LXIX. INSULIN AND INCREASE IN WEIGHT OF YOUNG ANIMALS.

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ALL those who have made use of rabbits for the assay of insulin have noted that most of the animals gain rapidly in weight during the first few weeks. On the other hand, according to Long and Bischoff [1930], insulin has no influence on the growth curves of rabbits. It has also been observed that depancreatized dogs treated with insulin and maintained on a diet of meat, raw pancreas and sucrose can be made to put on fat by increasing the proportion of sucrose, allowing at the same time one extra unit of insulin for every 2·5–3 g. of sugar [Macleod, 1926]. It is also well known that most diabetic patients who are allowed a liberal diet with sufficient insulin to prevent hyperglycaemia tend to put on weight rapidly. These experiences soon suggested to clinical workers that insulin might be of value in the treatment of malnutrition, particularly of children. The first observations in this direction were those of Pitfield [1923], and they have been followed by numerous others of which we will mention only those of Marriott and of Tisdall *et al.* Marriott [1924] concluded that rapid improvement in the nutrition of non-diabetic, malnourished children usually followed the intravenous injection of glucose and insulin; but this conclusion was not endorsed by Tisdall *et al.* [1925]. In view of these findings it seemed to us of interest to ascertain whether young pigs while being fed on a good fattening diet could be made to lay on fat more rapidly than ordinarily by injections of insulin. The insulin was supplied in solid form by the British Drug Houses, Ltd., and, after being dissolved in faintly acidulated water in suitable concentrations, was assayed by the rabbit method.

EXPERIMENTAL.

Twenty-four pigs of approximately equal weights were selected at weaning and placed on the succession of four graduated diets adopted in the Pig Department of this Institute as the most suitable for raising them for market purposes. Each diet was further supplemented by skim milk. The dry feed and skim milk, as well as water, were supplied to all animals *ad libitum*. The consumption of food per group was estimated daily, by weighing the unconsumed food. The pigs were weighed every third morning before feeding and, after three weighings, twenty animals of approximately equal weights were selected and

divided into two equal groups. The animals of Group I served as controls, and those of Group II were divided into two equal sub-groups (*a* and *b*) for injection with insulin.

The four pigs, which were not included in the above-mentioned groups, were used for studying the general effects of insulin. Two of them were deprived of food overnight and each was injected at about 10 a.m. with three units of insulin per kg. The blood-sugar, examined at hourly intervals in blood taken from the tail or ear, fell in the course of about three hours to below 0.05 % when hypoglycaemic symptoms developed, the characteristic features being rapid breathing with moderate hyperexcitability which was soon followed by muscular weakness and a state of coma with falling rectal temperature and marked cyanosis. In order to restore the animals, very large amounts of 50 % solution of glucose had to be injected subcutaneously. Although these injections were started as soon as the coma had become established, no improvement in the condition could be noted for nearly an hour. Recovery was then rapid in one of the animals, but very gradual in the other, both being, however, practically completely restored to normal by 5 p.m.

Other animals were injected with one unit of insulin per kg. body-weight, without restriction of food. The following figures show a typical effect on the percentage of blood-sugar.

Time	a.m.					p.m.			
	7.45	8.0	9.15	10.20	11.30	12.30	3.0	4.0	4.45
Blood-sugar mg. per 100 cc.	99	Insulin 1 unit per kg. Fed	69	60	73	83	94	Fed	121

In the light of these results it was decided to inject into each of the five pigs of Group II *a* 0.75, and into each of the five pigs of Group II *b* 1 unit of insulin per kg. body-weight twice daily, at 7 a.m. and 4 p.m.

The insulin was injected subcutaneously behind the ears, but no samples of blood were taken, since it was feared that the excitement and struggling which are unavoidable in collecting them might influence the results.

RESULTS.

There was no evidence of hypoglycaemic symptoms in any of the animals throughout the period of insulin administration, which lasted 21 days in the case of Group II *b* and 59 days in that of Group II *a*. The results are shown in Tables I and II.

Table I. *Average increase in weight, actual and percentage.*

	Initial weight 5. xi. 28 (lb.)	Increase in weight											
		11. xi. 28 (lb.)	(%)	17. xi. 28 (lb.)	(%)	23. xi. 28 (lb.)	(%)	29. xi. 28 (lb.)	(%)	20. xii. 28 (lb.)	(%)	3. i. 29 (lb.)	(%)
Group I*	71.8	5.5	7.7	12.4	17.3	19.4	27.0	25.3	35.2	47.8	66.6	64.2	89.4
Group II <i>a</i> †	75.4	7.3	9.7	14.8	19.6	23.0	30.5	27.6	36.6	51.5	68.3	64.7	85.8
Group II <i>b</i> ‡	68.1	6.6	9.7	12.9	18.9	18.5	27.2	25.2	37.0†	46.3	68.0	57.3	84.1

* Average of 10 pigs.

† Average of 5 pigs.

‡ Insulin stopped.

Table II. *Average food consumption (lb.), total and "per 1 lb." gain in weight.*

Group		5. xi. 28 to 11. xi. 28		11. xi. 28 to 17. xi. 28		17. xi. 28 to 23. xi. 28		23. xi. 28 to 29. xi. 28		29. xi. 28 to 20. xii. 28		20. xii. 28 to 3. i. 29	
		R		R		R		R		R		R	
		M	M	M	M	M	M	M	M	M	M	M	M
I	Total	18.6	27.9	19.6	29.4	21.6	32.3	23.2	34.8	81.7	122.5	55.8	83.8
	Per 1 lb. gain	3.2	5.1	2.8	4.3	3.1	4.6	3.9	5.9	3.6	5.4	3.4	5.1
II a	Total	22.6	33.9	23.6	35.4	25.1	37.7	26.5	39.8	95.6	143.4	56.2	84.3
	Per 1 lb. gain	3.1	4.6	3.1	4.7	3.1	4.6	5.8	8.6	4.0	6.0	4.2	6.4
II b	Total	18.0	27.0	19.9	29.9	21.7	32.6	22.9*	34.4*	84.6	126.8	56.2	84.3
	Per 1 lb. gain	2.7	4.1	3.2	4.7	3.9	5.8	3.4	5.1	4.0	6.0	5.1	7.7
		R Dry food.			M Milk.			* Insulin stopped.					

It can be seen that the average weight of the animals of Group II *a* increased decidedly more rapidly than that of the controls, especially during the first three weeks of the observation, but that ultimately the controls were well ahead of the injected animals. The animals receiving the larger doses of insulin (Group II *b*) did not at first put on weight as rapidly as those of Group II *a*, but they did so more rapidly than the controls. After discontinuance of insulin in this group, the animals fell behind the controls. These results are comparable with those obtained several years ago by Miss O'Brien and one of us (J. J. R. M.) who conducted a similar series of observations on groups of full-grown rabbits. The rabbits were all fed *ad libitum* with a diet rich in readily assimilable carbohydrate and certain of them were injected twice daily with sub-convulsive doses of insulin. During the first two or three weeks, the insulin-injected animals increased in weight more rapidly than the controls, but ultimately no difference could be detected between the two groups.

Attention is to be called to the fact that the early advantage shown by the injected animals does not necessarily mean that the insulin had endowed them with a greater power of converting available carbohydrate into fat or had led to retention of water in the tissues; it may merely have stimulated the appetite so that more food was ingested. It will be seen from Table II that this was the case at least during the earlier stages of insulin injection in the pigs of Group II *a*: the total food consumption was increased but the food consumption per pound of increase in weight was unchanged. At later stages in this group for each pound of increase in weight more food was required than in the controls, indicating that the insulin was now having the effect of diminishing, rather than increasing, the assimilative powers. The results of Group II *b* show that while insulin was given there was no influence either on the total food consumption or on the assimilative power. After insulin was discontinued, the latter seemed to be decreased, since each pound increase in weight required more food than in the controls. When the pigs were ultimately sold for butchering, no difference was noted between the injected and control animals.

Although these results show conclusively that insulin does not speed up the rate of fattening of normal pigs, it does not necessarily follow that it might not have this effect when injected into poorly thriving animals. It is well known to farmers that there are often one or more pigs in a litter which do not

put on weight at the average rate, without there being any obvious pathological condition to account for the state of malnutrition.

An observation was accordingly planned in which four such underweight pigs were used, two being used as controls and two injected twice daily with one unit of insulin per kg. body-weight. The period of observation was forty-two days and the following were the results.

		Initial weight	Percentage increases in weight after 42 days
Control pigs	1	96 lb.	36.4
	2	69 lb.	23.2
Insulin pigs	1	79 lb.	44.9
	2	89.5 lb.	42.5

This indicates a decided improvement as a result of insulin, but more observations would be required before it could be concluded that injections of this hormone can with certainty convert the "runts" into normal animals.

SUMMARY.

Two groups of 5 healthy pigs were given insulin daily in subcutaneous doses of 1.5 and 2 units per kg. body-weight and their weights compared with those of 10 animals fed on the same diet but receiving no insulin.

Insulin had only a very slight accelerating effect on the rate of increase in weight, which was evidently due to a correspondingly greater consumption of food and not to any metabolism-sparing action.

Other experiments suggested that insulin had a more marked effect on marasmic pigs.

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