('Liquemin', Hoffmann-La Roche) as an anticoagulant. The samples were kept frozen (−18 °C) until assayed.

Inhibitor substance. The ergot alkaloid 2-Br-α-ergocryptine-methane-sulfonate-CB-154 (kindly supplied by Sandoz Ltd., Basel) was used. The substance was dissolved in a solution of 40% ethanol and 60% saline, and was administered in 3 ml s.c.

Prolactin assay. Prolactin was measured by the radioimmunoassay technique described by SCHAMS and KARG[4], see also[3]. NIH-P-B_2 (19.9 IU/mg), kindly supplied by the National Institute of Health (USA), was used as reference preparation. The separation of the antigen antibody complex was done by the double – antibody technique.

Experiments and results. Details of treatment with CB-154, plasma prolactin level and milk yield/day are shown in Figures 1–3. Blood was collected from day 273 or 274 of pregnancy twice a day; before, during and after parturition at 6-h-intervals. 5 days after parturition samples were collected twice a day, and later only 3 times a week. The blood samples of the first 5 days showed the original individual prolactin levels. Thereafter treatment with CB-154 lasted for 12 days. During that period each cow was treated 8 times with 100 mg CB-154 on 2 successive days at intervals of 1 or 2 days.

Cow 'Kaliro' (Figure 1) was given the first injection on day 278 of pregnancy, the last injection on the 3rd day post partum; calving occurred on day 287.

Cow 'Nyschlos' (Figure 2) and cow 'Lado' (Figure 3) received the first injection on day 279 of pregnancy, the last injection on day 290; both cows calved on day 293.

All 3 cows had a normal delivery. The average gestation for the Brown Swiss breed is 287–288 days. Cow 'Lado''s calf was found dead. The two other calves developed normally and all puerperia were without complications. The

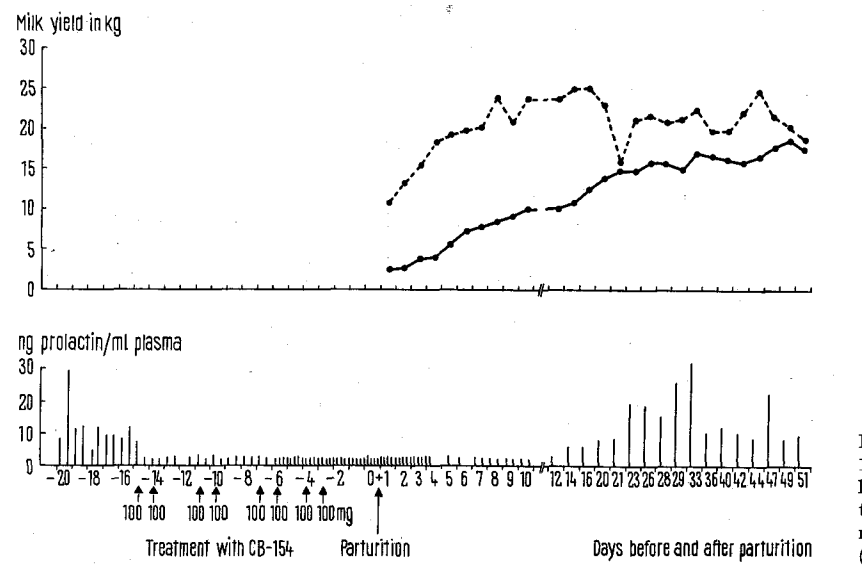

Fig. 2. Cow 'Nyschlos'; treatment with CB-154 before parturition; effect on plasma prolactin and milk yield. ●—●, milk yield after treatment (delivery Nov. 23, 1971); ○---○, milk yield 1 year before without treatment (delivery Dec. 2, 1970).

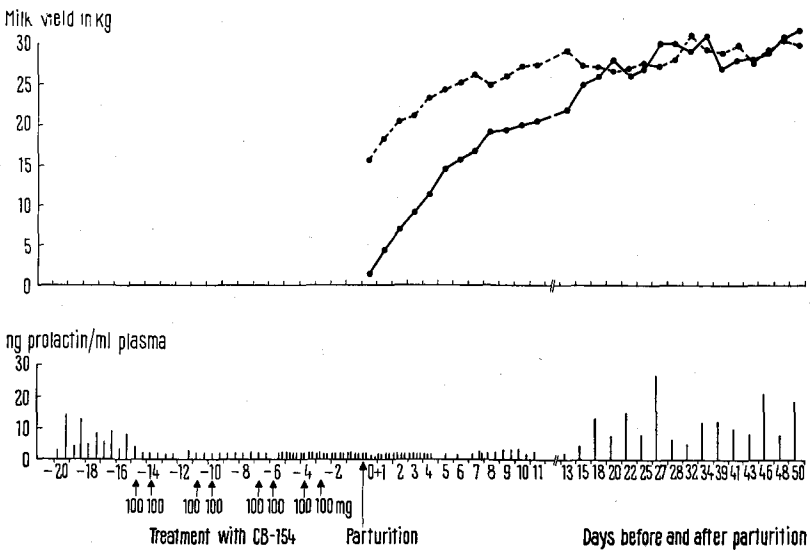

Fig. 3. Cow 'Lado'; treatment with CB-154 before parturition; effect on plasma prolactin and milk yield. ●—●, milk yield after treatment (delivery Nov. 23, 1971); ○---○, milk yield one year before without treatment (delivery July 8, 1970).

plasma prolactin levels decreased significantly after treatment with CB-154 in all 3 animals.

Before parturition the characteristic prolactin peak failed to appear completely. Prolactin values reached and rose beyond pretreatment levels approx. 3 weeks after the last injection of CB 154.

In all cows treatment with CB 154 had a strong depressive effect on the onset of lactation, although there were no abnormal clinical observations on the udder. In comparing the first 20 milk yields (10 days) of these cows of the year 1970 (untreated) with those of the year 1971, a regression of milk production of 'Kaliro' by 95%, of 'Nyschlos' by 68.9% and of 'Lado' by 46.9% was found. The colostral milk, especially that of cow 'Kaliro' showed a colour ranging from reddish to chocolate brown. The secretion became organoleptically normal for cow 'Kaliro' within 5 days, for cow 'Nyschlos' within 7 days and for cow 'Lado' within 2 days. The milk yield of cow 'Kaliro', treated with CB 154 for the last time on the 3rd day post partum, rose only slightly. The milk yield of cow 'Nyschlos' reached normal values within 49 days; that of cow 'Lado', within 18 days. Both animals received the last injection before parturition. An abnormal composition of casein has also been detected, especially in cow 'Kaliro', and will be described in a separate paper[7].

Discussion. The blocking effect of CB 154 on plasma prolactin could be demonstrated in all 3 cows. The deliveries were normal but the prolactin peak which had been reported to occur in connection with parturition[3–5] and has been detected by us without exception in 12 untreated cows, could not be seen.

The inhibitory action of CB 154 lasted for about 16 days after the last injection. A strong increase of prolactin could be noted afterwards, especially in cow 'Kaliro', which suggests the occurrence of a rebound effect.

In contrast to our earlier experiments[3] concerning galactopoiesis (maintenance of lactation), we could now demonstrate a pronounced effect on lactogenesis (onset of lactation). The question arises how to explain the individually different lactogenetical performances inspite of maximal prolactin inhibition in each case. The time of administration in correlation to the endogenous functional status of the prolactin blocker is obviously of fundamental importance. Cow 'Kaliro', which was treated with CB 154 shortly before but also after parturition, practically failed to come into lactation (see Figure 1). Even 2 months later her milk production is not comparable to that of the previous year.

In the 2 other cows, treatment with CB 154 being interrupted 3 days before parturition, the onset of lactation was only retarded. Their milk yield, however, rose to a normal level within 49 or 18 days, respectively. Qualitative abnormalities of the first milk yield (especially as observed in cow 'Kaliro') can sometimes also be seen in normal calving cows. From this experiment we conclude for the bovine species: a) The prolactin peak known to occur approx. 24 h ante partum is not functional but symptomatical for parturition. b) Prolactin is a principal hormone inducing lactation (lactogenesis. c) Yet it is not clear whether the depression of lactogenesis after administration of CB 154 is due to the depression of the prolactin peak or to the inhibition of the basic prolactin values alone. Having in mind results from a former experiment, in which lactation was induced by corticoid administration before parturition[5,6], we are rather in favour of the latter possibility.

Zusammenfassung. An drei Kühen wurde um den Zeitpunkt der Geburt der Effekt eines spezifischen Prolaktininhibitors (2-Br-α-Ergokryptin-Methan-Sulfonat = CB-154, Sandoz, Basel) auf den Plasmaprolaktinspiegel und das Einsetzen der Laktation untersucht. In allen drei Fällen konnte eine starke Hemmung der Prolaktinbasiswerte als auch eine Unterdrückung des normalerweise vor der Geburt auftretenden Prolaktingipfels erreicht werden. Ebenfalls wurde die Laktation (vergleichsweise zum Vorjahr) eindeutig gehemmt. Maximal zeigte sich die relative Unterdrückung der Milchleistung bei der Kuh, welche kurz vor und auch noch nach der Geburt mit CB-154 behandelt wurde. Prolaktin wird somit für das Rind als das massgebliche Hormon der Laktogenese – im Gegensatz zur Galaktopoese – angesehen.

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[8] This wirk was supported by the Deutsche Forschungsgemeinschaft.