GALACTOPOIETIC ACTIVITY OF PURIFIED ANTERIOR PITUITARY GROWTH HORMONE

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THE anterior pituitary factors concerned in the *initiation* of lactation are different from those capable of amplifying an existing milk flow (see reviews, refs. 1, 2), and Folley and Young[3] suggest that the term 'galactopoietic' be applied to an anterior pituitary substance which can augment established lactation irrespective of whether or not it can initiate the secretion of milk. Bergman and Turner[4] independently suggested the use of the words 'galactopoetic' or 'galactogogue' in a similar sense.

Asimov and Krouze[5] first showed that a single injection of a crude ox anterior pituitary extract can exert a substantial galactopoietic effect in milking cows. Folley and Young[3,6], estimating the galactopoietic potency of pituitary extracts by comparing the mean milk-yield of cows in declining lactation for two days before and two days after a single subcutaneous injection of anterior pituitary extract, obtained effects much greater than could be accounted for by the prolactin content of the extracts. We adopted the same procedure in the experiments reported here, and employed groups of cows the mean initial milk-yields of which varied between 26 and 42 lb./cow/day.

In a survey of the physiological activities of galactopoietic pituitary fractions, Folley and Young[6] observed a close association between the galactopoietic and 'anti-insulin' activities of different ox pituitary fractions, and later unpublished experiments have indicated that diabetogenic anterior-pituitary fractions are galactopoietic. Since Cotes Reid and Young[7] have shown that purified growth hormone is highly diabetogenic in the intact cat (see also Milman and Russell[8]), we have examined this hormone for galactopoietic activity with and without the addition of possible pituitary synergists such as prolactin and adrenocorticotropin. The growth hormone employed was prepared at University College, London, from fresh ox anterior pituitary tissue by the method of Wilhelmi *et al* [9]. The adrenocorticotropin used in the experiment at Shinfield was made at Shinfield by Mr. J. A. F. Rook from ox pituitary glands by a method essentially that of Li *et al.*[10]; that employed in the experiment at Bucksburn was generously supplied by Armour and Co., Chicago; for the gift of the latter we are grateful to Dr. E. E. Hays and Dr. I. M. Bunding, of the Armour Laboratories. The prolactin was prepared at University College by Mr. M. Stack-Dunne from ox anterior pituitary tissue essentially by the method of Li *et al.*[11], its potency being about 30 I.U./mgm. The crude extract was prepared from fresh ox anterior pituitary tissue as described by Young[12].

The results, which are summarized in the accompanying table, show that growth hormone is highly galactopoietic. We have previously reported that 10 ml. of our crude ox anterior pituitary extract, 1 ml. of which is equivalent to 0·25 gm. of fresh ox anterior lobe tissue, gives an almost maximal

Influence of a single subcutaneous injection of anterior pituitary preparations on the milk yield of cows in declining lactation. *A*, the mean increase in milk yield for the two days after treatment expressed as percentage of the mean yield for the two days before treatment. *B*, net increase, that is, difference between *A* and the mean percentage increase of the corresponding saline-treated group. Standard errors follow the means.

Treatment	Shinfield Farm			Craibstone Farm			Duthie Farm			Combined results for all farms		
	No. of cows	*A*	*B*	No. of cows	*A*	*B*	No. of cows	*A*	*B*	No. of cows	*A*	*B*
Saline	4	−0·50 ± 2·16		4	−3·16 ± 2·50		4	−3·52 ± 4·15		12	−1·89 ± 1·52	
15 mgm. growth hormone							4	2·78 ± 4·15	6·30 ± 5·87	4	2·78 ± 4·15	6·30 ± 5·87
30 mgm. growth hormone	4	6·49 ± 2·16*	6·99 ± 3·05	4	6·36 ± 2·50*	9·52 ± 3·53**	4	5·51 ± 4·15	9·03 ± 5·87	12	6·31 ± 1·52**	8·20 ± 2·15**
60 mgm. growth hormone				4	2·94 ± 2·50	6·10 ± 3·53	4	4·76 ± 4·15	8·28 ± 5·87	8	3·42 ± 2·14	6·68 ± 3·03
5 ml. *FGS*				4	2·87 ± 2·50	6·03 ± 3·53				4	2·87 ± 2·50	6·03 ± 3·53
10 ml. *FGS*				4	5·94 ± 2·50*	9·10 ± 3·53**	3	9·13 ± 4·89	12·65 ± 6·53	7	6·60 ± 2·22**	9·90 ± 3·11**
40 mgm. prolactin				4	−2·34 ± 2·50	0·82 ± 3·53				4	2·34 ± 2·50	0·82 ± 3·53
40 mgm. prolactin + 30 mgm. growth hormone				3	7·94 ± 2·94**	11·10 ± 3·86**				3	7·94 ± 2·94**	11·10 ± 3·86**
7 mgm. *ACTH*	4	−7·44 ± 2·16**	−6·94 ± 3·05				3	−2·64 ± 4·73	0·88 ± 6·53	7	−6·61 ± 1·96	−5·54 ± 2·76
28 mgm. *ACTH*							4	−10·13 ± 4·15*	−6·61 ± 5·87	4	−10·13 ± 4·15*	−6·61 ± 5·87
7 mgm. *ACTH* + 30 mgm. growth hormone							3	4·28 ± 4·89	7·80 ± 6·53	3	4·28 ± 4·89	7·80 ± 6·53

FGS = Crude alkaline extract of ox anterior pituitary tissue; *ACTH* = adrenocorticotropic hormone. * Significant at 5 per cent level. ** Significant at 2 per cent level.

galactopoietic response[13] and contains 30–50 mgm. of growth hormone[7]. The results show that the galactopoietic activity of 30 mgm. of growth hormone is probably greater than that of 5 ml. of our crude ox anterior pituitary extract and little different from that of 10 ml. Thus, in these short-term experiments, the whole of the galactopoietic activity of the crude extract may well be accredited to the growth hormone it contains. No positive galactopoietic effect of prolactin or of adrenocorticotropin was observed with the doses we employed, nor was the simultaneous administration of these hormones with growth hormone found to influence significantly the galactopoietic activity of the latter (see table). In long-term experiments, involving repeated injections of crude extract (for example, over a period of three weeks[3,13]), pituitary thyrotropin might play a part, since the galactopoietic action of the thyroid hormone is well attested (see Bailey *et al.*[14]). In such experiments of longer duration, it is possible that the galactopoietic action of the crude extract might be greater than could be attributed to the growth hormone it contained; but this is a matter for further investigation.

The table shows that 60 mgm. of growth hormone has no greater galactopoietic effect than has 30 mgm., such an observation being in agreement with the previously observed almost maximal galactopoietic effect of 10 ml. of our crude extract[13]. Indeed, the effect of 60 mgm. of growth hormone is slightly smaller than that of 30 mgm. (though the difference is not statistically significant on the basis of our results), and if this possible difference is real we are at present unable to account for it.

The administration of 28 mgm. of adrenocorticotropin induced a significant depression of milk yield, and a similar tendency (statistically significant only at Shinfield) was also observed with a dose of 7 mgm. of this hormone. On the other hand, Dr. A. Roy, in earlier experiments in our laboratories, found that under some conditions adrenocorticotropin could exert a substantial galactopoietic action (see Young[2]). It is clear that the magnitude of the dose of adrenocorticotropin may be of critical importance in such experiments, and this possibility is under investigation.

We believe the galactopoietic action of growth hormone to be of physiological significance. Treatment with pituitary growth hormone may induce growth (H. M. Evans), the secretion of extra milk (present paper) or diabetes[7,8], according to the age, species and condition of the treated animal. The diabetogenic action of growth hormone can be regarded as "the pathological outcome of an excessive stimulation of those processes (depression of oxidation of carbohydrate with enhancement of protein storage and of fat combustion) which, under more physiological conditions, lead to such deposition of new tissue as is associated with growth" (Young[15]; see also refs. 8, 16). As was pointed out some years ago: "Growth, including fœtal growth, and milk production are processes requiring a special type of metabolic control, in that they both necessitate the preservation from oxidation of foodstuff that would otherwise, in an animal in equilibrium, be oxidized. . . . Since growth, galactopoiesis and diabetogenesis all involve a restraint on oxidative processes, it would not be surprising if there were some relationship between the hormonal mechanisms concerned with the control of these phenomena" (Young[2]). Our demonstration of the galactopoietic activity of growth hormone, already known to be diabetogenic under some conditions, satisfactorily conforms with the expected concinnity of physiological pattern.

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RADIATION EFFECTS DUE TO PHOSPHORUS-32 IN FERTILIZER EXPERIMENTS

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It has been shown in water culture[1] that the rate of phosphorus absorption by plants is, under certain conditions, significantly reduced when activities of phosphorus-32 as low as 10 microcuries per litre are used as a tracer. Root-growth is also depressed; nevertheless, the development of the aerial parts of plants provides no consistent index of radiation damage. These effects are explained by the metabolic accumulation of labelled phosphorus, which may cause the root tips of rapidly absorbing plants to be exposed to radiation many hundred times more intense than that in the culture solution.

Effects resulting from the addition of labelled fertilizers to the soil are now being investigated. Plants are grown in pots containing 1,500 gm. soil, to which a constant level of potassium dihydrogen phosphate, labelled with varying activities of phosphorus-32, is added in solution. The full results will be described in due course in the *Journal of Experimental Botany*. This report is made since, despite the preliminary nature of the present results, they indicate that the seriousness of radiation damage in fertilizer experiments can be considerably greater than has frequently been supposed. The interpretation of radiation effects due to tracers in the soil is more complex than in water culture, since naturally-occurring soil phosphates are always present, and