Endocrine control of pig growth

By D. Lister, *ARC Meat Research Institute, Langford, Bristol BS18 7DY*

The title I was given for this contribution implies that a definitive statement can be made about the hormonal control of the growth of pigs. Any such expectation must be dismissed at the outset for there is enough debate about how pigs grow to prevent it, let alone how the neuroendocrine system controls it. Nevertheless, if we are to establish food requirements, solve the problems of assessing energetic efficiencies or predict and manipulate carcase and meat quality we must define the precise nature of the fundamental physiological mechanisms which bring about major differences in the performance of animals. Moreover, since we probably know as much about these topics in relation to pigs as we do for men or beasts generally a perspective, at least, is possible.

The first obstacle to our understanding of the endocrinology of growth is that the measurable changes in the size and form of animals represent the net consequences of the anabolic and catabolic aspects of metabolism. Fat and protein accretion are easy to assess in the body but the endocrinologically-induced differences in the balance between lipogenesis and lipolysis or protein synthesis and proteolysis, are not. Similarly, for a full understanding, we ought to consider the physiological basis of variations in the flow of blood to tissue due to environmental effects or feeding, for all contribute to these net effects. It is extraordinarily difficult for the mathematical modellers to illustrate the interplay between the calculated energetics of biochemical transformations and experimental results, but it is well-nigh impossible for the physiologist to define the nature of all the control mechanisms which operate simultaneously in vivo. Thus, we must resort to the examination of the very simplest of models in the search for clues.

Variations in the growth of pigs

I am continually surprised that seemingly large differences in the over-all growth and development of pigs stem from so few physiological functions. This view is not shared by everyone and attempts to settle it are plagued by difficulties in the interpretation of the commonly-collected information (Elsley, 1976; Lodge *et al.* 1978). It is best seen in comparisons between the performance of extremes of the range of physiological and metabolic types of animal. Table 1, for example, describes some aspects of the development of a slow-growing, lean pig and one which is faster-growing and fat. A heavier birth weight is a common advantage which usually persists and, in this example, at 20 weeks of age the Gloucester Old Spots still weighed 40% more than the Pietrains. Between 12 and 20 weeks the Gloucesters ate 1·5 times as much food which resulted in their retaining slightly more lean and bone in their carcases, but more than twice as much fat. The

0029-6651/80/3923-3803 $01.00 © 1980 The Nutrition Society

https://doi.org/10.1079/PNS19800025 Published online by Cambridge University Press

Table 1. *The growth and carcase composition of Pietrain and Gloucester Old Spot (GOS) pigs**

(Mean values with their standard errors)

	Pietrain (*n* 10)		GOS (*n* 12)	
	Mean	SE	Mean	SE
Birth wt (kg)	1·16	0·064	1·55	0·124
Wt at 12 weeks (kg)	27·7	1·41	34·1	2·07
Wt at 20 weeks (kg) (slaughter)	57·5	3·02	80·6	2·01
Food eaten (kg) from 12–20 weeks†	86·0	5·07	132·9	2·56
Food eaten/unit body-wt gain (12–20 weeks)	2·89	0·063	2·86	0·073
Wt of fat in carcase (kg)	8·4	0·42	18·3	0·53
Wt of lean in carcase (kg)	24·5	0·27	26·5	0·36
Wt of bone in carcase (kg)	4·3	0·12	5·4	0·13

*(Lister and Lovell, unpublished observations).
†Free access to food for 2×45 min periods each day.

efficiency of food utilization over this period was very similar in the two breeds. Thus, the extra cost of fat deposition in the Gloucesters was balanced presumably by a greater heat production in the Pietrain, for the energy value of their gain was considerably less.

In practical pig production differences in performance may not be quite so clear cut when judged against age or time. On the other hand, small differences may be exaggerated by comparing animals at the same body-weight (Lodge *et al.* 1978). Nevertheless, the simple example of Table 1 serves to illustrate what is the situation in all, namely, that there are three overwhelmingly-important reasons for variations in the growth and form of pigs. These are fat deposition, food intake and heat production. Fat deposition as a primary and measurable characteristic of all this is therefore, a good starting-point from which to look for associations with the neuroendocrine control of growth. Moreover, fat formation, lipogenesis and lipolysis are amongst the best researched topics in endocrinology.

Hormones and growth

We have no reason to suppose that the pig differs from other mammals in requiring the usual complement of hormones described in every biology textbook. Yet, although a great deal is known about the structure and activity of hormones, especially in vitro, and their likely role in certain diseases, we have yet to find a conclusive answer to the practical question of how hormones are organized to bring about the normal range of growth and form in animals.

A practical outcome of the fundamental studies was the development of an array of assays for estimating the concentrations of hormones especially in human plasma but, more recently, in that of other species. These assays have been of great value in the study of diseases but their application to investigations of normal

https://doi.org/10.1079/PNS19800025 Published online by Cambridge University Press

growth has not been widespread. There are two reasons for this. First, man, for whom there are the best prospects of assessing hormonal status, is not a good subject for studies on growth for his period of growth is long, his diet cannot be strictly controlled and the composition of his bodily gain cannot be described accurately. Animal scientists, on the other hand, have always been able to make detailed investigations on the growth and development of their experimental subjects. Their difficulties stemmed from a lack of appropriate techniques to look at the endocrinological issues involved. But even when this seemed possible it quickly became apparent that more was needed to identify the relation between hormonal function and growth than could be provided by measurements of the circulating levels of the various hormones which mainly reflect the net consequences of secretion and utilization. Other approaches had to be considered many of which, at first sight, seem not to be pertinent to the general question of the endocrine control of growth. The investigation of the hormonal control of fat deposition in pigs is a good example of how enquiry into the nature of a specific physiological mechanism can lead to encouraging advances in the study of hormones, metabolism and growth generally.

Hormones and fat. There were several indications in the literature of the early years of this decade that individual pigs, like human beings, differed in their lipolytic response to environmental stress (Marple *et al.* 1972; see also Bogdonoff & Estes, 1961; Taggart *et al.* 1973). It was also known that animals with less subcutaneous backfat frequently suffered a greater lipolytic response to fasting (Bakke, 1975). These observations were followed up by Gregory *et al.* (1977) and Wood *et al.* (1977) in their studies of the nature and control of fat mobilization in Pietrain and Large White pigs. Wood *et al.* (1977) proposed that the leaner carcases of Pietrain pigs (see also Table 1) could well be the result of their greater ability to mobilize fat. Pietrains showed higher concentrations of plasma free fatty acids (FFA) during fasting than the fatter Large Whites and greater sensitivity to noradrenaline infused during anaesthesia. Gregory *et al.* (1977) confirmed that Pietrains had a poorer insulin-secreting ability and lower antilipolytic sensitivity to it, and concluded that although Pietrains are not chemically diabetic their plasma insulin response to infused glucose suggested them to be prediabetic. Obesity, on the other hand, is associated with the normal secretion of insulin but mild insensitivity to it (Wangsness *et al.* 1977).

Hormones and metabolism. The unusual combination of reduced insulin sensitivity and secretion is difficult to explain but the involvement of the sympathetic nervous system (SNS) is a possibility (Mayhew *et al.* 1969). There are indications, moreover, that the ease with which the SNS of Pietrains is stimulated is important elsewhere. The syndrome known as malignant hyperthermia (MH) is an unusual and commonly fatal reaction of certain 'lean' breeds and types of pig, notably Pietrain and Poland China and some strains of Landrace (see Table 2) to several drugs, including Halothane and Suxamethonium, physical exercise and even to mental stress. (Lucke *et al.* 1979). The metabolic and biochemical events of the reaction are well documented (Berman *et al.* 1970;

https://doi.org/10.1079/PNS19800025 Published online by Cambridge University Press

Table 2. *Incidence of positive Halothane reaction in different breeds (Allen* et al. 1979)

Breed	No. of pigs tested	Incidence (%)
Pietrain/Hampshire	266	19·9
Norwegian Landrace	157	4·5
Hampshire	116	0·9
Yorkshire	50	0
Duroc	85	0
Pietrain*	>500	>95
Poland China*	>50	>50

*MRI records.

Lucke *et al.* 1976; Gronert & Theye, 1976*a,b*). They are similar to those which follow violent physical exercise and in sensitive animals during the slaughter process (Lister, Lucke *et al.* 1976). Typically there is acceleration of the biochemical and physical changes in muscle post-mortem which, in animals destined for meat, produces the characteristic pale, soft and exudative (PSE) pork (Briskey, 1964; Cassens *et al.* 1975). There are indications of a common aetiology for MH and PSE pork for both can be prevented by pretreatment of potential reactors with dantrolene (Dantrium—Eaton Laboratories) which is also the only drug known to be consistently effective in reversing an established MH episode (Harrison, 1977; Gronert *et al.* 1976; Hall *et al.* 1977; D. Lister, unpublished results).

The first suggestions for the involvement of hormones came from the fall in circulating thyroid hormones (Lister, 1973) which led later to the identification of a marked rise in circulating catecholamines (Lister, Hall *et al.* 1974, 1976; Gronert & Theye, 1976*a,b*; Van den Hende *et al.* 1976). α-Adrenergic stimulation can induce MH (Hall *et al.* 1977) and a reaction will not occur in adrenalectomized pigs which are blocked with bretylium (Lucke *et al.* 1978). α-Adrenergic blockade will not reverse an established reaction but will prevent one if it is infused before administration of the triggering drug (Lister, Hall *et al.* 1976).

With such clear involvement of catecholamines and the SNS in the metabolic aspects of MH one might predict a concomitant stimulation of glycogenolysis and lipolysis. Hyperglycaemia is commonly found but there is little or no increase in insulin secretion. Similarly there is only a small rise in plasma cortisol which, presumably, like the failure of insulin secretion, is due to the raised concentration of plasma catecholamines (Mayhew *et al.* 1969; Wilcox *et al.* 1975). Lipolysis is certainly increased but this is seen as an increase in plasma glycerol and not plasma FFA which tend to fall possibly as a result of increased re-esterification.

There is no doubt, therefore, that catecholamines and the SNS play an important role in the aetiology of MH. Whether this is primary or a secondary consequence of the reaction is still debated. The evidence from MH and of fat mobilization by susceptible pigs, however, supports the notion that these animals

https://doi.org/10.1079/PNS19800025 Published online by Cambridge University Press

have at least a lower threshold of sensitivity to autonomic or, in particular, sympathetic nervous stimulation. In conscious man this can be tested by the Valsalva manoeuvre but there is no way in which conscious pigs may be persuaded to hold their breath.

N. G. Gregory (unpublished results), used a Valsalve-like-manoeuvre in anaesthetized Pietrain and Gloucester Old Spot pigs to attempt to identify possible differences in SNS response. In these experiments, pigs, taken shortly before slaughter from the experiment from which Table 1 was prepared, were anaesthetized and ventilated and fitted with blood pressure and ECG monitors. After an appropriate delay pancuronium was given to block spontaneous respirations and the intrathoracic pressure was raised to 40 cm H_2O for 90 s by switching off the ventilator and holding the pressure manually. The Pietrain pigs could be distinguished by their greater compensatory rise in heart rate but not by the rise in blood pressure when the Valsalva was completed.

Future perspectives

The pattern of approach in the investigations just described is typical of those usually employed. Success is dependent on good measures of slog and serendipity. In the normal course of events one would turn next to study the endocrine control of protein deposition, food intake or heat production and so on until a scheme of hormonal pathways could be drawn up like those for metabolic pathways which festoon the walls of biochemical laboratories. Further investigations would include attempts to modify the growth of animals by substituting, inhibiting or augmenting these pathways by the use of drugs and hormones.

Within the foreseeable future there will be a continuing need for the mechanistic approach. But there are signs of a major change in direction in the application of fundamental advances in endocrinology. This has been brought about by the recognition that the endocrine system can be manipulated to modify the expression of individual genes or loci. The MH syndrome again provides a useful introduction to the philosophy.

The Pietrain pig is noted for its outstanding carcase quality, its poor quality meat and its sensitivity to Halothane. It was of interest, therefore, to know whether those pigs in any population which reacted adversely to Halothane also developed the other characteristics. Eikelenboom *et al.* (1976) developed a test based on the reaction of pigs which were forced to inhale Halothane over a period of 3–4 min. They and others (Eikelenboom, 1979; Webb & Jordan, 1979) discovered that positive reactors were shorter, leaner and had poorer meat quality and that these characteristics were inherited by their progeny.

The genetic inheritance of Halothane sensitivity is much debated. Now, the consensus is that it is due to a single recessive gene (Minkema *et al.* 1976) or a major locus (Andresen & Jensen, 1977) associated not only with meat quality but also with genes controlling the H blood-group (Jensen *et al.* 1976) and the enzyme phosphohexose isomerase (*EC* 5.3.1.9) locus (Jørgensen *et al.* 1976). Thus, the use of blood groups as specific genetic indicators of potential meat quality in animals

https://doi.org/10.1079/PNS19800025 Published online by Cambridge University Press

destined for slaughter or, more importantly, for breeding may be possible (Andresen *et al.* 1979).

In man, blood groups are inherited characters which involve antigen–antibody interactions of the immune system. There is a pair of genes, or of linked genes, for each blood-group system and the immunological techniques used in their identification are particularly precise and specific for given genotypes. Immunoreactive mechanisms may similarly give us a previously-undreamt-of measure of specificity in the manipulation of genetic potential via the endocrine system. One good example of this is in pigs.

The entire boar is remarkable for its rate of growth and efficiency of food conversion. But the accumulation of the volatile testicular steroid, androstenone, in its bodily tissues, especially fat, may give rise to an unpleasant odour when the meat is cooked. Historically, castration was the method chosen to prevent this but the desirable characteristics of male growth were also lost. It is now possible, however, to immunize young boars against the androstenone produced by their testes and it is not then deposited in the fat. The simple treatment requires one or two injections of androstenone rendered antigenic by linkage to a large carrier protein. Because this is a selective immunization only the androstenone is sequestered by the induced titre of antibodies. Thus, the serum concentrations of androstenone and the taint of the meat are reduced whilst the hormones, e.g. testosterone, responsible for the superior growth of the male are unaffected (D. E. Williamson, unpublished results). This approach has evolved from a comparable procedure which can be used to induce autoimmunity to the hypothalamic peptide, luteinizing hormone-releasing hormone. In rats (Perry *et al.* 1979) this leads to gross impairment of gonadal development whilst allowing the growth and efficiency of food use to be maintained in males and substantially improved in females. There is little doubt that this principle has important implications for domestic and farm species for the techniques used induce a self-perpetuating, self-activating system which interrupts the endocrine chain of command in an absolutely specific manner.

Another different approach which also has important implications in the modification of gene transcription and translation is the exposure of the foetus or neonate, at critical periods of development, to exogenous hormones which, thereby, permanently alter the actions of the same or other endogenous hormones. Thus, a single dose of testosterone to the neonatal female rat, for example, will permanently prevent the oestrogen stimulation of pituitary luteinizing hormone secretion and render the animal infertile. At the same time the rate and efficiency of growth is increased towards those of the male even when normal or raised levels of oestrogen are present in the circulation.

These manipulations of aspects of sexuality in animals represent the tip of the iceberg for what is theoretically possible. Work has already begun on the pig and substantial developments are likely to come about over the next 3–5 years. In the longer term we must surely look at the roles of neural peptides which possess opiate and hormone (e.g. insulin)-like activity (Fuxe *et al.* 1979) in modifying growth and development. At the moment we know very little about their

https://doi.org/10.1079/PNS19800025 Published online by Cambridge University Press

physiological roles in, for example, neurotransmission or the control of pituitary function but the rapid expansion of this area of research must certainly make considerable impact on animal science over the next 5 or 10 years.

The author is grateful to Drs B. N. Perry and N. G. Gregory and Miss D. E. Williamson for helpful discussion in the preparation of this paper.

REFERENCES

Allen, W. M., Cheah, K. S., Imlah, P., Lister, D., Steane, D. E. & Webb, A. J. (1980). *Livest. Prod. Sci.* (In the Press).
Andresen, E., Barton-Gade, P., Hyldgaard-Jensen, J., Jørgensen, P. F., Nielsen, P. B. & Moustgaard, J. (1979). *Acta Agric. scand.* **29**, 291.
Andresen, E. & Jensen, P. (1977). *Nord. Vet.-Med.* **29**, 502.
Bakke, H. (1975). *Acta Agric. scand.* **25**, 113.
Berman, M. C., Harrison, G. G., Bull, A. B. & Kench, J. E. (1970). *Nature, Lond.* **225**, 653.
Bogdonoff, M. D. & Estes, E. H. (1961). *Psychosom. Med.* **23**, 23.
Briskey, E. J. (1964). *Adv. Fd Res.* **13**, 89.
Cassens, R. G., Marple, D. N. & Eikelenboom, G. (1975). *Adv. Fd Res.* **21**, 71.
Eikelenboom, G. (1979). *Acta Agric. scand.* **21**, Suppl. 413.
Eikelenboom, G., Minkema, D. & van Eldick, P. (1976). *Proc. 3rd int. Conf. Production Diseases in Farm Animals*, p. 183. Wageningen: Pudoc.
Elsley, F. W. H. (1976). *Proc. Nutr. Soc.* **35**, 323.
Fuxe, K., Hökfelt, T. & Luft, R. (editors) (1979). *Central Regulation of the Endocrine Systems*. New York and London: Plenum.
Gregory, N. G., Lovell, R. D., Wood, J. D. & Lister, D. (1977). *J. agric. Sci., Camb.* **89**, 407.
Gronert, G. A., Milde, J. H. & Theye, R. A. (1976). *Anesthesiology* **44**, 488.
Gronert, G. A. & Theye, R. A. (1976*a*). *Anesthesiology* **44**, 36.
Gronert, G. A. & Theye, R. A. (1976*b*). *Br. J. Anaesth.* **48**, 513.
Hall, G. M., Lucke, J. N. & Lister, D. (1977). *Anaesthesia* **32**, 472.
Harrison, G. G. (1977). *Br. J. Anaesth.* **49**, 315.
Jensen, P., Staun, H., Bräuner Nielsen, P. & Moustgaard, J. (1976). *Commun. Natn. Inst. Anim. Sci., Copenhagen* no. 83.
Jørgensen, P. F., Hyldgaard-Jensen, J., Eikelenboom, G. & Moustgaard, J. (1976). *Proc. 3rd int. Conf. Production Diseases in Farm Animals*, p. 200. Wageningen: Pudoc.
Lister, D. (1973). *Br. med J.* i, 208.
Lister, D., Hall, G. M. & Lucke, J. N. (1974). *Br. J. Anaesth.* **46**, 803.
Lister, D., Hall, G. M. & Lucke, J. N. (1976). *Br. J. Anaesth.* **48**, 831.
Lister, D., Lucke, J. N. & Hall, G. M. (1976). *Proc. 3rd int. Conf. Production Diseases in Farm Animals*, p. 144. Wageningen: Pudoc.
Lodge, G. A., Lister, D., Wood, J. D. & Wolynetz, M. S. (1978). *Anim. Prod.* **27**, 345.
Lucke, J. N., Denny, H. R., Hall, G. M., Lovell, R. D. L. & Lister, D. (1978). *Br. J. Anaesth.* **50**, 241.
Lucke, J. N., Hall, G. M. & Lister, D. (1976). *Br. J. Anaesth.* **48**, 297.
Lucke, J. N., Hall, G. M. & Lister, D. (1979). *Ann. N.Y. Acad. Sci.* **317**, 326.
Marple, D. N., Aberle, E. D., Forrest, J. C., Blake, W. H. & Judge, M. D. (1972). *J. Anim. Sci.* **35**, 576.
Mayhew, D. A., Wright, P. H. & Ashmore, J. (1969). *Pharmac. Rev.* **21**, 183.
Minkema, D., Eikelenboom, G. & van Eldick, P. (1976). *Proc. 3rd int. Conf. Production Diseases in Farm Animals*, p. 203. Wageningen: Pudoc.
Perry, B. N., McCracken, A., Furr, B. J. A. & MacFie, H. F. H. (1979). *J. Endocr.* **81**, 35.
Taggart, P., Carruthers, M. & Somerville, W. (1973). *Lancet* ii, 341.
Van den Hende, C., Lister, D., Muylle, E., Ooms, L. & Oyaert, W. (1976). *Br. J. Anaesth.* **48**, 821.
Wangsness, P. J., Martin, R. J. & Gahagan, J. H. (1977). *Am. J. Physiol.* **233**, E104.

https://doi.org/10.1079/PNS19800025 Published online by Cambridge University Press

Webb, A. J. & Jordan, C. H. C. (1979). *Acta Agric. scand.* **21** Suppl., 418.
Wilcox, C. S., Aminoff, M. J., Millar, J. G. B., Keenan, J. & Kremer, M. (1975). *Clin. Endocr.* **4**, 191.
Wood, J. D., Gregory, N. G., Hall, G. M. & Lister, D. (1977). *Br. J. Nutr.* **37**, 167.

Printed in Great Britain

https://doi.org/10.1079/PNS19800025 Published online by Cambridge University Press