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Stimulation of Growth in Pigs by Iodinated Casein and Stilboestrol*

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During the last few years attempts have been made in this Institute to affect various endocrine glands of the pig by giving by mouth synthetic preparations, and to find effects on rate of growth and food utilization which might have a practical application.

The results of trials with iodinated casein (Braude, 1947*a*) showed that with some pigs a slight increase in the rate of growth and food utilization could be obtained by stimulating their metabolic activity with thyroid-active preparations. No practical application, however, could be envisaged because of the very limited dose range in which the giving of the drug had a positive effect, and because of the great variation between individual animals in response to the treatment. It should, however, be mentioned here that Reineke, McMillen & Bratzler (1948) claim that growth and development of pigs can be accelerated by suitably controlled administration of thyroprotein.

In another series of experiments with fattening pigs (Braude, 1947*b*, and unpublished data), it was observed that a slight increase in the rate of growth of castrated male animals, coupled with more efficient utilization of food, resulted from the giving of small amounts of stilboestrol, which acts on the pituitary gland. For practical application the effect was not substantial enough to warrant the trouble and expense connected with the treatment.

Much more promising results are now reported from four trials in which iodinated casein and stilboestrol were fed simultaneously. A preliminary note on the first two of these trials has been published (Braude, 1948).

EXPERIMENTAL

Tests with pigs

In all experiments, home-bred Large White pigs were used. At the end of the test all pigs were slaughtered and carcass measurements were taken according to the procedure described in detail by Shorrock (1940). The thyroid and pituitary glands were collected for histological examination.

* Read in part before the International Congress of Biochemistry (Braude, 1949).

Exp. 1. In the first experiment, six pairs of castrated male litter-mates, 10–11 weeks old at the commencement of the experiment, were used. One pig from each pair was chosen by lot to receive the treatment while the other acted as control. The treatment consisted in giving each pig, by mouth, 500 mg. iodinated casein and 30 mg. stilboestrol daily. The drugs were added to the food, straight into the troughs, just before the afternoon feeding. Both treated and control pigs received the same meal mixture which consisted of fine wheat offal 50, barley meal 20, maize meal 20, fish meal 10 %. In addition, each pig received 30 g. cod-liver oil once weekly. The meal was given as a wet mash, 3 lb. water being allowed for 1 lb. meal. The pigs were weighed three times weekly and were fed individually, the quantity of meal given being based on live weight and a scale for fattening pigs (cf. Braude & Foot, 1942). The test commenced on 21 July 1947 and lasted for 19 weeks.

Exp. 2. In the second experiment, another six pairs of castrated litter-mates were used and all experimental details were as described above. The test commenced on 5 August 1947 and lasted for 19 weeks.

Exp. 3. In the third experiment, nine pairs of castrated litter-mates, 11–12 weeks old, were used. The meal allowance was increased by 10 % but other details remained unchanged. The test commenced on 24 November 1947 and lasted for 19 weeks.

Exp. 4. The doses of iodinated casein and stilboestrol given by mouth to the pigs in the first three trials were chosen empirically from evidence relating to single drug treatment. In this test an attempt was made to enhance the effect by varying the dose.

Sixteen castrated male weaners, 11–12 weeks old, out of four litters were divided into four groups so that each litter was represented by one pig in each group. Individual feeding was used and one of the following four treatments was allocated at random to each of the groups:

Treatment	Iodinated casein (mg. daily)	Stilboestrol (mg. daily)
(1) Control	None	None
(2) Low dose	340	20
(3) Medium dose (as Exp. 3)	510	30
(4) High dose	680	40

All pigs received fattening meal of the same composition as in Exps. 1–3 and, as in Exp. 3, the meal was rationed at 10 % above the normal scale and was given mixed with water. The drugs were given in the form of tablets, each containing 85 mg. iodinated casein and 5 mg. stilboestrol, i.e. pigs on treatment 2 received two, on treatment 3, three, and on treatment 4, four, tablets, added directly to the food in the troughs at each morning and afternoon feeding. The experiment commenced on 11 November 1948 and lasted for 19 weeks.

Test of suitability for human consumption of meat from animals treated with iodinated casein and stilboestrol

Before proceeding with large-scale field trials to test, under conditions prevailing in commercial piggeries, the usefulness of drug treatment for increasing production of pigmeat, it was thought advisable to investigate whether the meat from treated animals was safe for human consumption. For this purpose the carcasses of two of the pigs

that received the high dose of the drugs in Exp. 4 were cut into 2 lb. pieces and these were stored at a temperature of $-25°$ until required for the test. The carcasses of the other two pigs on the same treatment were made into bacon and were stored at normal cold-storage temperature.

The clinical tests depended on the effect of pork and bacon on women suffering from menopausal symptoms. Such women may be regarded as the most sensitive subjects to oestrogen administration. An account of the daily number of hot flushes was kept for a fortnight before the administration of pork and bacon was started. Four lb. of pork and 3 lb. of bacon were then issued to each patient once a week for 2 weeks with instruction to eat as much as possible, and the hot flush counts were continued. The results show no difference in the hot flush count or in the clinical symptoms to suggest that during the time the pork and bacon was taken it induced any oestrogenic effects in the patients. Although the number of patients who completed the test was rather limited, all indications point to the conclusion that the meat from pigs treated with small doses of iodinated casein and stilboestrol is safe for human consumption.

RESULTS

Exps. 1–3

Table 1 gives the relevant data. The results of the three trials showed a statistically significant increase in the rates of growth and food utilization of the animals receiving a daily dose of 500 mg. iodinated casein and 30 mg. stilboestrol. During the fattening period, the treated animals gained on the average 14·8 lb. more weight and required 0·32 lb. less meal to produce 1 lb. live-weight gain than the control litter-mates. No untoward effects of the treatment were observed.

Table 1. *Exps.* 1–3. *Live-weight gain and food utilization of pigs given* 500 *mg. iodinated casein and* 30 *mg. stilboestrol daily for* 19 *weeks, compared with those of control litter-mates*

	No. of pigs	Average initial weight (lb.)	Average final weight (lb.)	Average gain (lb.)	Average daily gain (lb.)	Efficiency of food utilization (lb./lb. live-weight gain)
Exp. 1						
Control animals	6	41·0	201·5	160·5	1·21	3·79
Treated animals	6	41·8	219·3	177·5	1·33	3·63
Exp. 2						
Control animals	6	43·5	218·8	175·3	1·32	3·76
Treated animals	6	42·7	235·0	192·3	1·45	3·44
Exp. 3						
Control animals	9	50·3	199·6	149·2	1·12	4·39
Treated animals	9	49·3	210·4	161·1	1·21	3·96
Three experiments						
Control animals	21	45·7	205·6	159·9	1·20	4·03
Treated animals	21	45·3	220·0	174·7	1·31	3·72
Mean difference, treated-control, and its standard error				$+14·81 \pm 3·879$		$-0·316 \pm 0·0651$
t*				3·82		4·86

* The appropriate significance levels of t for twenty degrees of freedom are

5 %	2 %	1 %	0·1 %
2·086	2·528	2·845	3·850

The results of the carcass measurements are summarized in Table 2. These show that the treated animals were longer in the leg and tended to be longer in the body, though the latter point cannot be definitely established on the above data alone. As regards fat measurements, there seems to be no difference in shoulder fat (*A*) and loin fat (*B*), but the measurements for rump fat (*C*) are all greater in the control group. Taking into account the length of the body and the length of the hind leg it appears that the control pigs were fatter than the treated pigs, both absolutely and in relation to their length.

The thyroid glands were weighed and, after fixation in 10 % formalin, paraffin sections were prepared and stained with haematoxylin and eosin. The glands from treated pigs weighed on an average 7·2 g. and were significantly lighter than those from the control litter-mates which averaged 9·9 g. They were usually also smaller in size. The acini were, on the average, smaller than in the control pigs and most of them showed more acinar epithelium of the low cuboidal or flattened types. The acini in the treated and in the control pigs were well filled with colloid.

The pituitary glands were also examined but several difficulties encountered in interpretation of the findings make it unwise to draw conclusions on the effect of the treatment

Exp. 4

Table 3 summarizes the relevant data. As in the first three experiments there was a considerable improvement in the growth rate and efficiency of food utilization of the pigs receiving the drugs. Pigs on the medium dose, treatment 3, gained on the average 25·2 lb. more than their control litter-mates and required 0·32 lb. less meal for 1 lb. live-weight gain. They gave a much better response than the pigs receiving either the lower or the higher dose. A closer analysis of the data, Table 4, confirmed the observation made during the progress of the experiment, that the medium dose, which was kept constant throughout the experimental period, was most probably too high during the early stages, and too low during the late stages, of the experiment. It can be seen from Table 4 that during the first 10 weeks of the test the pigs receiving the lower dose showed the best response both in live-weight gain and efficiency of food utilization. During the same period the pigs receiving the highest dose were obviously adversely affected by the treatment. Their rates of growth and the efficiency with which they utilized food were below normal. On the other hand, during the last 9 weeks of the test the pigs on the highest dose improved in weight, while the pigs receiving the lowest dose grew at a rate comparable with that of the control litter-mates (after allowing for one pig on treatment 2, which was ill during part of this period). During the last few weeks of the test the beneficial effect of the highest dose became more pronounced, and the figures for the last 3 weeks confirmed that during this time the pigs on this dose gained weight faster than any others in the experiment.

Table 5 gives the average carcass measurements of the pigs on test. Because of the rather limited number of animals involved, it is only possible to comment on the trends which the figures show. The treated pigs were heavier at the time of slaughter than the control animals and were also longer in body and had longer legs, while being less fat. This confirms the results obtained in the first three experiments.

Table 2. *Exps.* 1–3. *Carcass measurements of pigs given* 500 *mg. iodinated casein and* 30 *mg. stilboestrol daily for* 19 *weeks, compared with those of control litter-mates*

	No. of pigs	Average carcass weight (lb.)	Average dressing percentage	Average length of body cavity (mm.)	Average length of hind leg (mm.)	Average fat measurements (mm.)				
						Shoulder fat *A*†	Loin fat *B*†	Rump fat		
								C_1†	C_2†	C_3†
Exp. 1										
Control animals	6	149·0	74·0	790	591	54·3	24·3	34·7	27·5	38·0
Treated animals	6	163·3	74·5	797	604	53·3	25·0	32·5	25·2	36·7
Exp. 2										
Control animals	6	163·0	74·6	792	577	48·8	28·0	35·0	29·0	38·8
Treated animals	6	173·5	73·8	809	589	49·8	24·3	27·8	24·3	32·0
Exp. 3										
Control animals	9	175·6	76·7	800	596	59·4	28·2	39·8	33·9	47·8
Treated animals	9	187·9	78·0	807	601	59·1	29·6	39·3	34·1	45·8
Three experiments										
Control animals	21	164·4	75·3	795	589	54·9	28·4	37·0	30·7	42·4
Treated animals	21	176·8	75·8	805	598	54·8	28·2	34·1	28·8	39·2
Mean difference, treated-control, and its standard error		12·38 ±3·26		+9·86 ±6·95	+9·14 ±4·04	−0·14 ±1·71	−0·19 ±1·01	−2·86 ±1·04	−1·90 ±0·93	−3·19 ±1·07
*t**		3·80		1·42	2·26	0·08	0·19	2·73	2·05	2·98

* The appropriate significance levels of *t* for twenty degrees of freedom are

5 %	2 %	1 %	0·1 %
2·086	2·528	2·845	3·850

† *A*, at the thickest point over shoulder; *B*, at the thinnest point over middle of back; C_1, C_2, C_3, at three places over rump muscle.

Table 3. *Exp.* 4. *Live-weight gains and food utilization of pigs given for* 19 *weeks different doses of iodinated casein and stilboestrol compared with those of control litter-mates*

Treatment	No. of pigs	Average initial weight (lb.)	Average final weight (lb.)	Average gain (lb.)	Average daily gain (lb.)	Efficiency of food utilization (lb./lb. live-weight gain)
No supplement	4	58·3	219·0	160·8	1·21	4·27
340 mg. iodinated casein + 20 mg. stilboestrol	4	61·3	227·5	166·3	1·25	4·11
510 mg. iodinated casein + 30 mg. stilboestrol	4	61·5	247·5	186·0	1·40	3·95
680 mg. iodinated casein + 40 mg. stilboestrol	4	59·0	221·3	162·3	1·22	4·27

Table 4. *Exp.* 4. *Live-weight gain and food utilization of pigs at various stages of the experiment*

Treatment	Whole experimental period of 19 weeks	First 10 weeks	Last 9 weeks	Last 3 weeks
Average daily live-weight gain (lb.)				
No supplement	1·21	1·15	1·28	1·44
340 mg. iodinated casein and 20 mg. stilboestrol	1·25	1·34	1·15*	1·39
510 mg. iodinated casein and 30 mg. stilboestrol	1·40	1·23	1·59	1·64
680 mg. iodinated casein and 40 mg. stilboestrol	1·22	0·96	1·51	1·73
Efficiency of food utilization (lb./lb. live-weight gain)				
No supplement	4·27	3·53	5·01	4·91
340 mg. iodinated casein and 20 mg. stilboestrol	4·11	2·94	5·65*	4·54
510 mg. iodinated casein and 30 mg. stilboestrol	3·95	3·51	4·38	4·63
680 mg. iodinated casein and 40 mg. stilboestrol	4·27	4·13	4·39	4·24

* One pig was ill during the first part of this period.

DISCUSSION

The results indicate that the addition of small quantities of two synthetic hormones to the feed increases the rate of growth and improves the food utilization. This, if confirmed under commercial conditions, might be of considerable benefit to the pig industry. It is not intended to speculate at this stage on the mode of action of the two drugs and on their apparent complementary effect. The question of the nature of the weight increase also remains open. At present, it can only be stated that the treated pigs were leaner than their control litter-mates, indicating that the substance of the increase in weight was not due to the deposition of fat. It can also be stated that human beings are not harmed by meat from treated animals.

One further point might be of interest. In experiments now in progress, L-thyroxine is being used instead of iodinated casein. The recent development of new methods of synthesis of thyroxine holds promise that the hormone will, in future, be available cheaply and in quantities sufficient for large-scale application to domesticated livestock.

Table 5. *Exp.* 4. *Carcass measurements of pigs given different doses of iodinated casein and stilboestrol for* 19 *weeks, compared with those of control litter-mates*

Treatment	No. of pigs	Average carcass weight (lb.)	Average dressing per-centage	Average length of body cavity (mm.)	Average length of hind leg (mm.)	Average fat measurements (mm.) Shoulder fat *A**	Loin fat *B**	Rump fat C_1*	C_2*	C_3*
No supplement	4	166·0	75·5	803	601	62	31	34	29	39
340 mg. iodinated casein + 20 mg. stilboestrol	4	174·5	75·5	809	613	59	32	33	26	36
510 mg. iodinated casein + 30 mg. stilboestrol	4	187·7	75·8	831	627	57	30	35	27	40
680 mg. iodinated casein + 40 mg. stilboestrol	4	162·7	73·6	798	615	55	26	30	26	33

* See footnote to Table 2.

SUMMARY

1. In three experiments, twenty-one castrated male pigs which received 500 mg. iodinated casein and 30 mg. stilboestrol daily for 133 days grew faster and utilized their food more efficiently than control litter-mates.

2. In a fourth experiment, the daily dosage for each animal covered the range of 340–680 mg. iodinated casein and 20–40 mg. stilboestrol. Good response was obtained with the medium dose, 510 mg. iodinated casein and 30 mg. stilboestrol. The low dose appeared to be too low towards the latter part of the experiment, whereas the high dose was too high at the commencement.

3. Meat from treated animals was tested and found suitable for human consumption.

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