Sponsors

Biotechnology for control of growth and product quality in swine Implications and acceptability

Résumés in French and Chinese

Proceedings of an international symposium
organized by the Wageningen Agricultural University,
12-14 December 1988, Wageningen, Netherlands.

P. van der Wal, G.J. Nieuwhof, R.D. Politiek (Editors)

Pudoc Wageningen 1989

Printed in the Netherlands.

ORGANIZING COMMITTEE:

Chairman:	R.D. Politiek	Wageningen Agricultural University	NL
Secretariat:	P. van der Wal	Wageningen Agricultural University	NL
assistant:	G.J. Nieuwhof		
Members:	H. Karg	München Technical University,	DE
	K.F. Fung	South China Agricultural University, Guangzhou,	CH
	R.G Zimbelman	American Society of Animal Science, Bethesda MD,	US

CHAIRMEN AND DISCUSSION MODERATORS:

K. Aibara	Food and Drugs Research Center, Kanagawa,	JP
L.L. Christian	Iowa State University, Ames,	US
G. Van Dijk	Wageningen Agricultural University,	NL
F. Ellendorff	Institut für Tierzucht und Tierverhalten, Mariensee,	DE
B. Hoffmann	Justus Liebig University, Giessen,	DE
R.L. Kline	National Pork Producers Council, Des Moines IA,	US
G.E. Lamming	University of Nottingham, Sutton Bonington,	GB
O.G. Pedersen	Danish Bacon and Meat Council, Copenhagen,	DK
A.A. Rerat	Institut National de Recherche Agronomique, Jouy-en-Josas,	FR
L. Reijnders	Stichting Natuur en Milieu, Utrecht,	NL
P. Wiepkema	Wageningen Agricultural University,	NL

CONTENTS

4. EFFECT ON REQUIREMENTS AND WELLBEING OF THE TARGET ANIMAL

PHYSIOLOGICAL MODE OF ACTION

NUTRIENT AND MANAGEMENT REQUIREMENTS

HEALTH AND IMMUNE RESPONSE

SIDE-EFFECTS

EFFECT ON REPRODUCTION AND LACTATION

5. CONSUMER ASPECTS

SAFETY OF EDIBLE PRODUCTS

NUTRITIONAL AND SENSORY CHARACTERISTICS

6. ENVIRONMENTAL AND ECONOMIC IMPACT

7. ADOPTED CONCLUSIONS OF SESSIONS

8. FRENCH RESUME:

9. CHINESE RESUME:

SCOPE OF THE SYMPOSIUM

SCOPE OF THE SYMPOSIUM

The availability of meat products of good quality at affordable prices is a generally accepted right for an increasing part of world's population. Meeting consumers demand for these animal products was made possible by making use of achievements in animal science. A sharpening of the scientific tools by developing modern biotechnology is probably essential for meeting future demands while coping simultaneously with the increasing constraints in production.

Acreage for growing crops for animal feed is limited and the capacity of the environment to absorb polluting excreta has already been exceeded in some areas. The sustainability of the animal production system can therefore no longer be taken for granted. The requirements for product quality and safety are defined more sharply. The wellbeing of the animals asks for a higher priority.

Advancements in biotechnology create widening perspectives for meeting these requirements effectively. Significant improvements in efficiency and quality in animal production come within reach.

It is the objective of this symposium to study in a global context the potentials and constraints of emerging new technologies for controlling growth and product quality, in meeting requirements for consumer, animal and environment.

Priorities for improving animal production

Improving the conversion efficiency of feed into meat offers in many ways the most promising perspective for the long term sustainability of the animal production system. **It reduces the acreage of feed crops** to be grown for animal production and leads to **lower meat** costs. Last but not least it is a most effective way for **reducing the environmental pollution** from animal excreta.

Product quality has to reflect demand for **more lean** and less fat as a result of the increasing awareness that excessive calory intake forms a human health hazard. **Product safety** as well as **taste and tenderness** remain a high priority.

The **wellbeing of the animals** as expressed in health and behavioral parameters can be studied more effectively by advancements in animal physiology, ethology and immunology.

Emerging biotechnologies

For an analysis at this symposium, physiologically related technologies have been selected with demonstrated potentials in combining effectiveness with intrinsically favourable safety aspects. The technologies relate to the somatotropin axis.

Growth of food producing animal species is controlled by the genome, expressing its potentials via this **interacting system of Somatotropin releasing factor (GRF) - Somatostatin - Somatotropin - Somatomedins.**

Since 6,000 years man has affected this axis by gradual modification of the genome of the animals through systematic selection and breeding in order to tune animal production to demand.

In the last decades this process accelerated considerably through introduction of artificial insemination and embryotransfer while other advanced technologies are emerging.

A more selective modification of the genome has recently been achieved by the **insertion of growth controlling genes** in the genome of food producing animals.

An even more selective impact on the growth controlling physiological axis has been obtained by changing the level of the various earlier mentioned messengers. This has been achieved by direct **administration of Somatotropin and Somatotropin Releasing Factor.**

7

The latest addition to the techniques allowing for impact on constituents of the somatotropin axis stems from **immunization techniques**. Potentiation of somatotropin and binding of somatostatin proved to be feasible with antibodies.

Evaluation of safety and efficacy

The common mode of action of these technologies leads in many ways to comparable effects on the target animals, their products and on the environment. It makes therefore sense to study them jointly for their common denominators.

Since biotechnology made key elements of the growth controlling system in the somatotropin axis separately available for animal research, a better understanding of the effects has been obtained in recent years.

With the rapidly accumulating scientific data it is increasingly possible to analyze the potential implications and acceptability aspects of the three above mentioned interrelated categories of new technologies for control of growth.

Introductions of earlier innovations in animal production demonstrated repeatedly that such achievements easily lead to long lasting divergencies of opinion on their acceptability. **Consumer safety aspects** have been a central issue for a long time. More recently **target animal safety, environmental impact** and repercussions for the **structure of the production system** are taken into consideration as well.

Questions on acceptability aspects of new technologies have often been defined rather late during their development. Insufficient awareness of the nature of these upcoming questions prevented their timely incorporation in the experimental designs. As a result relevant answers were produced later and at higher costs than necessary.

To provide adequate **guidance for research** as well **as for regulation** of applications of these technologies, much can be gained by timely international consultations within the scientific research community involved. Such a consultation is visualized in this symposium.

The state of the art is reviewed and further research priorities defined in an interaction between scientist from universities, industrial research groups and from the institutions which carry regulatory responsibility. The sponsorship and participation from all three sides illustrates the common awareness of the use of this joint scientific evaluation.

The symposium may contribute furthermore to a **harmonization** in the approach of the technologies at stake in the geographic theaters which are at present of relevance. The negative consequences of discrepancies between these regions in acceptance and regulation need not to be elaborated upon for demonstrating the urgency of a joint scientific evaluation.

THE CHALLENCE

BIOTECHNOLOGY, COMPETITIVENESS AND ACCEPTABILITY: THE CHALLENGE TO EUROPE

M.F. Cantley

Head of CUBE (Concertation Unit for Biotechnology in Europe) Commission of the European Communities

Summary

The author is not a biological specialist, but is involved in the conception and implementation of a strategy for biotechnology in Europe. Questions of implications and acceptability have in recent years become prominent particularly regarding the applications in agriculture of recent advances in biological knowledge and biotechnology.

An outline of the Community strategy is presented; its basic orientation is international competitiveness, assumed to underpin the pursuit of the broader objectives of the EEC Treaty. Public and political criticisms of biotechnology introduce broader dimensions, including ecology, economic structural impacts in agriculture, animal welfare, ethical issues, consumer rights and consumer safety. Those who perceive threat or feel outrage on one dimension seek allies amongst other critics.

In this broader context, issues of global responsibility and societal or cultural values complicate the conventional emphases on economic competitiveness, but do not negate the benefits of innovation, and of competition within a common global framework based on shared perceptions of common interests - which can be pursued simultaneously in a liberal world trade system under GATT rules, or under agreed constraints for the benefit of the global ecosystem (cf. the limitations now agreed internationally on the production of chlorofluorocarbons).

To promote these shared perceptions and raise the standard of public and political debate, more effective communication between the interested parties must be promoted in the public interest.

Keywords: biotechnology, European Community, market competition, acceptability, swine.

Introduction: The Community strategy for biotechnology in Europe, 1983-89

This conference takes place at a time when the dramatic progress of recent decades in the life sciences is being translated into practical applications in many fields - notably, health care, and agriculture. These practical applications in many fields have been summarised in a broad and diffuse but convenient word : "biotechnology".

The multi-disciplinary character and multi-sectoral applications of biotechnology pose many policy challenges to public authorities, at national or European Community level. It was in order to help respond to these multi-dimensional policy challenges that the Commission established in 1984 its Biotechnology Steering Committee, with a supporting secretariat and working groups. This is not the occasion for a long history of the development and implementation of the Community

11

strategy for biotechnology in Europe, but in summary, it has over the past 5 years comprised action on six separate priorities :

– **Research and Training:** the Biomolecular Engineering Programme ("BEP": 15 MECUs 1982-86) focussed on aspects of genetic engineering and enzymology of relevance to their applications in agriculture and the food industry. It has been followed by the broader Biotechnology Action Programme ("BAP" : 55 MECUs 1985-89), which is uniting laboratories throughout the EEC area around various topics relevant to the reinforcement of Europe's capabilities in biotechnology. In particular, this programme has pioneered the concept of "European Laboratories Without Walls", and is attracting growing interest from industry. Proposals for a 100 MECUs successor programme (1990-1994), provisionally entitled "BRIDGE" (Biotechnology for Innovation Development and Growth in Europe) are currently in preparation.

– **Agriculture:** new price regimes for sugar and starch were introduced in 1986, to facilitate and encourage the industrial uses of such materials.

– **Regulations:** guided by a Biotechnology Regulation Interservice Committee established in July 1985, the Commission is seeking to promote a harmonised regulatory approach to biotechnology; adding to the specific Community sectoral regulations (e.g. for foodstuffs, for pharmaceuticals, for agricultural products, etc.) three general proposals (March 1988) concerning the confined industrial use of recombinant micro-organisms, the field release of modified organisms, and the protection of workers against possible hazards of exposure to biological agents.

– **Intellectual Property:** as in the area of regulations for biotechnology, the Commission is seeking to promote a harmonised Community-wide approach to the protection of intellectual property in biotechnology. Its October 1988 proposal would confirm the patentability of living organisms, subject to the exclusion (imposed by the European Patent Convention 1974) of animal and plant varieties.

– **Demonstration Projects:** in order to promote the development and application of biotechnology, and to encourage the growth of new opportunities for adding value to the products of European agriculture, the Community has proposed the launching of programmes worth 105 MECUs (1988-1992) to promote biotechnology-based developments at the interfaces between agriculture and industry. A paper on agro-industrial demonstration activities has also been prepared following the February 1988 request to the Commission at the European Council (of prime ministers of the Member States).

– **Concertation:** in order to promote awareness of the challenges of biotechnology, and greater coherence of policy responses across the Commission services and between Commission and EC Member States, the earlier mentioned Biotechnology Action Programme includes a "concertation action" charged with a range of strategic monitoring, information and coordination tasks.

A five-year-old strategy is ripe for renewal, review and modification; especially given that action has already been initiated on each element of the old strategy.

The renewal of Community strategy: biotechnology in Europe in the 1990s

Amongst the many changes in the environment of biotechnology over the past five years, or in prospect during the coming years, particularly relevant are the following :

– the Uruguay Round of **GATT negotiations,** and in particular their possible implications for some liberalisation of agricultural trade.

— the **Single European Act**, which came into effect from 1 July 1987. Reinforcing and updating the founding treaty of the EEC, this Act :

  • reinforces the role of the directly-elected European Parliament in the adoption of new Community policies and programmes;

  • facilitates (by the wider use of qualified majority voting by the Council of Ministers) the adoption of the harmonisation measures needed to create by 1992 a true Common Market;

  • adds a specific section on "Research and technological development" to the EEC Treaty;

  • defines in hard economic terms the objective of the Community's R&D activities (Article 130F,1): "The Community's aim shall be to strengthen the scientific and technological basis of European industry and to encourage it to become more competitive at international level". This must be pursued with an awareness of Article 130A: "In order to promote its overall harmonious development, the Community shall develop and pursue its actions leading to the strengthening of its economic and social cohesion".;

  • requires the preparation of an overall, multi-year "Framework Programme" for Community R&D activities (to be unanimously agreed by the Member States), within which action has to be implemented through specific programmes (each to be adopted by majority decision); the current Framework Programme (1987-91) was agreed in September 1987.

These considerations emphasise international competitiveness and the achievement of internal common market as strategic aims for Community policies for biotechnology. However, there are both broader social and global issues, to which biotechnology is relevant or central; and narrower technical issues relevant to Community policy initiatives. A possible inventory of **strategic aims for biotechnology** might therefore be summarised as follows :

— **Overall, continuing, long-term goal:**

  • The beneficial application of biotechnology to the maintenance and improvement of health and wellbeing, local environments and the global ecosystem.

— **Major policies with specific implications for biotechnology:**

  • Competitiveness and innovation in the bio-industries, with particular reference to the formation and growth of small and medium-sized enterprises;

  • Harmonised internal market (regulations, patents, standards), taking **international** dimensions into account;

  • Research (basic, pre-competitive and infrastructure), development and training;

  • International collaboration (scientific, technological and industrial).

— **Other current priority actions in support of the above goal and policies:**

  • European biotechnology information policy (for infrastructure and competitiveness);

  • Communication : public, consumers, political leaders and legislators.

Of these seven strategic aims, some are particularly relevant to the topics of the current conference, and in the following sections, these are the points emphasised.

The benefit and the necessity of biotechnology

Of the seven proposed strategic aims above, only the first can be defended as unequivocally worthwhile in itself. The pursuit of this goal is not optional; it is a fundamental imperative. Biotechnology is by definition the collected knowledge relevant to purposeful use or maintenance of living systems, whether the system be a micro-organism or an inhabited planet. We hope to

sustain a human population rising from the current five billion to a likely 10 billion within our grandchildren's lifetimes. To sustain such a growing population in civilised conditions without destroying the planet's continuing ability to support human and other life, will call for all the intelligence and understanding which we possess concerning the management of living systems.

The other six aims are essentially instrumental, in support of this over-riding goal; and the subject of this conference, the pursuit of growth and product quality in swine, is one important example of the competitiveness which features next on the list of strategic aims. We review below the implications and acceptability of this pursuit.

Do we want competitiveness, intensification and productivity growth in agriculture ?

Doubts have in recent years been expressed about the pursuit of higher productivity in agriculture. These doubts reach beyond economic arguments, to areas which the classical economist might term "externalities" - and then ignore. The attack on productivity has several bases, of which four are particularly emphasised :

— deleterious effects on the environment;

— concern for the suffering and "rights" of animals;

— recepticism about the need for higher output in agriculture, at least in areas of the world characterised by saturated markets and apparent structural surpluses;

— disruptive impacts on economic structures, particularly if the "rationalisation" of agriculture into fewer, larger, units is accelerated.

These are seen as some of the implications which influence the acceptability of biotechnology, or at least, of some of its specific applications in agriculture.

Biotechnology and environment

Consider first the concern sometimes expressed about the impact of biotechnology on agriculture and the environment. Around the world, some two hundred million people are engaged in "slash and burn" agriculture. Of course, they are driven by their local necessities; but by their actions, they are destroying the remaining areas of tropical forest, with a loss of species estimated at several hundred per day. We are likely to lose half of all current species within twenty years; it is an environmental catastrophe, a species extinction of a magnitude unparalleled since the death of the dinosaurs. It is not hypothetical; it is happening now. Yet biotechnology can offer the means to feed the world's whole population more than adequately, using far less land than we cultivate today.

Further major gains in agricultural productivity are now seen to be possible, such as those deriving from our ever-increasing understanding of animal and plant nutrition and metabolism. By pursuing higher productivity, we can reduce the pressure on environmentally sensitive areas, such as the uplands and the wetlands, the unique ecological habitats. Biotechnology offers the means to defend our forest, be it in temperate or in tropical zones, and to restore our environment, replanting appropriate species in degraded areas such as, here in Europe, parts of our Mediterranean littoral.

The political and economic difficulties should not be understated. But it is essential that interest groups seriously concerned with the maintenance and restoration or enhancement of the environment, of ecosystems, should recognise the potential of the recent advances in biotechnology for enabling their objectives to be achieved.

Clearly mismanagement of intensive agricultural systems can create environmental problems, for example from the waste products of intensive animal units. But both public regulations and

economic self-interest militate in favour of reducing the volume of such wastes, by enhancing the animal's food conversion efficiency. Moreover, the methods for treating wastes and for converting them into acceptable or even useful products are themselves a matter of biotechnology.

Biotechnology and animal rights

Turning to the questions of animal suffering and rights, the industry must recognise constraints, and adjust its methods to remain within the limits of what is acceptable in our societies for the treatment of sentient fellow-species. This is currently given operational and legal definition through such instruments as the Council of Europe conventions on the treatment of animals used in agriculture, and of animals used in research. There is, in my opinion, no new problem of principle posed by the advances in genetics or biotechnology, relative to the issues of humane treatment with which we are already familiar. It may reasonably be argued that a healthy and more productive animal has higher value, and is therefore likely to be better cared for.

In some cases, we may hope that advances in biotechnology may enable us to diminish the use of animals in laboratory experimentation, for example through the use of in vitro tests. For meat animals, or animals castrated to control their behaviour, there is no escaping what some writers term, the associated "mixture of necessity and guilt" short of a completely vegetarian ideology. This remains a minority conviction, albeit a growing one. Biotechnology will again offer, if the market or the vegetarians demand it, the means for developing meat substitutes, of texture and flavour ever closer to the natural product. The ICI-RHM "Quorn" from the fusarium fungus, tastes better than the textured vegetable proteins of a few years ago; and in terms of land use, must be a substantial gain in the population sustainable from a given land area.

Pursuing this line of argument, one might in a hungry world draw a moral distinction, between the monogastrics (pigs and poultry) competing with human diet; and the polygastric, cellulose-digesting ruminants traditionally used as scavenging animals on terrain not otherwise adaptable to human sustenance. In a world less hungry, where the cattle are fed on oil-seed cake, the moral distinction is difficult to sustain, and the choice of production routes for protein supply returns to questions of economics. It should not be assumed, however, that the "consumer" is a "theoretical economic individual", indifferent to the means used, the circumstances and the origins of the products and services offered for consumption. To the acceptability issue we return below. Let us first consider the critique based on the "surpluses" argument.

Biotechnology and surpluses

The pursuit of higher productivity in agriculture is currently out of fashion in some political circles in Western Europe. This is a simplistic and dangerous reaction to the short-term problems of surpluses. It is worth reiterating the several reasons why the pursuit of efficiency and productivity remains vital.

The most obvious reason is the general welfare : it is clearly in the interest of the consumer and of society as a whole to produce needed goods with less materials energy or other costly inputs.

Agricultural surpluses in the European Community are a soluble and transient problem. The policy instruments - primarily prices, quotas and stabilisers - are already in operation, to bring supply and demand into balance over the next two or three years.

To satisfy current demands for agricultural products with a lower level of inputs provides a welfare gain. The distribution of this gain between the supplier of better inputs to the farmer, the farmer himself, the consumer, or the Community taxpayer, is a matter for political decision, or economic negotiation through the marketplace. Few consumers complain of a surplus of spending power.

Biotechnology and economic structure

The above aggregate economic arguments do not describe the detailed structural implications associated with the "lower level of inputs" - including the input of labour. This means a declining number of farms and farmers, for the rate of progress of productivity in agriculture is likely to continue to exceed the rate of growth of population, certainly in the developed world, and fortunately also on a global basis. In spite of the sometimes traumatic personal consequences of this structural change, it is difficult to dispute the desirability of a continuing decline in the real costs of agricultural production and the consequent capacity to supply food at affordable prices for a growing world population.

Europe cannot isolate its agriculture from these trends. It is above all a bloc of trading countries - more so than the United States or Japan - as the following figures make clear :

	United States	Japan	EC Member States *
Imports as % of GNP	8,8	6,5	22,8
Exports as % of GNP	5,2	10,8	22,8

Source: The OECD in figures, July 1988; figures relate to 1986
* the fact of including intra-Community trade does not diminish the force of the argument.

Agriculture forms a major element of this trade. France alone is second only to the United States in the value of its agricultural exports. Whatever the current differences between the groups negotiating in the GATT Uruguay round, it seems certain that the coming years are going to see some greater liberalisation of world trade in agriculture with a concomitant dismantling of production supports.

Any country or region which seeks to become or to remain a major participant in agricultural trade in the 1990s must therefore continue to pursue increased efficiency and productivity in agriculture, in particular via research and extension or training, and the application of advanced biotechnology in agriculture.

Consumer and political acceptability, and the need for communication

In reviewing some of the criticisms levelled at the pursuit of competitiveness through biotechnology, we have sought to defend it as a pursuit essential for the overall aims of health, wellbeing and environment. Most of the other earlier listed aims - the harmonised internal market, research, international collaboration, information infrastructure - contribute also to the pursuit of competitiveness. There remains the proposed aim: "Communication: to public, consumers, political leaders and legislators".

The emphasis on this aim is related to the aims of this conference, and to the criticism reviewed above : the implications of applying biotechnology for competitiveness in agriculture are far from accepted. Even within a general acceptance of the aim, there is extensive debate about specific practices going far beyond the traditional regulatory concerns of quality, safety, efficacy, and safety for the environment.

It is one of the Community's stated aims to raise the level of public understanding of the nature, potential and risks of biotechnology. An educated public is fundamental to democracy, and it is clear that a growing and influential proportion of today's consumers want to be as fully informed as possible. Such purchasers of goods and services are not indifferent to the production technology, to

the suffering of animals, or to the impacts on the environment (witness the companies now seeking to profit from alternatives to chlorinated fluorocarbons as aerosol propellants).

In a recent work (Elkington et al., 1988) the "Green Consumer" gets frank and detailed advice on how to shop for a better environment - how to "buy products that don't cost the earth". Industrialists may bow to such demands, or argue with them, but above all will be expected to offer transparency and integrity.

Scientists acquainted with biotechnology can easily see why potentially, and generally in practice, biotechnology can be the perfect ally of such trends in consumer behaviour; and this has been argued above. But such arguments are by no means self-evident and there are strong opposing voices. Some of these criticisms are fair. They may be motivated by ecological concerns over what are in fact bad and short-sighted agricultural practices, by sincere objections to the use of animals as food producers, or simply by a deep-seated conservatism that yearns in vain for a stable and organic society[1]. Other criticisms are less honest, either masking a self-interested sectoral protectionism in the guise of pretended concern for consumer safety, or participating in a misleading and alarmist attach on modern science and its applications.

Lady Warnock (1988), for example writes of "the barbarians at the gate, seeking to take us back to the Middle Ages. What alarms me today is that the power of antiscientific rhetoric has grown so quickly that it may be impossible for us to set up a regulatory body not prey to such rhetoric".

There is indeed in some countries and in some interest groups an upsurge of public disquiet about the implication of progress in the life sciences, and their applications. The reasons are less a fear of specific consequences, than a fear of the unknown, and a facile transfer of concerns appropriate to one specific danger to other areas in which they may be irrelevant.

Such sloppy thinking is dangerous; it costs lives. As the Bodmer report (1985) puts it, in the absence of widespread understanding, we "shy at kittens and cuddle tigers".

Issues are not resolved by statistical analysis, however, but by public confidence; as Harry Otway has expressed it : "if the public cannot evaluate the risk, they will evaluate the regulator". Confidence has to be built upon trust and the trust has to be built upon regulations and practical experience which are scientifically based and scientifically evaluated.

The scientific method is one of the supreme achievements of human culture over the past three or four centuries, and is the direct lineal descendant of Renaissance humanism. It is the most effective societal learning instrument ever developed. It is naturally international in character.

Key features of science are its cumulative character - we build on the achievements of our predecessors - and its openness to correction. In spite of its achievements, this openness to correction implies an essential humility, which Karl Popper expressed in his phrase "the conjectural status of knowledge". All scientific knowledge is hypothesis, subject to refutation or refinement by new evidence or experiment.

Thus to refuse the further expansion of science, or to be nervous of its application to useful purposes, implies a failure of self-confidence in human capacities and of confidence in our societies' abilities to learn, to correct and to improve.

Biotechnology is important for human progress, and for the management of the global ecosystem, a responsibility which we cannot escape or "leave to nature".

Public understanding, attitudes and acceptance will increasingly be of strategic significance for the progress of biotechnology. Public education/information is therefore of strategic importance; arguably, the single most important strategic instrument in a society's self-management, learning and survival, and whether we define "society" in global, regional or national terms.

To the process of enlightenment of the public and our political leadership, conferences such as this can greatly contribute.

---

[1]The phrase "organic society" is here used, as by Karl Popper (1945), in antithesis to the less rooted but more liberal and iconoclastic "open society" characteristic of the Western economies.

References

Bodmer, W., 1985. The public understanding of science. Royal Society working group, under the Chairmanship of Sir Walter Bodmer. The Royal Society, London.

Elkington, J. and J. Hailes, 1988. The Green Consumer Guide. Victor Gollanez, London, 1988.

Popper, K., 1945. The Open Society and its Enemies. Routledge & Kegan Paul, London.

Warnock, M., 1988. Religious Fundamentalism Threatens to Block Scientific Progress. The Scientist, 5 September 1988.

THE FRAMEWORK

BIOTECHNOLOGICAL 'TOOLS' TO REGULATE GROWTH IN SWINE

R.Dean Boyd and Diane Wray-Cahen
Department of Animal Science, Cornell University, Ithaca NY 14853-4801

Summary

Growth is a highly orchestrated process invoking a multiplicity of hormones and requiring substantial quantities of nutrients. The hormone somatotropin (ST) has been shown to exhibit regulatory effects on metabolism and to occupy a central role in determining how absorbed nutrients will be partitioned postnatally. Exogenous administration of ST markedly alters the rate and pattern of tissue growth in growing swine by directing nutrients toward or diverting them from specific tissues in a highly coordinated manner. Unprecedented increases in lean tissue accretion have been observed, coincident with a simultaneous decrease in the rate of lipid accretion. Strategies that increase the blood concentration of this naturally occurring polypeptide will provide swine producers with the opportunity to simultaneously effect dramatic changes in production efficiency and to provide consumers with a truly lean food constituent. Recent innovations in biology are giving rise to new biological 'tools' which will permit Animal Scientists to employ a variety of approaches to achieve the ST response. In this review, we will discuss five potential approaches which are presently under systematic study. Techniques discussed are (a) exogenous ST and (b) secretogues of ST, (c) insulin-like growth factor (IGF-1), (d) immunological manipulation of ST secretion or potency and, (e) gene insertion or regulation of gene expression (eg., ST, GRF). In the 'near' future, the ST response may be achieved through exogenous ST, appropriate secretogues of ST release, or by employment of site specific antibodies which enhance the biological activity of the endogenous hormone. Important biological questions remain before Scientists can determine if mediation of the ST response by IGF-1 is appropriate for commercial development. In the 'long-term', it seems conceivable that the ST 'axis' may be manipulated genetically as techniques for genetic improvement evolve to sophisticated and specific methods for controlled gene expression (ie., gene amplification) or gene insertion (ie., gene optimization - ST, GRF). We anticipate that approaches for manipulating the ST 'axis' may be of sufficient breadth to accommodate directed nutrient partitioning while satisfying public mandates against the use of certain technologies in meat animal production. Finally, the over-riding importance of ST is that it has become an invaluable 'probe' into the mechanisms of postnatal growth and metabolic regulation.

Keywords: biotechnology, growth regulation, nutrient partitioning, somatotropin, insulin-like growth factor, gene insertion, swine.

Introduction

The mission of Animal Science Research is to provide biological and management 'tools' to animal agriculture which facilitate efficient animal production and products acceptability. Productive efficiency of growing swine is determined by the growing of nutrients partitioned to fat relative to muscle and by the rate at which tissue accretion occurs (ie., dilution of total maintenance cost). Acceptability of the meat product is markedly influenced by fat content. A recent report from

21

the National Research Council (1988) cites the recommend of both medical and health professionals who urge reduced consumption of dietary fat; particularly that of animal origin. Furthermore, consumers are becoming more health conscious with a growing preference for leaner meat. Present efforts by Animal Scientists in the area of growth regulation are timely indeed. By attempting to alter the rate and composition of gain, we simultaneously address the issues of productive efficiency and product acceptability.

Techniques for altering the balance between lean and adipose tissue growth in swine have previously involved genetic selection and employment of a variety of management strategies (eg., intact males, limit feeding, lower slaughter weights). Recent advances in recombinant DNA technology are giving rise to a technological revolution that will permit Animal Scientists to employ new 'tools' which dramatically alter growth and development. For example, we now have the ability to produce recombinant products such as somatotropin (ST) which exhibits regulatory effects on metabolism during postnatal growth. Administration of ST to young growing swine has yielded unprecedented results with respect to the rate, efficiency and composition of gain (Evock et al., 1988; Campbell et al., 1988; Boyd and Bauman, 1988). These achievements would normally have required 10 to 20 years of intense genetic selection (Table 1).

The data in Table 1 show the estimated rate of progress achievable through a genetic selection program. The paper by Mitchell and co-workers (1982) was selected for presentation because the selection objectives and criteria for simultaneous emphasis were most relevant to the needs of commercial swine production. The response to ST affirms that considerable time would be required for similar changes to be achieved by selection alone. Further, genetic capacity is far greater than is presently expressed in the growing pig and circulating levels of ST are clearly a limit to expression of growth potential. Its administration should be considered as an adjunct to genetic selection since even highly selected strains exhibit a marked response (Campbell - this volume) and since performance 'maxima' are not yet evident. Although the responses to ST (as shown in Table 1) are dramatic, they are nevertheless conservative. We now appreciate that the ST response is a function of diet adequacy and that increases in the order of 30-40% are achievable for rate and efficiency of gain. We published theoretical estimates of the amino acid requirements for growing swine (50-100 kg) in a recent report (Boyd et al., 1988b). These have served as the basis for subsequent studies in which greater relative responses were observed. We have assumed an amino acid requirement appropriate for accretion of 300 grams of protein per day in highly selected strains of swine (Krick and Boyd, unpublished data).

Table 1. Comparison of relative responses to genetic selection and somatotropin administration.

Item	Genetic Selection[a] Absolute Change per Generation	% Change	Somatotropin[b] Absolute Change	% Change
Daily gain, g/d	+ 5.0	+ 0.7	+ 100.	+ 10.5
Feed:gain, units	- .03	- 1.0	- .87	- 28.5
Daily intake, g/d	- 7.3	0.4	- 590.	- 20.3
Lean gain, g/d	+ 6.0	+ 2.1	ND	—
Feed:lean gain	- .17	- 2.4	ND	—
Loin eye area, mm^2	+27.	+0.8	+ 449.	+ 13.1
Backfat depth, mm	- 1.8c	- 5.5	- 7.	- 25.0
Carcass protein, g/d	ND	—	+ 54.	+ 54.0
Carcass lipid, g/d	ND	—	- 204	- 69.0

[a] Data from Meat & Livestock Commission (1970-1977), Mitchell et al., 1982.
[b] Boyd et al., 1986; Boyd and Bauman, 1988 (120 ug ST/kg BW).
[c] Cleveland et al., 1982 (5 generations of selection).

The absolute levels of performance are not evident from Table 1, however, a minimal statement is warranted so that the capacity for response is evident. For example, rates of carcass protein accretion in the order of 250-280 gram/day (50- 100 kg pigs) have been achieved while simultaneously accruing only 30-50 gram lipid/day. This alteration in rate of tissue development makes it possible to achieve feed to gain (live weight) ratios of 1.6-1.8 in swine (50-100 kg), which are highly selected for lean tissue growth and feed conversion (Boyd and Krick - Unpublished data; Campbell - personal Communication). It is important to appreciate that levels of performance achieved in practice depend on the genotype and blood levels of ST achieved by the delivery system.

Control of somatotropin secretion

Somatotropin is a protein secreted by the anterior pituitary gland. An overview of the controls on ST secretion and its direct and indirect involvement in tissue metabolism is portrayed in Figure 1. Since exogenous administration of ST enhances the rate and composition of growth, any strategy that increases blood concentrations of ST would potentially be a feasible approach for manipulating growth. For example, manipulation of endogenous ST secretion can occur by overriding the inhibitory effects of somatostatin or by increasing the secretory stimulant -- growth hormone releasing factor (GRF). Also, one component of the ST response is an increase in the concentration of insulin-like growth factor I (IGF-I). Since IGF-I appears to mediate many of the effects ascribed to ST, it has been considered as a possible 'target for manipulation.
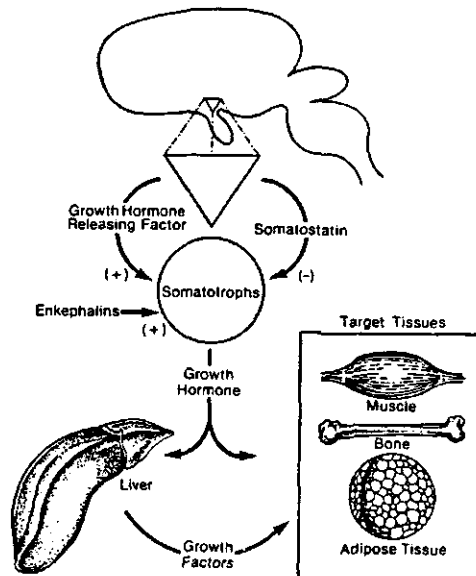
Figure 1. Regulation of somatotropin synthesis and secretion is determined by the hypothalamic hormones, growth hormone releasing factor (GRF-stimulatory) and somatostatin (SRIF-inhibitory)(Figure from Convey, 1987).

Given the technologies which presently exist and our understanding of the biology, there are at least 5 'targets' or approaches to manipulation of the ST 'pathway':

— Exogenous ST;

— Exogenous GRF or other ST secretogues;

— Insulin-like growth factor - 1;

— Immunological manipulation of ST secretion or potency;

— Gene Insertion (ST, GRF).

Pharmacological alternatives also exist and are under investigation (eg., repartitioning agents such as β-adrenergic agonists). A discussion of these is beyond the scope of this paper. We intend to confine our discussion to those techniques associated with the ST 'axis' and which are under serious and systematic investigation.

Somatotropin

Somatotropin appears to be a family of peptides with the major component being a 22 kDa form consisting of 191 amino acid residues. A recent paper from laboratory demonstrates that the potency of ST can be increased by structural modification of the ST molecule. We compared the biological activity of a novel recombinantly derived 21 kDa variant of porcine ST to the 22 kDa form (Boyd et al., 1988a). This form is missing a deletion peptide (amino acids 32-38). In preliminary experiments with heterologous models, the variant form of ST exhibited substantially greater activity as determined by rat liver membrane receptor binding and the hypophysectomized rat growth bioassay systems. The variant also exhibited significantly greater nutrient partitioning activity in swine, with improvements in compositional gain (lipid, protein) and in the efficiency of growth. A parallel example is cited below for GRF in which the potency was markedly improved (ten fold) by structural alteration.

The limiting step in administering ST to farm animals is in the development of a suitable delivery system. ST must be administered in a vehicle that provides controlled delivery over a sustained period of time (eg., 30 days). It is difficult to assess the progress in this area since much of the research is occurring within the private industry sector. Reports have been published recently by researchers from Monsanto Company (Knight et al., 1988) and by Wang and Kothe (1988).

Alternative strategies to ST administration may be sought for reasons other than administration mode and cost effectiveness. For example, exogenous administration represents to some a 'hormone' approach to animal production. Even if concerns of safety to animal and consumer are completely satisfied by regulatory agencies, approaches appearing to be more 'natural' (eg., immunological route) may in some cases prove to be publicly more acceptable. This may be especially true for some European countries.

Somatotropin releasing factor and releasing peptides

As shown in Figure 1, ST secretion is regulated by two hypothalamic neuropeptides - GRF and somatostatin. GRF is a potent and specific stimulant of ST release. In the short time since the isolation and characterization of human GRF (hGRF; Guillemin et al., 1982; Rivier et al., 1982), it has proven to be an effective treatment for ST-deficient children (Gelato et al., 1984; Thorner et al., 1985) and to have potential application to farm animal species for performance enhancement. There is considerable sequence homology between hGRF (1-44)-NH_2, and that isolated from several animal species. This is particularly true for the first 29 amino acid residues from the NH_2 terminus (Schanbacher, 1986). Structure-activity studies have shown that full activity lies within this region.

Porcine GRF is identical to hGRF in the 1-29 amino acid region, hence the expectation that hGRF or expression of the hGRF gene might elicit biological activity in swine similar to porcine GRF.

GRF increases serum ST concentration in a dose dependent manner in humans and in a number of farm animal species (Schanbacher, 1986; Convey, 1987) including swine (Kraft et al., 1984; Etherton et al., 1986; Johnson et al., 1988). There are few published studies, however, on the effects of long-term administration of GRF on the growth performance of swine or meat animals in general. Early attempts to investigate the effect of GRF administration involved intermittent injections. This was due to evidence in rats which suggested that a pulsatile pattern of administration (versus continuous infusion) was necessary to cause ST release (Clark & Robinson, 1985; Jansson et al., 1982). However, studies with GRF given either in multiple injections or as a continuous infusion have yielded equivalent increases in nitrogen retention in growing calves (Moseley et al., 1887) and in milk production for dairy cows (Enright et al., 1986) and ewes (Hart et al., 1985). This observation dispelled early concerns that pituitary somatotrophs may become refractory to continuous GRF exposure and suggests that GRF or other ST releasing peptides are viable 'targets' for promoting growth.

Recently, a series of studies were conducted with growing swine using a novel and potent analogue of hGRF (1-29) (Heimer et al., 1988). These studies demonstrate the potential for a GRF-mediated route of growth promotion and show the merit of using structural modification to enhance biological activity. Scientists at Hoffman-La Roche altered the biologically active region of hGRF by substitution of 3 amino acids. The molecular basis for the structural modification and evaluation for activity are published in an excellent paper by Heimer and co-workers (1988). The tri-substituted GRF (des-NH_2 Tyr_1, D-Ala_2, Ala_{15}, [GRF 1-29 NH_2]) exhibited greater potency in swine than the 1-44 hGRF construct (approximately ten fold). The increase in potency was attributed to the enhanced stability of the NH_2-terminus to enzymatic degradation by a plasma diaminopeptidase. This enzyme degrades GRF by metabolizing GRF(1-44)NH_2 to GRF(3-44)NH_2. Since the structurally modified GRF is a poor substrate for the diaminopeptidase, its clearance rate is considerably slower than observed for the parent compound.

Table 2. Effect of a potent analog of hGRF (1-29) on growth performance and carcass characteristics of growing swine[a]

Item	Saline	hGRF[b]	SE	% Difference
No. Swine	16.	16.	--	--
Gain, g/d	1.06	1.12[c]	.02	+ 5.7
Feed/Gain	2.97	2.38[c]	.07	-19.9
Feed Intake, g/d	3.01	2.57[c]	.03	-14.6
Loin area, cm^2	34.1	38.4[c]	.8	+12.6
Backfat, mm	27.1	19.5[c]	1.0	-28.0
Dissected: No.	8.	8.	--	--
Ham				
- Muscle kg	5.35	6.05[c]	.16	+13.1
- Fat kg	2.65	1.94[c]	.14	- 26.8
- Bone kg	.92	1.03[c]	.04	+12.0
Shoulder				
- Muscle kg	5.69	6.61[c]	.15	+16.2
- Fat kg	2.70	2.34	.14	-13.3
- Bone kg	1.36	1.72[c]	.03	+26.5

[a] Dubreuil et al., 1988 & Pommier et al., 1988. Selected trts. Start wt. 49 kg; End wt. 106 kg.
[b] Desamino - Tyr^1 - Ala^2...Ala^{15} - hGRF(1-29)NH_2 Analog. Injected 3 times daily.
[c] $P < .05$.

Following a study to determine the optimum dose and periodicity of injection (Pelletier et al., 1988), Canadian scientists administered this analogue to growing swine (6.7 ug/kg BW three times

daily) to determine the effects on growth performance and carcass characteristics (Pommier et al., 1988; Dubreuil et al., 1988). Results were similar, in magnitude, to those achieved when ST is administered exogenously (Table 2). It is noteworthy that the dose of GRF analogue required to elicit dramatic changes in performance and composition of gain is relatively low. This and the fact that the peptide is relatively small are attractive features for potential commercialization.

Other approaches to stimulation of endogenous secretion of ST include small somatotropin releasing peptides such as the enkephalin analog, Tyr-D-Tyr-Gly-Phe-Met-NH$_2$ (Bowers et al., 1981). This peptide is also specific for ST secretion. Another compound of this series (His-D-Trp-Ala-Trp-D-Phe-Lys-NH$_2$) has been shown to increase serum ST concentration in growing swine (Doscher et el., 1984) and cattle (Kraft et al., 1984), but we are not aware of demonstrated effects on performance of farm animals by either of the ST releasing peptides.

Mediation of somatotropin effects - IGF-1

Another possible way to elicit the ST response is via a 'down-stream approach'-administering factors which mediate the ST response. One component of the ST response is an increase in IGF-1 (somatomedin-c) concentrations. Since many of the growth-promoting effects observed with ST administration are thought to be mediated by these elevated levels of IGF-1, it is reasonable to speculate that direct administration may enhance growth performance. The most direct evidence for the 'somatomedins hypothesis' is that IGF-I can stimulate growth in rats. Several researchers have reported increases in growth indices when hypophysectomized rats (Schoenle et al., 1982; Schoenle et al., 1985; Skottner et al., 1987; Guler, 1988) and normal rats (Hizuka et al., 1986) received infusions of IGF-I. In general, the growth response elicited by direct administration of IGF-I has not been as great as that observed with ST. In many of these studies the blood levels of IGF-I achieved by infusion were not as high as those achieved with ST administration even though the amount of IGF-I infused was quite large. This may account for the reduced response. Most experiments designed to study the effects of IGF-I on various tissues have been performed in vitro and often using supra-physiological concentrations of IGF-I; many of the effects observed in such studies may be due to IGF-I binding to the insulin receptor. To date, there has not been enough IGF-I available to study the in vivo effects of long-term administration of exogenous IGF-I in farm animals.

In swine, somatotropin treatment results in an elevation of IGF-I levels (Chung et al., 1985; Etherton et al., 1987; Campbell et al., 1988; Evock et al., 1988). Low levels of IGF-1 have been observed in small breeds of dogs (toy poodles; Eigenmann, 1985) and swine (minipigs; Buonomo et al., 1987), although levels of ST were normal. Elevation of circulating IGF-I levels may be necessary for the expression of ST's effects on growth performance. However, IGF-I may not be an effective growth promoter without the interaction with ST. ST may modulate some of the effects of IGF-I on target tissues -- either directly or via induction of the 150 kDa binding protein (Zapf and Froesch, 1986). Walton et al. (1987a,b) demonstrated that pST suppresses insulin- and IGF-I-stimulated lipogenesis and that the 150 kDa binding protein can block the IGF-I insulin-like lipogenic response in porcine adipose tissue.

The large (150 kDa) IGF binding protein is ST-dependent, while the small (40 kDa) IGF binding protein appears to be ST-independent. When ST is administered the large binding protein increases in concentration along with IGF-I (Etherton, 1988; Zapf and Froesch, 1986; Buonomo et al., 1987); the concentration of this binding protein is greatly depressed in hypophysectomized swine (Buonomo et al., 1987). The large binding protein thus may be playing an important role in the regulation of IGF-I function. For instance, the binding proteins could be maintaining IGF-I levels in the blood stream, allowing their effects to be sustained. Or perhaps the large binding protein could inactivate locally produced IGF-I by binding and transporting it to catabolic sites. Its affinity for IGF-I is quite high and the half-live of IGF-I is greatly increased when bound. When IGF-I is infused into rats very little of the free form is detectable. While a single bolus of IGF-I disappears

rapidly, a constant infusion of IGF-I in rats seems to allow the IGF-I to equilibrate with the binding protein, allowing blood levels to rise (Zapf et al., 1985). However, a constant infusion of IGF-1 in lactating cows does not result in an elevation of blood IGF-I (Plaut et al., 1988) and free IGF-I injected into swine disappears rapidly (Etherton, 1988). The binding proteins in both cases appear to be saturated. Although IGF-1 infusion has been shown to reproduce many of the effects of ST administration, much more IGF-1 is required to achieve the same level of response as ST. On a molar basis ST is 10- to 15-fold more potent than IGF-I (Clemmons et al., 1987). Structurally modified forms of IGF-I which are more potent than the native compound have now been produced (Cascieri et al., 1988). However, other problems with IGF-1 as a growth promoter exist. It is not clear what the active form of IGF-1 is in vivo (bound vs free). Unbound IGF-1 mimics insulin, stimulating lipogenesis and causing hypoglycemia in pigs (Etherton, 1988); neither is desirable in meat producing animals. It is uncertain whether or not binding protein synthesis would be induced with IGF-1 administration and without its presence (or that of ST) the insulin-like effects of IGF-1 would ensue. Although Guler (1988) reported that the epididymal fat pad was decreased in hypophysectomized rats treated with IGF-I, it appears that the decreased adipose accretion rates observed in ST-treated pigs are a direct effect of ST (Boyd & Bauman, 1988). Local production of IGF-I (stimulated by ST) may be more important than circulating IGF-I levels. Such a scenario would mean that only a transgenic approach -- insertion of the IGF-I gene and possibly that of the binding protein into the genome of farm animals -- would be likely to succeed.

At least two problems must be seriously considered when discussing IGF-I as an alternative to ST for growth promotion. First, it is unclear whether IGF-I is capable of orchestrating the diverse effects on tissue metabolism ascribed to ST. Particularly important may be the direct effects ST seems to have on bone and adipose (Boyd & Bauman, 1988). Second, it is possible that any technique which does not increase production of the binding protein in conjunction with elevation of IGF-I may not be effective. The roles of ST, binding proteins, and local IGF-I production in the regulation of IGF-I must be more completely understood before the application of direct administration of IGF-I can be considered commercially as a means of achieving the ST response.

Immunological intervention

The recent ban by the European Economic Community (EEC) on hormone- based growth promotants has focused attention on alternatives to exogenous hormone administration. Immunological manipulation of specific endocrine events is an attractive alternative since it may be perceived as a more 'natural' means of promoting growth. Certain immunological approaches appear to improve the efficiency of ST use or mimic its action. This suggests possible advantages in the cost-benefit relationship. Strategies presently under investigation include (1) active immunization against somatostatin to increase ST secretion, (2) use of monoclonal antibodies with specific antigenic determinants to increase biological activity of ST and, (3) use of 'surrogate' molecules to mimic the ST effect.

Somatostatin, which is the counter-regulatory peptide of ST secretion, inhibits GRF release. Neutralization of somatostatin was conceived early in the search for alternatives to ST administration. Attempts to alleviate the effects of somatostatin by immunization has resulted in mixed results to date with respect to plasma ST concentration and growth enhancement in ruminants (Schanbacher, 1986; Schelling & Byers, 1988). We are not aware of any credible report on somatostatin immunization in swine, however, given the relative response of swine to ST, this might be the more sensitive species. Nevertheless, failure to achieve more consistent and dramatic results in growing sheep and cattle, in addition to a lack of specificity for ST (eg., inhibits at least 8 other hormones) seem to make this a less likely 'target' for manipulation.

A novel and intriguing biological phenomenon results when specific monoclonal antibodies (Mab) interact with ST. Mab have been shown to enhance the effectiveness of hST with respect to the rate, efficiency and composition of gain in dwarf mice (Aston et al., 1986; Holder & Aston,

27

1988). This find is unequivocal, nevertheless unexpected since binding of antibodies to hormones generally inhibits hormone activity. At the present time, the mechanism of Mab-mediated enhancement of ST action is unclear and speculative.

The first report testing the possibility of Mab-enhanced ST action in farm animals was by Pell and coworkers (1988). They observed that Mab, with specific antigenic determinants, increased milk production of lactating ewes treated with bST, above that elicited by bST alone. We are not aware of any report on the effects of Mab on growth and composition in meat animals. However, the results provide incentive for further pursuit of this route to improve the efficiency of ST use by farm animals.

Another immunological strategy for manipulation of growth is to use the immune system's anti-idiotype network to produce antibodies which structurally resemble ST and which are capable of mimicking its action (Hannah report, 1986; Flint, 1987). Such antibodies (or hormone 'images') have been raised to rat and ovine ST. They effectively compete with ST for liver and adipose receptors of the respective species (Hannah report, 1986). Hypophysectomized rats have responded with an increase in body weight gain similar to that observed with ST administration. Although we are not aware of any report demonstrating this to be a feasible approach for ST enhancement of growth in meat animals, this is a conceptual possibility worthy of careful consideration. The attractive feature of this and other immune approaches is the induction of antibodies in high concentrations which would be expected to circulate in the bloodstream for prolonged periods without further treatment.

Transgenic technology

The emergence of recombinant genetic technology and embryo manipulation have provided the facility for controlled genetic alteration of the genome via gene insertion. Significant developments in biology are still required, however, before this tool for increasing endogenous production of ST can be commercialized. This technology integrates the most sophisticated approaches from a number of fields of investigation and represents another alternative to administration of peptide hormones.

Rat (Palmiter et al., 1982) and human (Palmiter et al., 1983) structural genes, ligated to a metallothionein-I (MT) promoter or regulatory region, were introduced into mice via micro-injection of fertilized eggs. Mice that incorporated and expressed the foreign gene produced large quantities of ST and grew more rapidly than littermate controls. Similarly, the MT-hGRF gene clone has also been introduced into mice. Those expressing the gene had elevated ST levels resulting in marked increases in weight gain relative to littermate controls (Hammer et al., 1985a). In neither instance, unfortunately, was the composition of gain determined. This information is essential for determining the effectiveness of a growth promoter in meat animals.

Recently, genes coding for ST and GRF have been inserted into the genome of farm animals via micro-injection into the pronucleus or nucleus of fertilized ova. The first report to transgenesis in swine involved insertion of the structural gene for hST with a MT-I promoter region (Hammer et al., 1985b). Since then structural clones for the gene of bovine (Pursel et al., 1987; Wieghart et al., 1988) and rat (Ebert et al., 1988) ST have been inserted into the genome as has that for hGRF (Pursel - personal communication). With the exception of a recent paper by Vize and co-workers (1988), the gene construct cloned for insertion has been non-porcine. Despite the enormous effort to produce swine with enhanced ability for ST secretion, only one study has had sufficient 'littermates' to document the potential for improved growth and carcass composition of transgenic pigs (Pursel et al., 1988a; Table 3).

Results presented in Table 3 clearly demonstrate that enhanced rate and efficiency of gain may be achieved in swine with insertion of the ST gene. In accordance with studies using exogenous ST treatment, subcutaneous fat was dramatically decreased, thereby implying increased lean mass. Ultrasonic estimates of backfat thickness (10th rib, approximately 90 kg) were 20.5 mm and 7.9 mm

for control and MT-bST pigs respectively (Pursel et al., 1988b). However, this is a slight overestimate of the actual backfat thickness since skin thickness over the respective rib was approximately 1 mm thicker than in the littermate controls. Although transgenic pigs grew more rapidly and efficiently, they also exhibited a number of adverse effects. These included lameness, ulcers, lethargy and susceptibility to stress, hence the disproportionate number of animals actually completing the study as noted in Table 3. These adverse effect are believed to be caused by prolonged exposure to the pharmacological levels of plasma ST expressed by most of the transgenics studied thus far by Pursel and co-workers.

Table 3. Growth potential of Metallothionein-bST transgenic swine fed ad libitum from 30 to 90 kg body weight.[a]

Period	Treatment	No./Trt	Gain, g/d	Intake, kg/d	Feed:Gain
30-60 Kg	Control	8	761 ± 35	$2.08 \pm .05$	$2.77 \pm .14$
	Transgenic	4	988 ± 44^b	$2.12 + .07$	$2.21 + .17^b$
	%Difference	--	+30%	ND	-20%
60-90 Kg	Control	7	884 ± 28	$2.93 \pm .11$	$3.33 \pm .18$
	Transgenic	3	948 ± 38	$2.39 \pm .15^b$	$2.58 + .25^b$
	%Difference	--	+ 7%	-18%	-22%

[a] Pursel et al., 1988a and personal communication. Diet contained 18% CP with .25% Lysine. Eight pigs allocated per treatment with disproportionate numbers of transgenic pigs due to health problems.
[b] $P < .05$.

The remarkable accomplishments of transgenesis must not over-shadow the fact that critical biological questions must be addressed before application to farm animals can be truly successful. First, the basic mechanisms responsible for regulation of gene expression in mammalian cells are not yet understood. There are several levels of gene control, hence different control elements may exist. This facet is discussed in a review by Wagner and Jochle (1986). Second, the process of insertion into the genome of the germ-line is largely 'random'. At present, there is generalized incorporation across tissues and uncertainty relative to the determination of gene placement and integrity of associated genomic sequences (ie., those on either side). Finally, the specific approach to transgenesis will undoubtedly evolve and have multiple approaches for a given endpoint as we learn more about the biology, recognize specific points of regulation, and determine how amenable they are to regulation at the gene level.

References

Aston, R., A.T. Holder, M.A. Preece and J. Ivanyi, 1986. Potentiation of the somatogenic and lactogenic activity of human growth hormone with monoclonal antibodies. J. Endocrinol. 110:381.

Bowers, C.Y., F.A. Momany, G.A. Reynolds, D. Chang, A. Hong and K. Chang, 1981. Endocrinol. 116:663.

Boyd, R.D. and D.E. Bauman, 1988. Mechanisms of action for somatotropin in growth. In: D.R. Campion, G.J. Hausman and R.J. Martin (Eds.) Animal growth regulation. Plenum Press. (In press).

Boyd, R.D., D.E. Bauman, D.H. Beermann, A.F. DeNeergaard, L. Souza and W.R. Butler, 1986. Titration of the porcine growth hormone dose which maximizes growth performance and lean deposition in swine. J. Anim. Sci. (Suppl. 1):218 (Abstr.).

Boyd, R.D., D.H. Beermann, K.R. Roneker, T.D. Bartley and K.D. Fagin, 1988a. Biological activity of a recombinant variant (21 kD) of porcine somatotropin in growing swine. J. Anim. Sci. 66 (Suppl. 1):256 (Abstr.).

Boyd, R.D., D. Wray-Cahen and B. Krick, 1988b. Implications of somatotropin on nutrient requirements of growing swine. Proc. Cornell Nutr. Conf. p. 81.

Buonomo, F.C., T.J. Lauterio, C.A. Bayle and D.R. Campion, 1987. Determination of insulin-like growth factor 1 (IGF-1) and IGF binding protein levels in swine. Dom. Anim. Endocrinol. 4:23.

Campbell, R.G., N.C. Steele, T.J. Caperna, J.P. McMurtry, M.B. Solomon and A.D. Mitchell, 1988. Interrelationships between energy intake and exogenous porcine growth hormone administration on the performance, body composition and protein and energy metabolism of growing pigs weighing 25 to 55 kilogram live weight. J. Anim. Sci. 66:1643.

Cascieri, M.A., R. Saperstein, N.S. Hayes, B.G. Green, G.G. Chicchi, J. Applebaum and M.L. Bayne, 1988. Serum half-life and biological activity of mutants of human insulin-like growth factor 1 which do not bind to serum binding proteins. Endocrinol. 123:373.

Chung, C.S. , T.D. Etherton and J.P. Wiggins, 1985. Stimulation of swine growth by porcine growth hormone. J. Anim. Sci. 60:118.

Clark, R.G. and I.C.A.F. Robinson, 1985. Growth induced by pulsatile infusion of an aminated fragment of human growth hormone-releasing factor in normal and deficient rats. Nature 314:281.

Clemmons, D.R., M. Dehoff, R. McCusker, R. Elgin and W. Busby, 1987. The role of insulin-like growth factor 1 in the regulation of growth. J. Anim. Sci. 65(Suppl. 2):168.

Cleveland, E.R., P.J. Cunningham and E.R. Peo Jr., 1982. Selection for lean growth in swine. J. Anim. Sci. 54:719.

Convey, E.M., 1987. Advances in Animal Science: Potential for improving meat animal production. Proc. Cornell Nutrition Conf. p. 1.

Doscher, M.E., P.K. Baker, L.A. Kraft and C.A. Ricks, 1984. Effect of a synthetic growth hormone releasing hexapeptide on serum growth hormone levels in barrows. J. Anim. Sci. 59 (Suppl. 1):218 (Abstr.).

Dubreuil P., S. Pommier, P. Gaudreau, G. Pelletier, D. Petitclerc, C.Farmer, H. Lapierre, Y. Couture and T.F. Mowles, 1988. Effect of dose and frequency of a potent analog of human growth hormone-releasing factor (hGRF) on growth performance and carcass characteristics of growing pigs. J. Anim. Sci. 66 (Suppl. 1):296 (Abstr.).

Ebert, K.M., M.J. Low, E.W. Overstrom, F.C. Buonomo, C.A. Bayle, T.M. Roberts, A. Lee, G. Mandel and R.H. Goodman, 1988. A Moloney MLV-rat somatotropin fusion gene produces biologically active somatotropin in a transgenic pig. Molec. Endocrinol. 2:277.

Eigenmann, J.E., 1985. Growth hormone and insulin-like growth factor in the dog: clinical and experimental investigations. Dom. Anim. Endocrinol. 2:1.

Enright, W.J., L.T. Chapin, W.M. Moseley, S.A. Zinn and H.A. Tucker, 1986. Growth hormone-releasing factor stimulates milk production and sustains growth hormone release in holstein cows. J. Dairy Sci. 69:344.

Etherton, T.D., 1988. The mechanisms by which porcine growth hormone improves pig growth performance. Proc. Internal. Symp. on Biotech. in Growth Regulation. (In press). Cambridge.

Etherton, T.D., J.P. Wiggins, C.S. Chung, C.M. Evock, J.F. Rebhun and P.E. Walton, 1986. Stimulation of pig growth performance by porcine growth hormone and growth hormone-releasing factor. J. Anim. Sci. 63:1389.

Etherton, T.D., J.P. Wiggins, C.M. Evock, C.S. Chung, J.F. Rebhun, P.E. Walton and N.C. Steele, 1987. Stimulation of pig growth performance by porcine growth hormone: determination of the dose-relationship. J. Anim. Sci. 64:433.

Evock, C.M., T.D. Etherton, C.S. Chung and R.E. Ivy, 1988. Pituitary porcine growth hormone (pGH) and a recombinant pGH analog stimulate pig growth performance in a similar manner. J. Anim. Sci. 66:1928.

Flint, D.J., 1987. Endocrine manipulation of animal growth. J. Endocrinol. 115:365.

Gelato, M., J. Ross, 0. Pescovitz, F. Cassorla, M. Skeeda and G.R. Merriam, 1984. Acceleration of linear growth after repeated doses of growth hormone-releasing hormone. Pediat. Res. 18:167A (Abstr. 430).

Guillemin, R., P. Brazeau, P. Bohlen, F. Esch, N. Ling and W.B. Wehrenberg, 1982. Growth hormone-releasing factor from a human pancreatic tumor that caused acromegaly. Science 218:585.

Guler, H.P., 1988. Growth promotion using recombinant IGF-I. Proc. Internat. Symp. on Biotech. in Growth Regulation. (In press). Cambridge.

Hammer, R.E., R.L. Brinster, M.G. Rosenfeld, R.M. Evans and K.E. Mayo, 1985a. Expression of human growth hormone releasing factor in transgenic mice results in increased somatic growth. Nature 315:413.

Hammer, R.E., V.G. Pursel, C.E. Rexroad Jr., R.J. Wall, D.J. Bolt, K.M. Ebert, R.D. Palmiter and R.L. Brinster, 1985b. Production of transgenic rabbits, sheep and pigs by microinjection. Nature 315:680.

Hannah Research Institute, 1986. Mammary physiology and biochemistry: Anti-idiotypic antibodies as surrogate hormones. Ayr, Scotland. p. 43.

Hart, I.C., P.M.E. Chadwick, S. James and A.D. Simmonds, 1985. Effects of intravenous bovine growth hormone or human pancreatic growth hormone- releasing factor on milk production and plasma hormones and metabolites in sheep. J. Endocrinol. 105:189.

Heimer, E.P., M. Ahmad, T. Lambros, T. McCarty, C.T. Wang, T.F. Mowles, S. Maines and A.M. Felix, 1988. Synthesis and biological evaluation of growth hormone releasing factor, structural linear and cyclic analogs. Proc. UCLA Peptide Symp. (In Press).

Hizuka, N., K. Takano, K. Asakawa, M. Miyakaw, I. Tanaka, R. Hirikaw and K. Shizume, 1986. Insulin-like growth factor 1 stimulates growth in normal growing rats. Eur. J. Pharmacol. 125:143.

Holder, A.T. and R. Aston, 1988. Antigen-antibody complexes that enhance growth. Proc. Internat. Symp. on Biotech. of Growth Regulation. (In Press). Cambridge.

Jansson, J.O., K. Albertsson-Wikland, S. Eden, K.G. Thorngren, O. Isaksson, 1982. Acta Endocrinol. 99:24.

Johnson, J.L., M.T. Coffey and K.L. Esbenshade, 1988. Dose response of synthetic human growth hormone releasing factor (hGRF) on serum porcine growth hormone (pGH) in growing barrows. J. Anim. Sci. 66 (Suppl. 1):294 (Abstr.).

Knight, C.D., M.J. Azain, T.R. Kasser, M.J. Sabacky, C.A. Bayle, F.C. Buonomo and C.L. McLaughlin, 1988. Functionality of an implantable 6-week delivery system for porcine somatotropin (pST) in finishing hogs. J. Anim. Sci. 66 (Suppl. 1):257 (Abstr.).

Kraft, L.A., P.K. Baker, M.E. Doscher and C.A. Ricks, 1984. Effect of a synthetic growth hormone releasing hexapeptide (BI679) and growth hormone releasing factor (GRF) on serum growth hormone levels in barrows. J. Anim. Sci. 59 (Suppl. 1):218 (Abstr.).

Lanza, G.M., G.G. Krivi, L.A. Bentle, P.J. Eppard, L. Kung, R.L. Hintz, R.L. Ryan and M.A. Miller, 1988. Comparison of the galactopoietic activity of several recombinant bovine somatotropin variants and pituitary derived bovine somatotropin. Proc. 7Oth Endocrinol. Soc. p.81 (Abstr.).

Moseley, W.M., J. Huisman and E.J. Van Weerden, 1987. Serum growth hormone and nitrogen metabolism responses in young bull calves infused with growth hormone-releasing factor for 20 days. Dom. Anim. Endocrinol. 4:51.

Mitchell, G., C. Smith, M. Makower and P.J.W.N. Bird, 1982. An economic appraisal of pig improvement in Great Britain. Anim. Prod. 35:215.

National Research Council (NRC), 1988. Designing Foods: Animal Product Options in the Marketplace. National Academy Press, Washington, D.C.

Palmiter, R.D., R.L. Brinster, R.E. Hammer, M.E. Trumbauer, M.G. Rosenfeld, N.C. Birnberg and R.M. Evans, 1982. Dramatic growth of mice that develop from eggs microinjected with metallothionein-growth hormone fusion genes. Nature 300:611.

Palmiter, R.D., G. Norstedt, R.E. Gelinas, R.E. Hammer and R.L. Brinster, 1983. Metallothionein-human GH fusion genes stimulate growth of mice. Science 222:809.

Pell, J.M., I.D. Johnsson, R. Puller, D.J. Morrell, I.C. Hart, A.T. Holder and R. Aston, 1988. Potentiation of growth hormone activity in sheep using monoclonal antibodies. J. Endocrinol. (In Press).

Pelletier, G., P. Dubreuil, P. Gaudreau, C. Farmer, D. Petitclerc, S. Pommier, H. Lapierre and T.F. Mowles, 1988. Effect of dose and frequency of a potent analog of human growth hormone-releasing factor (hGRF) on serum components of growing pigs. J. Anim. Sci. 66 (Suppl. 1):295 (Abstr.).

Plaut, K., M. Harkins, D.E. Bauman and A.W. Bell, 1988. Evaluation of continuous infusion of insulin-like growth factor-1 (IGF-1) on systemic concentrations IGF-1 in lactating dairy cows. J. Anim. Sci. 66(Suppl.1):273 (Abstr.).

Pommier, S., P. Dubreuil, P. Goudreau, G. Pelletier, C. Farmer, D. Petitclerc, H. Lapierre, Y. Couture and T. Mowles, 1988. Effect of a potent analog of human growth hormone-releasing factor (hGRF) on the carcass composition of market pigs. J. Anim. Sci. 66 (Suppl. 1):295 (Abstr.).

Pursel, V.G., C.E. Rexroad Jr., D.J. Bolt, K.F. Miller, R.J. Wall, R.E. Hammer, C.A. Pinkert, R.D. Palmiter and R.L. Brinster, 1987. Progress on gene transfer in farm animals. Vet. Path. Immunopath. 17:303.

Pursel, V.G., R.G. Campbell, K.F. Miller, R.R. Behringer, R.D. Palmiter and R.L. Brinster, 1988a. Growth potential of transgenic pigs expressing a bovine growth hormone gene. J. Anim. Sci. 66 (Suppl. 1):267 (Abstr.).

Pursel, V.G., K.F. Miller, D.J. Bolt, C.A. Pinkert, R.E. Hammer, R.D. Palmiter and R.L. Brinster, 1988b. Insertion of growth hormone genes into pig embryos. Proc. Internat. Symp. on Biotech. in Growth Regulation (In Press). Cambridge.

Rivier J., J. Spiess, M. Thorner and W. Vale, 1982. Characterization of a growth hormone-releasing factor from a human pancreatic islet tumor. Nature 300:276.

Schanbacher, B.D., 1986. Growth hormone releasing factor (GRF): Physiological and immunological studies. In: P.J. Buttery, D.B. Lindsay and N.B. Haynes (Ed.): Control and manipulation of animal growth. Butterworths, London. p. 259.

Schelling, G.T. and F.M. Byers, 1988. Immunization of beef cattle against somatostatin. In: (National Research Council) Designing Foods: Animal Product Options in the Marketplace. National Academy Press, Washington, D.C.

Schoenle, E., J. Zapf C. Hauri, T. Steiner and E.R. Froesch, 1985. Comparison of in vivo effects of insulin-like growth factors 1 and II and of growth hormone in hypophysectomized rats. Acta Endocrinol. 108:167.

Schoenle, E., J. Zapf, R.E. Humbel and E.R. Froesch, 1982. Insulin-like growth factor 1 stimulates growth in hypophysectomized rats. Nature 296:252.

Skottner, A., R.G. Clark, I.C.A.F. Robinson and L. Fryklund, 1987. Recombinant human insulin-like growth factor: testing the somatomedin hypothesis in hypophysectomized rats. J. Endocrinol. 112:123.

Thorner, M.O., J. Reschke, J. Chitwood, A.D. Rogol, R. Furlanetto, J. Rivier, W. Vale and R.M. Blizzard, 1985. Acceleration of growth in two children treated with human growth hormone-releasing factor. New Eng. J. Med. 312:4.

Vize, P.D., A.E. Michalska, R. Ashman, B. Lloyd, B.A. Stone, P. Quinn, J.R.E. Wells and R.F. Seamark, 1988. Introduction to a porcine growth hormone fusion gene into transgenic pigs promotes growth. J. Cell Sci. 90:295.

Wagner, T.E. and W. Jochle, 1986. Recombinant gene transfer in animals: The potential for improving growth in livestock. In: P.J. Buttery, D.B.Lindsay and N.B. Haynes (Eds.): Control and manipulation of animal growth. Butterworths, London. p. 293.

Walton, P.E., T.D. Etherton and C.S. Chung, 1987 a. Exogenous pituitary and recombinant growth hormones induce insulin and insulin-like growth factor 1 resistance in pig adipose tissue. Dom. Anim. Endocrinol. 4:183.

Walton, P.E., R. Gopinath, B.D. Bureigh and T.D. Etherton, 1987 b. An acid-stable subunit of porcine serum IGF binding protein specifically blocks biological action of IGF-I on adipose tissue. J. Anim. Sci. 65(Suppl. 1):274 (Abstr.).

Wang, P.Y. and E. Kothe, 1988. Biocompatible implants for continuous delivery of growth hormones. J. Anim. Sci. (Suppl. 1):258 (Abstr.).

Weekes, T.E.C., 1983. The hormonal control of fat metabolism in animals. Proc. Nutr. Soc. 42:129.

Wieghart, M., J. Hoover, S.H. Choe, M.M. McCrane, F.M. Rottman, R.W. Hanson and T.E. Wagner, 1988. Genetic engineering of livestock -- transgenic pigs containing a chimeric bovine growth hormone (PEPCK / bGH) gene. J. Anim. Sci. 66 (Suppl. 1):266 (Abstr.).

Zapf J. and E.R. Froesch, 1986. Insulin-like growth factors/somatomedins: structure, secretion, biological actions and physiological role. Horm. Res. 24:121.

Zapf, J., E. Schoenle and E.R. Froesch, 1985. In vivo effects of the insulin-like growth factors (IGFs) in the hypophysectomized rat: comparison with human growth hormone and the possible role of the specific IGF carrier proteins. In: D. Evered, J. Nugent, J. Whelan (Ed.): Growth factors in biology and medicine. CIBA Foundation Symp. 116. John Wiley and Sons, London. p.169.

REGULATORY AND PUBLIC ACCEPTANCE OF BIOTECHNOLOGY FOR CONTROL OF GROWTH AND PRODUCT QUALITY IN SWINE

P. van der Wal
Wageningen Agricultural University, Wageningen, Netherlands.

Summary

Control of growth and product quality in swine can be achieved via the Somatotropin axis by administering its constituents, by affecting these through immunization and by inserting the related gene constructs in the genome of the animal.

The legal regulations for these three technologies differ according to type of technology and regulatory region. Yet they exert a comparable impact on efficacy and safety aspects by the same mode of action.

Harmonization of the requirements for approving these technologies is essential for serving effectively the purpose of guarding the safety of consumers, animals and environment and for creating well defined objectives for research and development.

The unprecedented challenge in animal and food sciences requires international cooperation in research. Such joining of efforts allows for coping adequately with generic issues in safety and efficacy of those technologies. The issues do not differ for regions and they require research capacity and specific expertise which is limited anywhere.

International tuning of expertise in these fields will contribute to international regulatory harmonization, the key to preventing disruptive disputes in international trade.

The somatotropin related technologies have for core issues in regulation a combination of effects in common.

For efficacy the impact on production efficiency and product quality, resulting from more protein accretion and less fat deposition, is characteristic.

For product safety the proteinic nature of the constituents of the somatotropin axis, which results in easy degradability in intestine and environment, offers good perspectives.

For public acceptance of these technologies adequate well balanced information about their potential contributions to cost and quality of foods and to safety of consumer, animal and environment is crucial.

There is no substitute for a strong and well staffed regulatory system in creating a solid base for consumer acceptance. Credibility of the system depends on optimizing guidelines and procedures and on ensuring compliance with regulatory decisions.

Keywords: growth control, biotechnology, somatotropin, acceptance, regulations.

Introduction

A variety of new biotechnologies for control of growth and product quality in animal production is at present in the pipeline. They already form increasingly effective tools for improving efficiency and product quality.

In view of the rapidly widening perspectives one can envisage a future where these technologies are indispensable tools for meeting the prime objectives of food production: adequate availability at affordable prices of food of good quality for the world population.

A manageable framework of guidelines for developing and implementing these technologies effectively and safely is therefore a matter of high priority.

The tap at the end of the pipeline with new technologies, to be passed for their introduction into the production system is virtually controlled by two mechanisms: regulatory approval and public acceptance of the technologies and the products derived therefrom (Figure 1).
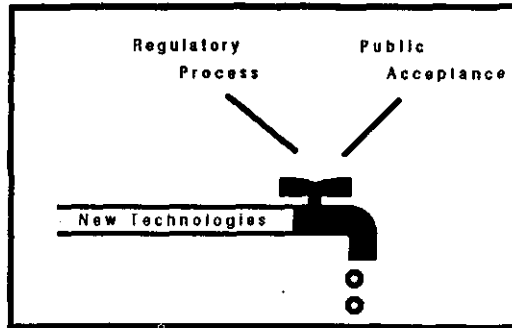
Figure 1. Controlling the introduction of new technologies.

Regulatory systems are operational in the highly industrialized countries for systematic evaluation of innovations in the production system on the basis of detailed requirements for efficacy and safety. Conclusions about regulatory acceptability of technologies reached here are often adopted or taken as guidelines by the rest of the world.

Public acceptance of the technologies and of the resulting food products follows a less well defined course but is obviously of decisive relevance for the successful implementation of new technologies.

Discrepancies in conclusions on acceptability of innovative technologies between the official regulatory agencies and the general public may present a problem. The prevention of a credibility gap should be feasible when recognizing that a sustainable production leading to an adequate supply of safe animal products forms a common goal.

The technical complexity of the criteria for evaluating technologies and end products for their safety and efficacy contributes to the confusion in discussions about their acceptability.

For closing the credibility gap it seems attractive to look for alternative, simplified and widely understood selection criteria as: natural, biological or long established.

Such selection criteria however have proved not to be effective. In the animal production system for instance one is well aware of the carcinogenic potential of biological naturals like aflatoxins on the one hand and the safe and benificial use of widespread synthetic chemicals like the amino acid methionine on the other hand.

Adherence to already well known technologies is sometimes seen as another realistic option for risk prevention. It would at present probably indeed not interfere with an adequate and affordable food supply for the affluent in the industrialized countries. However, to improve the perspectives for getting beyond that achievement, now and in the future, a sharpening and renewing of the technological tools for animal food production seems to be advisable, if not a must. Furthermore old production systems do not necessarily imply product safety either. Contaminations, for instance with pathogenic organisms or environment pollutants, can be more difficult to prevent as under advanced management and housing conditions.

While there seems to be then no simple substitute for a regulatory system based upon detailed, objective, scientific criteria for evaluating biotechnologies in animal production, it is essential that

the system is designed and operated in a credible way in the eyes of the general public, intended to consume the food.

This paper will deal with the regulatory systems, and the way they may effectively face the challenge of biotechnology for control of growth and product quality in animal production. Options for preventing a credibility gap between the system and the general public are considered. The systems in the EC and the USA, which at present are already being applied to the technologies of relevance, are primarily taken into account. To a lesser extent those in Japan and P. R. China are mentioned.

Objectives in food production, the core of regulatory requirements

The objectives in animal food production

In terms of efficiency and safety the animal food production system is facing increasingly sharp and detailed requirements. These requirements find their reflection in the regulatory systems for approval of technological innovations in the production system.

Meeting the demand for animals products, adequate in quantity and quality and available for affordable prices, requires efficiency in production. Increase in demand resulting from higher standards of living of an ever increasing world population lends priority to the development of efficient technologies which make optimum use of available resources.

Advancement of science and better standards of living have led to increasing emphasis on the safety aspects in animal production. Product safety for consumers has been a core issue for a long time. Safety for target animals and environment has recieved increased attention in the last decade.

The above mentioned objectives can be well measured by objective scientific criteria and are reflected in the regulatory requirements as summarized in Figure 2.


```
Efficacy
    Performance (availability
        and  costprice of products)
    Product quality (nutritional  and
        organoleptical   characteristics

Safety
    Human consumer
    Target  animal species
    Environment
    (Production system)
```
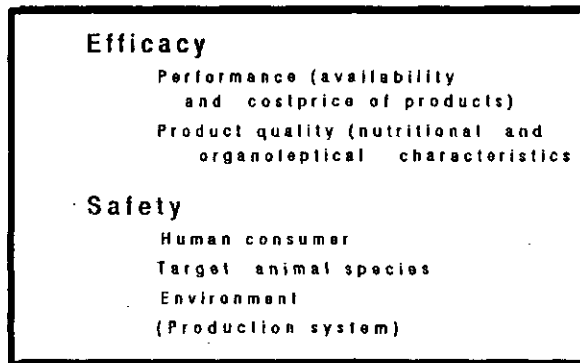
Figure 2. Objectives in animal food production reflected in regulatory requirements.

This is not yet the case for the socio economic impact of new technologies. The issue is hotly debated because of the difficulty in analyzing and measuring it objectively in a meaningful way. The criteria in this field seem to depend strongly on political preferences.

Regulatory systems serving a dual purpose

In animal production the regulatory system exerts its influence in two ways by:

– *Assuring efficacy and safety* for consumer, target animal and environment, leading to public confidence that in food production only useful technologies without risks are applied.

37

Meeting this objective in a credible way is essential for acceptance of new technologies and the derived products in domestic and export markets.

— *Setting targets for research and development in animal food production* for industry by defining criteria for approval of innovations for use. When these targets are considered by industry as realistic to reach, they will stimulate and guide research and development. Consistency in regulatory requirements over longer periods and objectivity of criteria allow for long term research planning. Advances in science can be translated into technology contributing to efficiency and quality in production.

When consumers feel uncertain that the first objective is met, a reluctance is seen in buying food of animal origin.

When in industry doubt predominates that regulatory requirements can be met, spending for research and development is hard to justify. Research efforts may then be suspended accordingly. A remote and possibly moving target is not readily aimed at.

A decrease in innovative research will slow down the improvements in production efficiency which have been achieved in the last decades. Such a decrease would interfere with future potentials in meeting demand and when not universally applied, have an impact on competitiveness on world markets.

Such a setback cannot easily be redressed. Building up research capacity and expertise in fields of high technology is both time consuming and costly.

Shaping of regulations an ongoing process; the challenge of biotechnology.

The gradual shift in emphasis on the objectives in food production as well as developments in science and technology have had a strong impact on regulatory requirements in the recent past. The fast developments in biotechnology form an unprecedented challenge for the regulatory system in the near future.

On the one hand the emerging potentials for improving efficiency and product quality in animal production make the definition of requirements a matter of urgency for creating a realistic and consistent framework for the necessary long term research and development efforts in the biotechnological and animal industry.

On the other hand the degree of novelty may interfere with public acceptance if the regulatory proces is not going to be handled in a way deserving and gaining credibility.

The regulatory systems

Regulations applicable; differences according to technology and country

The Somatotropin axis (Figure 3) for the physiological control of growth consists of Somatotropin itself, Growth hormone Releasing Factor or GRF (promoting its release), Somatostatin (inhibiting its release) and Somatomedin C or IGF-1 (mediating its effect).

Three categories of biotechnologies may be used for controlling growth and product quality of animals by affecting the Somatotropin axis. Figure 3 shows in which cases (+) research has demonstrated the feasibility of controlling the elements of this axis by their injection as such, by inserting the corresponding genes in the genome of the animals, or by means of immunological techniques.

The three types of biotechnology are at present subject to different sets of regulations and managed by different regulatory authorities.

When *administered by injection* to food producing animals, Somatotropin, GRF, and IGF-1 are regulated as Animal (production) Drugs in the USA and as Veterinary Medicinal Products in the EC. Established guidelines for evaluating their efficacy and safety have been applied for many years in

this field. Judging from the massive scientific evidence published on the impact of Somatotropin administration by injection, (Boyd, 1988; Fowler and Kanis, 1988; Fung and Qi, 1988; Steele 1988) this technology is a regulatory item of relevance for the immediate future.

	G . R . F .	Somato statin	Somato- tropin	Somato- medin
Genome Modifi- cation	+		+	+
Immuni- sation		+	+	
Admini- stration	+		+	+

Figure 3. Biotechnologies for control of growth.

In the USA the Center for Veterinary Medicin (CVM) of the Food and Drug Administration (FDA) of the Department for Health and Human Services is responsible for the implementation of the regulations. The Center provides for the evaluation of safety and efficacy of the drugs guidelines, based on the Federal Food, Drug, and Cosmetic Act (USA, 1906) and the pertinent regulations implementing the statutory provisions (USA, 1987). Sponsors may rely upon these guidelines for general safety evaluation, efficacy studies, and safety for target animals, with the assurance that, they describe procedures acceptable to FDA. The guidelines are detailed and are updated when necessary.

In the EC the Commission for Veterinary Medicinal Products (CVMP) of the Directorate-General III for Internal Market and Industrial Affairs is responsible for the regulation of animal production drugs, referred to here as "Veterinary Medicinal Products". The regulations, defined in Council Directives 81/851/EEC and 81/852/EEC (1981) have been adopted for high-technology products after procedural adaptations in Council Directive 87/22/EEC (1987), aimed at a further approximation of the laws in the member states.

For a further completion of the common market an updating of the directives is at present prepared to establish a fully centralized Community procedure.

In the P. R. of China the principles adhered to for the regulation of veterinary drugs seem somewhat less detailed in their definition (P.R.China, 1985). From the guidelines it can be concluded that largely the same criteria are used as in the EC and the USA. Data on safety and results of clinical trials have to be submitted to the Ministry of Agriculture.

In Japan drugs for animal use are regulated under the jurisdiction of the Ministry of Agriculture. For safety evaluation detailed guidelines for testing are provided by the Ministry of Health and Wellfare (Japan, 1984).

An *increase in the level or a potentiation of Somatotropin* can also be achieved in various ways by *immunological techniques*. Active immunization against Somatostatin has been shown to increase Somatotropin (Spencer et al., 1983). Enhanced Somatotropin activity by administering monoclonal antibodies has been demonstrated by Aston et al. (1986) and by polyclonal antibodies by Pell (1988).

Vaccination for control of growth and product quality has so far not been a regulatory item. It can hardly be covered satisfactorily by the regulations for vaccines for disease control.

In the USA these regulations fall under the Animal and Plant Health Inspection Service (APHIS) of the United States Department of Agriculture (USDA). However, if production improvements by other means then diagnosis, prevention or teatment of diseases are aimed at, a joint approach with the C.V.M. of FDA is foreseen. In the EC it has recently been proposed to apply for vaccines the same regulations as for the other "Veterinary Medicinal Products".

When an *increase* in the *Somatotropin* level of swine is obtained *by the insertion of ST gene constructs* in the genome of these animals, the effect on the metabolism, reflected in increased meatiness and less fat, is comparable to that in swine to which recombinant Porcine Somatotropin (rPST) has been administered by injection (Pursel, 1987; Wieghart et al., 1988).

The regulations for genome modifications and their application are still under development in the USA as well as in the EC. The definition and implementation of these regulations does not at present fall under the same authorities as the earlier mentioned animal production drugs. APHIS of the USDA is actively preparing the regulatory policy in the USA and the Directorate General VI for Agriculture has taken responsibility for the regulation of this technology in the EC.

At present in both theatres the patent situation, the ethical aspects, and the proper regulation of research with transgenic animals draw still more attention than the requirements to be met for safety and efficacy under production conditions.

We may conclude that the technologies under discussion, designed for the same production system, are under the present regimes going to be evaluated and eventually applied under different regulatory regimes. Yet, from the commonality in mode of action and from the available scientific evidence it can be expected that the impact on performance, product quality and product safety of all three technologies is to a large extent comparable.

Need for commonality in criteria for technologies of different origin

Harmonization and strong coordination, if not unification in the further definition and implementation of regulations in the above mentioned intertwined technologies seem necessary, both for equality in law and for an optimum use of the highly specialized expertise in the regulatory field. The alternative could well lead to disastrous confusion among producers and consumers.

Commonality in regulation of biotechnology and traditional technology is an explicit objective in the "Coordinated Framework for Regulation of Biotechnology" (USA; 1986). The Food and Drug Administration (FDA), the Environmental Protection Agency (EPA), the U.S Department of Agriculture (USDA), the Occupational Safety and Health Administration (OSHA), and the National Institute of Health (NIH) contributed for their respective fields. It is stated that: "The manufacture of food, the development of new drugs, medical devices, biologics for humans and animals and pesticides will be reviewed by FDA, USDA and EPA in essentially the same manner for safety and efficacy as products obtained by other techniques".

"Jurisdiction over the varied products is determined by their use, as has been the case for traditional products". This seems to ask for further coordination between the agencies for the closely related technologies for growth control as discussed above.

For "Veterinary Medicinal Products" the EC is heading for revised regulations which do no longer differentiate between biotechnological and traditional production in either procedure and criteria. A further harmonization will here be achieved when animal vaccines will be regulated, as intended, under the same directives.

Need for international harmonization of regulatory requirements

Although the various regulatory systems may cover largely the same safety and efficacy aspects, the remaining differences in criteria, and procedures allow for substantial discrepancies in the

admission of new drugs and technologies. The point is illustrated well enough by the case of the anabolic steroids, approved for selective use in the USA and banned in the EC.

The *advantages of better regulatory harmonization* are obvious enough to make its realization mandatory:

— *Frictions in the international trade* resulting from regulatory disagreements would be avoided. The present clash between the EC and the USA may easily lead to economic losses and further political irritations. They might be turned into a blessing when leading to the awareness that effective steps have to be taken for their elimination and for the prevention of their future recurrence.

— *Closer cooperation in research and development* would be facilitated. The development of effective and safe biotechnologies for animal production requires an unprecedented research effort in the related sciences. Effective, coordinated use of expertise and research capacity in the fields of relevance is nearly a must. Worldwide this research capacity is the bottle neck in developing and evaluating biotechnology. Defining jointly basic issues underlying the common regulatory objectives for efficacy and safety form an effective step towards a *common approach of generic potentials and problems in animal biotechnology.* Such issues, being largely precompetitive, lend themselves for involvement of governmental and industrial research groups.

International harmonization at the regional level is making progress at the EC, where a steady approximation of national laws of the member states is a key element in establishing the common market. The Community research programs contribute to this approximation. The enlargement of the economic and regulatory framework in Europe may allow for further intensification of research in animal biotechnology over its present level.

In North America commonality in regulations is aimed at, between the USA and Canada.

In Figure 4 research papers of the last three years have been quantified for the three main regions where experimental work on biotechnology for growth control has been performed with farm animals. (Database: Commonwealth Agricultural Bureau - CAB). The figure illustrates that research capacity and expertise are available and actively engaged in all three regions. Knowhow is however predominantly concentrated in North America. This is the case to an even larger extent than shown in Figure 4 because the production of the active ingredients and of the genetic constructs for the research in Europe and along the Western Pacific Rim is nearly exclusively located in the USA.
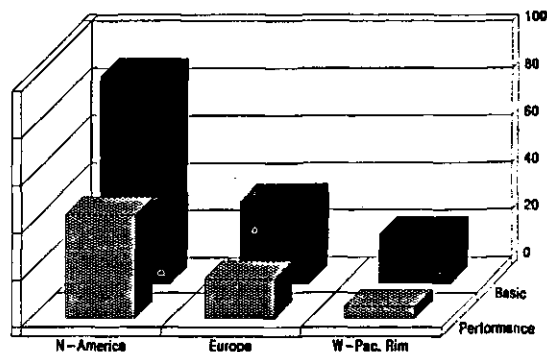
Figure 4. Research in biotechnology for growth control of farm animals. Technical papers 1986-1988

Effective contributions to worldwide international harmonization are being made within the framework of international organizations. Their successful examples encourage further steps in this direction.

The Organization for Economic Cooperation and Development (OECD) has contributed to the standardization of methodologies and to regulations for Good Laboratory Practice.

The Committee of the Codex Alimentarius for Residues of Veterinary Drugs in Foods (CCVRF) is active in defining internationally acceptable tolerance levels for residues of animal drugs.

Perspectives and constraints in regulatory acceptability

The technologies for control of growth and product quality via the Somatotropin axis (Figure 3) form a new regulatory ballpark in more than one way. The fact that the same impact is obtainable via three different technologies is without precedent. The major impact on product quality characteristics and the proteinic nature of the active substance were not met in earlier rounds of animal production drugs.

The regulations for evaluating efficacy and safety of Animal Production Drugs in the USA and the comparable category of Veterinary Medicinal Products in the EC have now been operational for many years. They offer a foothold for analyzing some perspectives for the related technologies for growth control as well. The regulations under development for these technologies will have to adopt largely the same approach anyhow.

Efficacy

The efficacy of somatotropin by injection on performance has been demonstrated already worldwide (Fowler and Kanis, 1988; Fung and Qi, 1988 and Steele et al., 1988). Comparable improvements in feed conversion efficiency in particular have not been shown before by growth promoting drugs for swine.

The strong improvement in product quality by the reduction of carcass fat in favour of lean tissue has not been achieved before with animal production drugs either. It can put especially fat breeds in a higher class of slaughter quality. In order to be able to evaluate the resulting product quality claims adequately, the Center for Veterinary Medicine of the FDA in the USA is updating its guidelines for testing efficacy. At FDA's request the American Society of Animal Science (ASAS) has established a committee to provide expertise in redefining the requirements for demonstrating improvements in product quality.

Product safety

The proteinic nature of the active elements of the Somatotropin axis puts them in a potentially safer category as earlier animal production drugs with regard to risk of residues. Even if an increase in residue levels might occur in consumable products, proteins are degradable in the intestinal tract "of consumers" and these large molecules are normally not absorbed from the intestinal tract anyway (Apostolou, 1988).

Firm data have to further substantiate the issue regarding the occurrence and safety of possible residues of active substances in edible products.

The considerable reduction in fat creates perspectives for improving nutritional safety by reducing the main threat for human safety attributed to animal products, namely excessive fat consumption. The earlier mentioned redrafting of the related regulatory requirements may assist in measuring the extent and the relevance of this effect of Somatotropin based technologies as well as determining its possible impact on other potentially positive or negative factors.

Target animal safety

Somatotropin injections so far have not shown any appreciable effects that can not be coped with in the existing regulatory requirements. The impact of somatotropin administration on a variety of physiological mechanisms (Boyd and Bauman, 1988) seems to be reasonably well balanced.

The potential repercussions of genetic modifications on the animals' physiology (Pursel, 1987 and 1988; Wieghart et al., 1988) have been shown to go beyond those obtained with the other two technologies. Scientific exploration of animal safety aspects of genome modifications requires adequate and early attention. Control of the expression of the inserted genes (Mc Crane et al., 1988) is considered by Pursel (1987) as a potentially effective tool in controlling negative effects on animals.

The results obtained with genome modifications so far raise the question as to whether in particular growth rate of domesticated animals will be changed by a quantum leap over their present ceiling by this technology. The genome has already been optimised for this parameter by selection during many generations. The observation that insertion of ST genes in swine affected leanness and feed conversion ratio rather than growth rate is here of interest.

By contrast, in mice strains, not selected for weight gain, bodyweight nearly doubled as a result of insertion of an MThGH construct (Nieuwhof and Kanis, 1988). A comparable increase in body weight of mice has been obtained by selection over several generations by Bakker (1974).

Environmental impact

The degradability of the active substances involved in Somatotropin related technologies seems to eliminate virtually the risk for environmental pollution with residues.

The potentially positive impact of its use on the environment deserves attention. The decreased excretion of pollutants as a result of the improved utilization of nutrients may prove to be of particular significance under present production conditions in some regions (Van Weerden and Verstegen, 1988).

Social and economic impact

Results reviewed by Fowler and Kanis (1988), Fung and Qi (1988) and Steele et al. (1988) show that the technologies under discussion will have a strong impact on production efficiency and product quality of swine.

The introduction of these technologies will therefore be of obvious significance for the competitiveness in pig production, both domestically and in export markets (Steele et al., 1988). As a consequence the survivability on these markets of farmers and countries which will abstain from the introduction of these technologies is going to be affected accordingly. This phenomenon forms a familiar pattern in animal industry when new technologies are emerging.

It seems to be a matter of political opinion rather than a regulatory issue, whether one should control competitiveness, domestically and internationally, by selectively deciding on the introduction of technological innovations on the base of their potential effectiveness. This viewpoint is obviously followed by the EC. It is proposed in the draft for revised regulatory directives to have in the EC the social and economic impact weighed and decided upon separately from the normal regulatory procedure.

The issue is of high and basic relevance because adoption of the proposal would introduce a double track system for the approval of new technologies. Objective and consistent paramaters for measuring social and economic impact will be difficult to define.

43

Public acceptance

Role of adequate information in public perception and acceptance

Public perception of biotechnology comprising only production tools with a high degree of novelty, seems to be gradually overcome by increasing awareness that such technology has contributed for ages in many forms to the production of food and more recently to the manufacture of pharmaceuticals.

Yet there is sometimes still a touch of magic in biotechnology. The eagerness to illustrate the advancement of science by claims which made the public unjustifiably believe that quantum leaps in animal production are around the corner evoked more emotions than necessary.

The decision to evaluate in the USA and the EC biotechnologically derived products essentially by the same criteria as traditional products contribute to placing biotechnology in the right perspective.

Recent reviews about public acceptance in the USA and Europe (Cantley, 1987; Van den Broek, 1988) lead to the conclusion that an open information and communication are crucial for acceptance. The report of the Office of Technology Assessment (1987) found that in the USA acceptance improves with increasing knowledge.

Public trust in University scientists proved to be particularly strong when it comes to evaluation of risks in biotechnology. It seems to imply a specific responsibility for the Universities with regard to risk assessment and acceptability of technological innovations.

Need for strengthening credibility of the regulatory system

Cantley (1987) points at the vulnerability of a society in developing innovative technologies effectively when the credibility of the regulatory system is low. The public, when unable to evaluate the risk, evaluates the regulator. When not satisfied, ways will be found for rejecting the regulatory decisions.

The need for strengthening the credibility of the regulatory system is being increasingly recognized as the key to public acceptance.

The regulation authority is the only institution where enough highly qualified expertise can be made operational for defining and handling effectively the rules for admission of innovative technology. Objectivity, consistency in policy, and therefore predictability in maintaining the rules seem essential for building public confidence and hence acceptance of regulatory decisions.

A further strengthening of the system will be allowed for in the EC as a result of the proposed centralization of the regulatory procedure. It seems to lead unavoidably to the creation of a central body with expertise which is already operational at the comparable Center for Veterinary Medicine of the FDA in the USA.

Making the regulatory system better known

In discussions about public acceptance, it is frequently overlooked that too often the general public is not aware of the unique power given to the regulatory authority in controlling the admission of new technologies and thus safeguarding public interests.

Even those who take widely publicized views in regulatory affairs tend to overlook that in principle the mechanism has been created to cope with problems regarding acceptability of new technologies. Regulatory agencies might be able to find ways to create and maintain more public awareness of their specific responsibilities and capabilities. The FDA in the USA has the benefit of having been operational for a long time and has gained public prestige in the proces.

Confusion from bypassing the regulatory system in making decisions

Participation in making decisions about the introduction of new technologies in animal production from outside the designated regulatory framework (Figure 5) is sometimes considered as necessary.

In the case of anabolic steroids, and more recently in the case of Bovine Somatotropin the European Parliament and the Council of ministers of the EC adopted resolutions and made decisions which affect the regulatory situation. The US Congress interfered in a technical regulatory issue by adopting the Delaney clause on carcinogens. In most of these cases public opinion exerted pressure on these institutions.

Conclusions have been reached and implemented here on specific items before the necessary facts had enabled the regulatory bodies to reach a decision. Control in this form is confusing for consumers and producers by the unpredictability of ad hoc applied criteria. The somewhat Babylonic situation is likely to interfere with confidence in the regulatory systems and with acceptance of its conclusions.
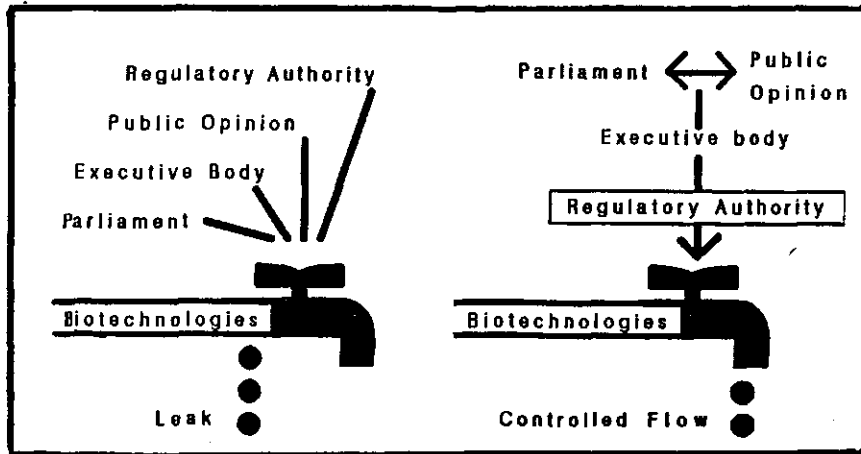
Figure 5. Options for controlling introductions of biotechnology.

If lack of acceptance of regulatory conclusions is spreading to the animal production system it may contribute to the leakage of technologies from the pipeline, thus reaching the food production system without passing through the officially controlled tap. A subsequent lack of consumer acceptance of food products, domestically or on export markets would not seem to be merely theoretical.

Increasing credibility by updating regulatory guidelines and procedures

The ad hoc interventions in the regulatory process signify a lack of consensus on the regulatory requirements that have to be met for accepting technological innovations for introduction.

Much might be gained in credibility and hence in acceptance of regulatory conclusions when such a consensus on requirements is reached by the usual democratic interaction between public opinion, parliament and executive body and is reflected in the regulations.

It can provide for a regulatory framework within which the regulatory authority can act indepently on objective and consistent guidelines without interference (Figure 5).

It does not in itself seem to be very far fetched, since it would merely reflect the practice already followed in the not unrelated field of civil procedures in law. That practice gained credibility for a long time because of adhering to well defined laws and their independent implementation.

Much of the discussion in this field will focus on the degree to which requirements on social and economic impact of new technologies shall and can be incorporated in the regulations, an item covered already earlier in this paper. While in the USA the item tends to be covered within the

context of the environmental impact, in the EC the discussion is initiated by provisions in new draft Directives.

Making key facts available to the public on generic issues

In meeting the demand for adequate public information the regulatory system could play a useful role.

There is a strict limit to the information that can be made available from dossiers for approving drugs for use. Proprietary data on specific technological achievements are gathered at a high cost and are of decisive relevance to the competitive position.

It is, however, information on the impact of a category of drugs or technologies, the generic effects, rather than the impact of a specific proprietary achievement which is of relevance for public acceptance. For instance, impact of somatotropin on their level in consumable products, impact of these substances on longevity and reproductive performance of breeding stock, and impact on the endocrine balance are largely inherent to the category of compounds. The availability of such information to the public might be promoted by regulatory institutions in conjunction with existing national or international cooperative research programs.

Before approving a new product or technology for use, a public hearing would serve the purpose of providing a possibility for bringing up questions at a place of relevance. Such questions can now only be addressed via informal channels not likely to produce expert answers, if any.

Compliance with decisions crucial to system credibility and acceptance

Bypassing the control tap of the regulatory authorities by illicit applications of biotechnological achievements is an obvious undermining of the credibility of the system. It interferes with public confidence in the safety of animal products. The enforcement of regulatory decisions is beyond the scope of this paper but it needs to be characterized here as an essential element in public acceptance of biotechnologically derived products.

Law enforcement is difficult to bring about if the law does not have firm roots in the sense of justice of those who have to comply. When doubts are rising about optimum compliance with regulatory decisions in the production system this aspect deserves more attention than it usually seems to get.

Safety related issues in animal production, as encountered in the EC with clenbuterol and anabolic steroids and in the USA with sulfa and aflatoxins can only be solved when industry and farmers are deeply aware that compliance with regulations is in their own best interest.

This awareness is stimulated when confidence is created that effective innovations are made available to the system when their efficacy and safety allow for it. Prohibition was not an effective instrument in preventing alcohol abuse.

Conclusions

A strong and credible regulatory system has a unique potential in serving both the development of new technologies for food production and public acceptance of these technologies.

The credibility of the system in adequately handling both objectives depends greatly on its application of objective scientific criteria in a consistent manner. Credibility can be ensured and strengthened further by:

- Guidelines and procedures which reflect the state of the art in technology and are accepted by parliamentary and executive bodies.
- International harmonization of guidelines and evaluation criteria.
- Qualified scientific staff for covering the various regulatory issues.
- Independent decision procedures with the right for appeal.

- Contribution to public information on generic safety and efficacy issues by initiating hearings and by stimulating cooperative research efforts in these fields.
- Ensuring compliance with regulatory decisions by effective enforcement and by contributing to the awareness of the participants in food production that law abidance is in their best interest.

References

Apostolou, A., 1988. Somatotropin safety- A short regulatory overview. J. Am. Vet. Med. Ass. 192:1698-1700.

Aston, R., A.T. Holder, M.A. Preece, and J. Ivanyi, 1986. Potentiation of the somatogenic and lactogenic activity of human growth hormone receptor using monoclonal antibody probes. J, Endocr. 110:381-388.

Bakker, H., 1974. Effect of selection for relative growth rate and body weight of mice on rate, composition and efficiency of growth. Med. Landbouwhogeschool Wageningen. 74-8.

Boyd, R.D. and D.E. Bauman, 1988. Mechanisms of action for somatotropin in growth. In: N.D.R. Campion, G.J.H. Hausman, and R.J. Martin: Animal growth regulation. Plenum Press N.Y.

Cantley, M.F., 1987. Democracy and Biotechnoloy. Swiss Biotech 5: 5-15 E.C. Council Directive 81/851/EEC on the approximation of the laws of the Member States relating to veterinary medicinal products. 1981. Off.J.E.C. 24:L 317.

E.C. Council Directive 81/852/EEC on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of veterinary medicinal products. 1981. Off. J. J.E.C. 24:L 317.

E.C., 1987. Council Directive 87/22/EEC on the approximation of national measures relating to the placing on the Market of high-technology medicinal products, particularly those derived from biotechnology. Off. J.E.C. 30:L 15 Japan, 1984. Ministry of Health and Wellfare. Toxicity test guidelines.

Fowler, V.R. and E. Kanis, 1988. Use of recombinant somatotropin (rPST) in Europe: research experience and perspectives. This symposium.

Fung, F.K. and S.Z. Qi, 1988. The prospects of using porcine somatotropin in chinese pigs. This Symposium,

McCrane, M.M., J. de Vente, J. Yun, J. Bloom, E. Park, A. Wynshaw-Boris, Th. Wagner, F.M. Rothman and R.W. Hanson, 1988. Tissue specific expression and dietary regulation of a chimeric Phosohoenolpyruvate Carboxykinase/ Bovine growth hormone gene in transgenic mice. J. Biol. Chem. 263:11443-11451.

Nieuwhof, G.J. and E. Kanis, 1988. Growth in transgenic (somatotropin) mice. In: S. Korver, H.A.M. van der Steen, J.A.M. van Arendonk, H. Bakker, E.W. Brascamp and J. Dommerholt (compilers). Proceedings of advances in animal breeding. Pudoc, Wageningen.

Pell, J.M., C. Elcock, A. Walsh, T. Trigg, and R. Aston, 1988. Potentiation of growth hormone activity using a polyclonal antibody of restricted specificity. Intern. symp. on biotechnology in growth regulation. Cambridge.

Pursel, V., 1987. Potential for inserting the Somatotropin gene into the swine DNA. Pork Industry Conf. Univ.of Ill. 12-18.

Pursel, V., R.G. Campbell, K.F. Miller, R.R. Beheringer, R.D. Palmiter and R.L. Brinster, 1988. Growth potential of transgenic pigs expressing a bovine growth hormone gene. J.An.Sc. 66: 267.

P.R.China, 1985. Ministry of Agriculture. Procedures for retrial and registration of Veterinary drugs carried out by foreign companies in China.

Spencer, G.S.G., G.J. Garssen and I.C. Hart, 1983. A novel approach to growth promotion using auto-immunisation against somatostatin. Livestock Prod. Sc. 10, 25-37

Steele, N.C., R.G. Campbell, T.J. Caperna, J.P. McMurtry and M.B. Solomon, 1988. PST efficacy in North America : management variables and advantages. This symposium.

U.S.A. Congressional Office of Technology Assessment. 1987. New developments in biotechnology. Background paper 2: Public perception of biotechnology.

U.S.A. Act of Congress. 1938. The Federal Food, Drug, and Cosmetic Act. Section, as amended. Title 21 US Code 409, 512, and 706.

U.S.A. Department of Health and Human services. Food and Drug Administration. 1987. Sponsored Compounds in Food Producing Animals; Fed. Reg. 52:49572-49589.

U.S.A. Executive Office of the President, Office of Science and Technology Policy. 1986. Coordinated Framework for Regulation of Biotechnology. Fed. Reg. 51: 23302-23393.

Van den Broek, J.M., 1988. Public opinion on biotechnology: (un)known, (un)loved ? Biot. in Ned. 5:259-269.

Van Weerden, E.J. and M.W.A. Verstegen, 1988. Effect of PST on environmental N pollution. This Symposium.

Wieghart, L., J. Hoover, S.H. Choe, M.M. McCrane, F.M. Rottman, R.W. Hanson and T.E. Wagner, 1988. Genetic engineering of livestock - Transgenic pig containing a chimeric bovine growth hormone (PEPCK/bGH) gene. J.An.Sc. 66:266.

IMPLICATIONS FOR PRODUCTION SYSTEM

Impact on performance and grading

Implications for Breeders

Implications for Processing industry

PST EFFICACY IN NORTH AMERICA : MANAGEMENT VARIABLES AND ADVANTAGES

N.C. Steele, R.G. Campbell, T.J. Caperna, J.P. McMurtry and M.B. Solomon

U.S. Department of Agriculture, Agricultural Research Service, Beltsville Agricultural Research Center, Nonruminant Animal Nutrition Laboratory and Meat Science Research Laboratory, Beltsville, MD 20705 USA and Animal Research Institute, Werribee, Victoria 3030 Australia

Summary

Various technologies now available to alter livestock growth and composition, specifically exogenous treatment with species-specific growth hormone (GH), GH releasing factor and somatostatin autoimmunization, all operate at some level of the GH axis and as such alter production, secretion or metabolism of this hormone. Exogenous administration of porcine GH, or somatotropin (PST), has marked effects on the growth and development pattern of swine favoring lean tissue gain with minimal fat deposition. World-wide interest in the use of this technology is based on the presumption that this technology would be equally efficacious regardless of management conditions. European swine management conditions favor such factors as limit-feeding, marketing of intact male pigs, heterogeneous mixes of dietary protein sources, division of growth for light and heavy pig marketing and similar factors. Western production practices as evident in North America favor ad libitum feeding, use of gilts and castrate males, comparatively high intake of good quality protein, and exclusively a heavy pig market. In several recently completed experiments, different management variables affecting PST efficacy have been evaluated. Results indicate PST is a major physiological constraint on lean tissue growth both for young pigs and animals in the fattening stage of growth. Additionally, feed intake, specifically energy intake, can constrain the response to PST; however, PST will essentially negate sex effects such that female and castrate male pigs will respond to PST and display protein accretion rates comparable to the intact male. Results of current research indicate that PST technology is adaptable within current management systems, but swine management practices characteristic of North America are particularly suited for application. This implies that pork production for the purpose of export to the global marketplace will become much more competitive in that a means for greater uniformity in the production of lean pork of high quality is now available.

Keywords: swine, growth hormone, composition, management.

Introduction

Growth hormone (GH), somatotropin and ST are synonyms for a single- stranded, 191 amino acid residue, nonglycosylated, protein containing two intramolecular disulfide bridges which is secreted by the anterior pituitary gland in response to positive (GRF; growth hormone-releasing factor) and negative (STH; somatostatin) effector secretions from the hypothalamus. GH has long been associated with growth processes (Walker et al., 1950), but only with the recent advances in recombinant DNA technology have sufficient quantities become available for long-term animal experimentation and to attract industrial interest toward product development for livestock

51

application. In the United States, the livestock industry represents a $61 billion market (Agricultural Statistics, 1987) and, specifically, the $9.8 billion swine industry has been targeted as likely clientele for this technology. Due to productive efficiency currently constrained by physiological factors, the inherent tendency to synthesize and deposit excessive quantities of body fat and a very negative public image with respect to pork as a healthful meat product, the swine industry should benefit greatly from this technology. Several excellent references are cited (Machlin, 1972; Chung et al., 1985; Etherton et al., 1987; Etherton et al., 1986; Boyd et al., 1986) for background on the use of GH in swine. The purpose of this report is to describe the recent experiments with porcine GH (pGH) conducted at the Beltsville Agricultural Research Center. As designed, these projects did not represent efficacy tests of the technology, but were intended to provide data which might have global interest in swine production practices. Less pragmatically, we wish to quantify the absolute ceiling or limit for protein deposition by swine and pGH represents only a tool in pursuit of this goal.

Overview of Growth Biology

Growth of any species represents the accumulation of body weight due to hypertrophy of component tissues. Those tissues most critical for survival of a species have the highest priority for nutrient use and as such are supported even in marginal nutritional environments at the expense of tissues less critical for species survival. Sir John Hammond expressed this priority for nutrient use in a treatise describing the concept of nutrient partitioning (Hammond, 1952). Figure 1 paraphrases the Hammond nutrient partitioning concept for growth of individual tissues and physiological function. On the abscissa, a qualitative weighing of genetic and environmental determinants of tissue hypertrophy are proposed. According to this model the elevation of extracellular nutrients occurs with increased plane of nutrition and neural and bone tissues extract with high priority nutrients for maintenance and growth. Once differentiated, the hypertrophy of muscle and adipose tissue will occur in response to environmental factors, including nutrition, only to the degree permitted by genetic composition. Livestock production practices have focused on the maximum yield of lean tissue with modest accretion of body fat and within the specialty of animal nutrition one often assumes that genetic potential toward this end point is fully realized.
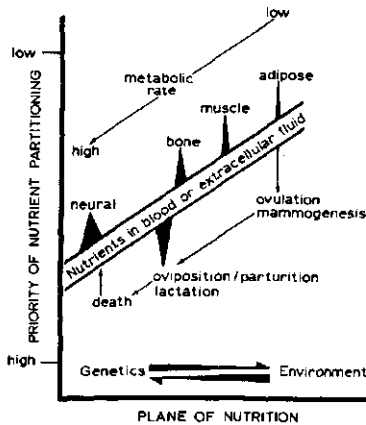

Figure 1. Hammond (1952) model of nutrient partitioning. Note that arrow boldness of a given tissue is indicative of the hierarchial need of the tissue for survival of the species and coincides with nutrient partitioning, or use, priority for maintenance and growth.

According to this model of nutrient partitioning the relative accretion of muscle and adipose tissues could be altered either by increasing the slope of the line or altering the position of adipose tissue priority relative to muscle growth. These possibilities can be classified as partitioning (i.e., slope change) or repartitioning (i.e., relative position of component tissue growth) strategies. Partitioning strategies rely on genetic tools (gene optimization, gene amplification and transgenic manipulations) to affect livestock performance.

Repartitioning strategies rely on pharmacological, site-specific, alterations of metabolism. Examples of the latter include beta adrenergic agonists, thyroid active compounds and steroid implants.

The genetic tool most recognized for the modification of livestock growth are the gene optimization procedures used by animal breeders. A classical example is the Beltsville selection experiment for or against subcutaneous fat thickness (Davey et al., 1969) which simultaneously effected both muscle tissue deposition and skeletal growth. Recently a strain of swine has been characterized with an apparent infinite capacity for protein growth compared to typical commercial strains (Campbell and Taverner 1985, 1988). In this genotype, appetite is the only factor limiting protein accretion. These examples emphasize that gene optimization techniques can markedly influence both adipose tissue and muscle protein priorities for nutrient use. Such techniques as practiced over many centuries of livestock domestication are characteristically very slow and costly, but highly effective and generally regarded as safe with respect to environmental concerns. Unfortunately, the lack of knowledge regarding specific genes involved in growth and development processes and the inability to manipulate such genes within large populations of animals prevents rapid progress to reduce fat and increase lean tissue deposition using gene optimization procedures.

Recent progress in foreign gene insertion and expression (Hammer et al., 1985) has led to the production of agriculturally important "transgenic" animals. The promise of this procedure is that not only the slope of the nutrient partitioning priority line, but also the absolute genetic ceiling for both muscle protein and fat accretion can be altered by the only method capable of truly altering genetic composition. However, elucidation of mechanisms involved in the control of gene expression and the subsequent impact on growth and development as well as the remarkable negative public image of this technique will require considerable research investment and a lengthy education of the consuming public to be realized.

Yet another technique available to alter nutrient partitioning priority would be to preferentially increase the efficiency of muscle protein deposition assuming that full genetic potential has been underestimated and constrained within normal physiological processes. In effect this strategy involves "gene amplification" and describes those efforts which manipulate rate and composition of growth by ST administration. With strategic application of species-specific ST to induce supra-physiological concentrations of primary growth stimulants, those genes normally involved with growth processes are activated more completely and over longer periods of time permitting a species to more fully express genetic potential for protein deposition. According to the Hammond model, pigs the size of steers, or steers the size of elephants, could not result from ST-induced gene amplification for protein deposition independent of proportionate increases in skeletal growth. However, pigs with feed efficiency comparable to broilers and dairy animals with 25% greater milk yields could enter the animal production system. This point is emphasized such that public concern regarding ST-induced growth alteration is not construed to be a violation of animal rights, specifically the genetic destiny of livestock.

An obvious example of naturally occurring gene amplification is the classic sex effect difference in rate and composition of gain comparing the intact male to the female pig (Campbell et al., 1985). Genetic composition does not differ greatly in this example, but expression of genetic potential for protein deposition is constrained in the female by the lack of androgen stimulation.

Porcine Somatotropin: Historical Information

Growth hormone has long been associated with long bone growth and nitrogen retention in laboratory animals (Li et al., 1948; Greenspan et al., 1949). Giles (1942) reported that injection of pigs with a pituitary-derived growth hormone preparation over a four month period increased the width of the epiphyseal growth plate of long bone, but otherwise was without biological consequence. The biological potency of the GH preparation and lack of sufficient experimental detail prevents discussion for the lack of growth promotion. Turman and Andrews (1955) reported that a porcine pituitary preparation increased the efficiency, but not rate, of body weight accretion in swine. Significant increases of body water and protein content with a reduction in body fat was reported. Again, the biopotency of the GH preparation was unknown, but the authors noted that of those animals treated at a high dose (6 mg/15 kg body weight daily), mortality rate was 100%. In these pioneering studies much of the same potential as apparent in contemporary experiments for GH to alter nutrient partitioning in swine was noted, but hormone purity confounded the design of experiments and interpretation of results.

More recently, the research by Machlin (1972) and the efforts by Pennsylvania State (Chung et al., 1985; Etherton et al., 1986; Etherton et al., 1987) and Cornell (Boyd et al., 1986) University investigators must be regarded as the basis for current interest in GH technology. Machlin found that treatment of growing pigs with a commercial preparation referenced to a rat tibia bioassay significantly improved rate and efficiency of body weight gain and the gain was generally of lean tissue mass and not lipid. In one experiment, GH treatment at levels of 220 and 1100 ug/kg body weight resulted in liver and kidney degeneration and a high mortality rate. Based on current information, doses used were far in excess for maximal biological benefit and reinforce that a dose-optimum does exist for pGH treatment.

With the resurgence of the National Pituitary Program in the early 1980's, Chung reported that daily administration of pGH (pituitary derived) at a dose level of 22 ug/kg body weight for a 30 day period improved rate of gain by 10%, efficiency of gain by 4%, increased muscle mass by 5% and did not influence adipose tissue mass. Blood plasma glucose and insulin concentrations were increased by pGH while blood urea nitrogen concentration was decreased. This study was significant in that anabolic actions of GH were apparent in young pigs over a relatively short period of hormone treatment without induction of animal health complications. Subsequently, the optimal dose was tested by animal bioassay using levels of pituitary GH ranging from 10 to 70 ug/kg body weight daily and various production and carcass characteristics as end point measurements. Rate and efficiency of gain improved over the doses tested and muscle mass continued to show fractional increase between a dose range of 35 and 70 ug/kg body weight.

Apparent in the Pennsylvania State University studies were the marked effects of pGH on nutrient partitioning in the pig and the potential for this technology to greatly alter swine production systems. However, of equal, if not greater, importance was the emergence of recombinant DNA technology permitting the mass production of species-specific rpGH to provide a commercial product with marketing potential in the pork industry. Etherton and co-workers (1986) were the first to report that rpGH, rpST, was indistinguishable from pituitary derived material in animal bioassay response. In a similarly designed dose response titration experiment Boyd and co-workers at Cornell University reported that pituitary derived pGH had optimal effects on most end point parameters at a dose of 90 to 100 ug/kg body weight daily. Therefore, in two independent studies the dose optimum of pGH, natural or recombinant, is approximately 70 to 120 ug/kg body weight daily.

A consistent effect of pGH treatment is the reduction of voluntary appetite which in itself confounds the quantitation of GH effects on carcass components from those effects attributable to feed restriction. In part, the greater improvement of feed efficiency compared to the effect on rate of gain would be anticipated considering the change in composition of gain (i.e., less fat and greater muscle protein and associated water). Several studies which have utilized either pituitary-derived (Wolfrom et al., 1986) or recombinant pGH (Kraft et al., 1986) found little if any benefit to growth

and composition in pigs; however, nutrient intake, in particular protein content and composition, was marginal. Boyd and co-workers (personnel communication) and recent efforts at Illinois (Easter, 1987) have revealed that protein intake can constrain realization of pGH benefit.

Porcine Somatotropin: Beltsville Studies

Within the discipline of nutrition one often loses the perspective that the mass and specific composition of the target tissue deposited defines the nutrient requirement of an animal. The diet with adjustments for obligatory losses associated with tissue deposition is merely the vehicle to supply the tissue requirement. With greater emphasis on lean tissue deposition and less lipid, the absolute and quantitative genetic potential for protein deposition is a very important concept in that this potential, or ceiling, defines the protein requirement of the pig.

Underlying efforts at the Beltsville Agricultural Research Center was the thought of defining in quantitative terms the genetic potential for protein deposition. To this end several studies have been conducted with designs to address this question. Simultaneously, several aspects pertinent to global swine production practices were addressed. Growth hormone within these experiments was used merely as a tool, albeit a very powerful tool, to maximize genetic potential for protein accretion.

Interaction of dietary energy intake and pST administration:

Common in US production practices is the use of ad libitum feeding systems which, to some extent, reflects the availability of grain resources. European feeding systems, in contrast, utilize limit-feeding due to the expense of grain resources, but additionally as a means to enhance lean tissue deposition. As reported (Etherton et al., 1987; Boyd et al., 1986) the beneficial effects due to pGH were confounded by ad libitum feeding and the reduction (10-15%) of voluntary appetite resulting from treatment.

Table 1. Effects of energy intake and porcine growth hormone (pGH) administration on the growth performance of pigs from 25 to 55 kg live weight.

Energy Intake	pGH dose (ug/kg/d)		Feed Intake (kg/d)	Energy Intake (Mcal/d)	Daily gain (g)	Feed:gain
		(No./trt.)				
Ad libitum (A)	0	(6)	2.32	8.10	905	2.57
	100	(6)	2.08	7.28	1052	1.96
80% Ad libitum (80%A)	0	(6)	1.64	5.72	670	2.45
	100	(6)	1.62	5.65	842	1.91
60% Ad libitum (60%A)	0	(5)	1.38	4.83	543	2.54
	100	(5)	1.34	4.70	681	1.95
SEM			.03	.09	22	.06
Model R^2			.98	.98	.93	.85
Significance of contrast, P<:						
0 pGH vs 100 pGH			.01	.01	.01	.01
A vs (80% A + 60% A)			.01	.01	.01	.31
80% A vs 60% A			.01	.01	.01	.27
pGH x (A vs (80% A + 60% A))			.01	.01	.80	.65
pGH x (80% A vs 60% A)			.76	.73	.42	.67

Therefore, dietary energy was selected as the initial nutrient variable to reconcile possible synergistic effects as intake and pGH alter nutrient partitioning. Additionally, Etherton and co-workers (1987) reported that benefit from pGH administration increased with increasing amounts of body fat. Shields et al. (1983) had previously reported that protein accretion rate was

greatest in pigs between birth and approximately 55 kg live weight and decreased slowly with further weight accretion. Therefore, the interaction of energy intake and pGH was examined over the live weight phase during which protein accretion is greatest (25 to 55 kg body weight).

Data in Table 1 summarizes the growth performance of barrows fed at one of three intake levels (AL- ad libitum, 80% AL or 60% AL) a common diet and injected daily into the extensor neck muscles with excipient buffer or buffer containing pituitary derived GH at a dose of 100 ug/kg body weight over the live weight phase of 25 to 55 kg. Pigs were individually penned and feed intake and GH dose was adjusted weekly based on change of body weight. Consistent with previous reports (Etherton et al., 1987; Boyd et al., 1986), GH reduced voluntary appetite (10%) of pigs fed AL.

Intake restriction masked this effect and animals consumed all feed offered regardless of GH dose. Growth rate increased linearly with increased feed intake and was amplified by 16 to 25% by GH treatment; however, feed efficiency was similar regardless of intake treatment and was consistently improved 23% by GH. During the course of the experiment two animals were removed due to problems unrelated to treatment.

Chemical analyses of carcass and visceral components permitted the calculation of accretion rates for water, protein, fat and ash (Table 2) and using standard energy values, maintenance energy expenditure was estimated from the protein and fat components of growth. Body water, protein, fat and ash all increased as a linear function with feeding level and, with pGH treatment, protein accretion increased by 35 to 49% while fat accretion was decreased by 25 to 32%. To emphasize this effect, pigs fed 40% less feed and treated with pGH (60% AL) exhibited protein accretion rates comparable to pigs fed AL and excipient-treated. Maintenance energy expenditure estimated at total energy retention of zero was increased by 17% due to pGH. This increased energy expenditure is due to the increase of lean body mass (i.e., metabolic rate of muscle > metabolic rate of adipose tissue) and a possible direct thermic effect of GH.

Table 2. Effects of energy intake and porcine growth hormone (pGH) administration on the rates of deposition of water, protein, fat and ash and the fat:protein ratio in the empty body of pigs at 55 kg live weight.

Energy intake	pGH dose (ug/kg/d)	Accretion rates, g/d:				Fat: Protein
		Water	Protein	Fat	Ash	
Ad libitum (A)	0	416	110	283	20.4	2.58
	100	567	151	193	36.8	1.28
80% Ad libitum (80%A)	0	310	85	171	15.4	2.04
	100	498	127	127	22.2	.99
60% Ad libitum (60%A)	0	279	78	110	11.9	1.41
	100	388	105	76	17.1	.73
SEM		18	4	11	2.2	.13
Model R^2		.88	.92	.89	.77	.85
Significance of contrast, P<:						
0 pGH vs 100 pGH		.01	.01	.01	.01	.01
A vs (80% A + 60% A)		.01	.01	.01	.01	.01
80% A vs 60% A		.01	.01	.01	.05	.01
pGH x (A vs (80% A + 60% A))		.91	.26	.01	.01	.05
pGH x (80% A vs 60% A)		.05	.02	.64	.69	.15

Related to the mechanism of GH action, several studies have suggested that GH acts primarily on adipose tissue to decrease basal and insulin-stimulated lipogenesis (Walton and Etherton, 1986; Walton et al., 1987). Thereby energy normally utilized to support fat accretion is available for protein synthetic processes. Data from this energy study revealed that the rate of lipogenesis as indicated by fat accretion rate is identical comparing excipient to pGH-treated pigs, but that the rate of body lipid turnover is increased. The increased feed energy required to maintain a unit of body

fat results in a net reduction of body fat deposition. These data circumstantially imply that GH acts primarily on muscle tissue because if muscle protein effects were secondary to those on fat tissue the slope of the line describing energy retained as fat should be reduced compared to the slope for excipient-treated animals; this was not observed.

The following list describes conclusions from the dietary energy x pGH experiment:

– GH is a limiting physiological factor for lean tissue deposition in the young pig. Accretion of body fat reserve is not a prerequisite to demonstrate benefit from pGH administration.

– GH markedly increases the rate of protein deposition, regardless of energy intake, and, therefore, pGH effects as reported are independent of and additive to the effects of such treatment on energy nutriture. The magnitude of benefit from pGH administration will be more fully realized with ad libitum feeding systems.

– As a qualification to the above statement, pGH increases maintenance energy expenditure by 17% and energy intake must be adjusted accordingly to realize full benefit from pGH treatment.

– Changes in rate and efficiency of growth attributed to pGH administration are direct consequences of stimulating protein deposition and energy associated with protein deposition combined with increased maintenance expenditure denies energy supportive of lipogenesis.

Interaction of dietary protein intake and pST administration:

In a recent study, the interrelationships between protein intake and pGH responsiveness were examined. Young crossbred barrows were used and dietary protein was varied between 11 and 27%. The diets were prepared to be isocaloric (3.8 Mcal DE/kg feed) and each formulation, regardless of protein content, contained the same lysine concentration (4.9 g lysine/ Mcal DE). Thus, the influence of protein intake could be evaluated independent of lysine which is the primary limiting amino acid for growth of pigs. Soybean meal provided the variable source of dietary protein and was diluted with corn starch to yield five diets containing 27, 23, 19, 15 and 11% crude protein.

Table 3. Effects of protein intake and porcine growth hormone (pGH) administration on growth performance and selected carcass characteristics of pigs.

Dietary Protein (%)	rpGH dose (ug/kg/d)	Initial weight (kg)	Final weight (kg)	Daily gain (g)	Feed: gain	Loin eye area (cm sq)	Average backfat (cm)
11	0	32.3[a]	51.8	464	3.39	19.4	1.66
11	100	32.1	56.0	569 (23%)[b]	2.90 (14 %)	21.5 (11 %)	1.24 (25 %)
15	0	30.6	51.8	504	3.07	22.5	1.58
15	100	31.2	62.1	736 (46%)	2.28 (26 %)	27.0 (20 %)	1.17 (26 %)
19	0	30.9	53.4	536	2.93	21.9	1.66
19	100	31.3	62.9	760 (42%)	2.23 (24 %)	28.0 (28 %)	1.09 (34 %)
23	0	30.8	52.7	520	3.05	22.5	1.59
23	100	30.6	64.0	796 (53%)	2.12 (30 %)	27.6 (22 %)	1.17 (20 %)
27	0	29.0	49.8	496	3.02	20.4	1.21
27	100	29.4	60.7	744 (50%)	2.15 (29 %)	27.8 (37 %)	0.99 (21 %)
SEM		1.3	2.1	33	0.12	1.2	0.15

[a] Values are means, n=6 pigs per treatment group.

[b] Values in parentheses represent percent change of pGH-treated pigs compared to excipient-treated controls.

The rations were limit-fed daily (approximately 20% restriction vs. ad libitum) to eliminate confounding effects of altered energy intake on interpretation of results. Recombinant pGH (rpST*) was injected daily (100 ug/kg) into five groups of six pigs (i.e. one group on each of the five dietary regimes). An equal number of control pigs were treated with a similar volume of excipient buffer. Pigs were placed on treatment at 30 kg live weight and were treated for 6 weeks. Amounts of feed and pGH were adjusted weekly based on change of body weight.

The purpose of this experiment was two-fold. First, to determine whether pGH could in fact stimulate lean tissue growth in diets deficient (or marginally deficient) in protein and second, to determine whether the protein requirement is altered for pigs treated with GH. At present only preliminary growth performance data are available and shown in Table 3. The data indicate that substantial changes in growth characteristics were evident at all levels of dietary protein intake as a result of pGH treatment. Generally, it is apparent that at 15% protein (and higher) growth characteristics were quite similar. Furthermore, the improvement in performance of pigs treated with pGH and fed diets containing 15 to 27% protein diets were similar, at least in the parameters examined. In contrast, at 11% protein the magnitude of improvement in daily gain, feed:gain and loin eye area was found to be approximately 50% that observed at higher levels of protein intake. However, the net change in backfat due to pGH administration was similar at all levels of protein intake. This finding is in agreement with data from the previous study which demonstrated that aspects of fat metabolism were energy dependent and that the influence of pGH on protein and fat metabolism could be separated by nutritional manipulation. Furthermore, final interpretation of these data must await proximate analysis of the whole body and determination of protein and fat accretion rates in these animals. From the data presented here, it seems unlikely that the protein requirement for growing pigs is altered greatly as a consequence of GH administration.

Effect of genotype on realization of pST benefit:

Virtually all reports of GH efficacy have utilized castrate males, barrows, which have the greatest rate of fat accretion and intrinsically the poorest rate of protein deposition. In addition, many countries market intact male pigs to take advantage of their superior growth characteristics.

Table 4. Effects of animal sex and porcine growth hormone (pGH) administration on the growth performance of pigs from 60 kg live weight and treated for 31 days.

Animal sex	pGH dose (ug/kg/d)		Weight (kg)	Feed Intake (kg/d)	Daily gain (g)	Feed: gain
		(no.trt.)				
Male (B; boar)	0	(6)	97.8	3.22	1186	2.72
	100	(6)	102.8	2.96	1342	2.21
Female (F;gilt)	0	(6)	91.8	3.38	1011	3.34
	100	(6)	98.8	2.73	1236	2.21
Castrate male(Ba;	0	(6)	93.7	3.67	1057	3.46
barrow)	100	(6)	98.1	2.84	1225	2.33
SEM			1.5	.13	43	.07
Model R^2			.53	.55	.57	.92
Significance of contrast, P<:						
0 pGH vs 100 pGH			.01	.01	.01	.01
M vs (F + Ba)			.01	.56	.01	.01
F vs BA			.68	.13	.69	.09
pGH x (Mvs(F + Ba))			.81	.04	.59	.01
pGH x (F vs Ba)			.38	.50	.50	.96

* rpST was generously provided by IMC-Pittman-Moore, Terre Haute, IN.

Therefore, genotypic effects were evaluated initially at the most fundamental level of genetic difference; animal sex. Subsequently, Campbell and Taverner (1988) repeated these efforts using pigs which differed not only in sex, but also realization of protein deposition potential through genetic optimization.

Data in Table 4 describes the response of female, castrate male and intact male pigs fed a common diet and treated with either excipient buffer or pGH (100 ug/kg) for a 31 day period starting at 60 kg live weight. Apparent in the data was the superior rate (excipient buffer treated; male > female and castrate by 15%) and efficiency (male > female and castrate by 20%) of gain of intact male pigs. The sex effect difference was minimized with respect to rate of gain and eliminated with respect to feed efficiency by pGH administration. Chemical analysis of the components of growth confirmed that the vast improvement of feed efficiency observed in females and castrates was the result of accelerated protein and associated water deposition (Table 5).

Table 5. Effects of animal sex and porcine growth hormone (pGH) administration on the rates of deposition of water, protein, fat and ash and the fat:protein ratio in the empty body of pigs treated for 31 days.

Animal sex	pGH dose (ug/kg/d)	Water	Accretion rates,g/d: Protein	Fat	Ash	Fat: Protein
Male (B; boar)	0	467	196	317	23.6	1.40
	100	676	238	202	29.9	1.02
Female (F;gilt)	0	342	148	411	24.1	1.84
	100	680	235	185	37.8	1.04
Castrate male (Ba;	0	383	139	462	27.4	2.17
barrow)	100	615	·225	223	29.2	1.22
SEM		29	9	27	1.9	.06
Model R^2		.84	.78	.79	.56	.91
Significance of contrast, P<:						
0 pGH vs 100 pGH		.01	.01	.01	.01	.01
B vs (F + Ba)		.01	.01	.01	.09	.01
F vs BA		.54	.26	.07	.17	.01
pGH x (Bvs(F + Ba))		.12	.01	.01	.66	.01
pGH x (F vs Ba)		.07	.99	.73	.01	.23

Therefore, GH technology will be of most benefit in those production environments which utilize pigs with the poorest protein accretion rates (i.e., female and castrate male pigs as typical in the US swine industry). Furthermore, the lack of pGH effects of the same magnitude when administered to intact male pigs did not suggest that androgens and GH are additive stimulants of growth and development processes.

The effect of pGH technology on strains of pigs which have diverged from commercial-type pigs with respect to growth characteristics was recently reported by Campbell and colleagues (1988; Table 6). Pigs of strain A represent a population with an infinite capacity for protein growth constrained only by appetite, while pigs of strain B are commercial-type animals typical of Australia. Intact male and female animals within strain were treated with either excipient buffer or pGH over the live weight phase of 60 to 90 kg and fed ad libitum a common diet. Consistent with the lack of GH x genotype interaction, pGH minimizes genetic differences. Within genotype, GH negates sex effects on the efficiency and composition of live weight gain.

Table 6. Genotype and sex effects on the responsiveness of growing pigs to exogenous growth hormone administration (Campbell and Taverner, 1988).

Strain:		A				B					
pGH dose:	0		100		0		100				
Item Sex:	M	F	M	F	M	F	M	F	SEM	AOV*
Daily gain, g	1177	894	1519	1250	992	737	1292	1080	17	G,S,GH
Intake,kg/d	3.14	3.05	2.76	2.63	3.24	2.77	2.61	2.48	.32	S,GH
Feed/Gain	2.70	3.43	1.90	2.10	3.28	3.76	2.07	2.23	.24	G,S,GH,S-GH
Backfat,mm	26.4	32.5	20.4	21.3	32.3	34.2	24.9	23.6	2.8	G,S,GH,S-GH
Visceral wt, kg	7.8	7.4	7.5	8.5	7.4	7.1	8.4	8.6	.74	GH,S-GH
Carcass length,cm	78.2	76.2	80.0	77.9	77.1	77.3	78.3	79.6	2.2	GH,S-GH

* P <.05. Effects: G=strain; S=sex; GH=pGH; and S-GH interaction.

With the original objective of defining protein accretion capacity in the pig, data in Table 5 has substantially refined the estimate. Previously, protein deposition capacity in the range of 180 grams/day has been considered an "ideal" reference (Whittemore, 1983). Regardless of animal sex, we report accretion rates for body protein between 235 to 250 grams/day. Considering the goal of animal agriculture to maximize protein output per animal unit, swine nutrition practices should adapt to satisfy this genetic potential. Considerable trade-offs exist in practical swine management, but the economic basis for these trade-offs must be recognized in the perspective that the genetic ceiling, or capacity, for protein growth in the pig is approximately 40% greater than previously estimated.

Sustained effect of pST administration:

Ideally any manipulation of animal growth should involve those processes described as homeorhetic adaptations. Homeorhesis is defined as the chronic integration and coordination of metabolic processes to support a specialized physiological state (Bauman et al., 1982). Both for economy of GH used in the treatment of animals and ease of animal management, some advantage

Table 7. Effects of porcine growth hormone (pGH) administration from 30 to 60 kg live weight on the growth performance of pigs.

pGH dose (ug/kg/d)	Live weight (kg)	Days	Feed intake (kg/d)	Daily gain (g)	Feed/gain
(Treated)					
0	30-60	39.8	1.98	798	2.84
100		29.5	1.94	1041	1.86
SEM		.6	.04	35	.04
Significance of contrast, P<:					
0 pGHvs 100 pGH		.01	.50	.01	.01
(Withdrawal)					
0 (0)	60-90	32.7	3.30	887	3.75
100 (0)		29.1	2.96	1020	2.92
SEM		.7	.96	31	.14
Significance of contrast, P<:					
0 pGH vs 100 pGH		.01	.02	.01	.01
(Overall)					
0	30-90	73.6	2.58	804	3.08
100		58.7	2.43	1009	2.41
SEM		.9	.04	12	.10
Significance of contrast, P<:					
0 pGH vs 100 pGH		.01	.02	.01	.01

to the treatment of relatively small growing pigs could be realized if the pGH effects were sustained during the finishing phase of growth. In part, this challenges the homeorhesis theory of hormone action with respect to GH effects on growth. Assuming GH action is primarily exerted on those mechanisms controlling muscle protein deposition (i.e., satellite cell integration into myofibrils), decompensation of benefit following treatment withdrawal should not occur. This concept is also relevant should licensing approval mandate a lengthy withdrawal period following hormone treatment.

Barrows were treated daily with either excipient buffer or buffer containing pituitary derived pGH (100 ug/kg body weight) over the live weight phase of 30 to 60 kg. Pigs treated with excipient buffer were pair-fed to the intake noted in pGH-treated pigs to avoid energy consumption as a confounding factor. From 60 to 90 kg live weight no further injections were performed and all pigs were fed ad libitum. Growth performance segregated by live weight period is summarized in Table 7. Of the original 36% benefit in daily gain favoring pGH treatment, a 14% residual benefit was sustained during the finishing phase of growth. The 28% improvement of feed efficiency observed during the treatment phase deteriorated slightly (-6%) during the finishing phase of growth. Overall, treatment of young pigs with pGH accelerated growth velocity sufficient to reduce by 15 days the time interval to achieve 90 kg live weight utilizing 22% less feed.

Accretion rates of water, protein and ash were significantly increased during the treatment phase, while carcass fat accretion rate was decreased, compared to excipient-treated control pigs (Table 8). During the withdrawal period, carcass water, protein and ash deposition rates were significantly greater in pigs previously treated with pGH compared to excipient-treated, control, animals. Fat deposition rate was comparable regardless of prior treatment. These data indicate that, at minimum, the pGH benefit to somatic components of growth (i.e., water, protein and ash) are maintained over control values during withdrawal and do not decompensate. The increased fat deposition of pigs previously treated with pGH suggested that the decrease in magnitude of stimulated protein deposition in effect created an energy surplus resulting in a large increase of lipogenic rate. Whether these data provide evidence for a homeorhetic adaptation is inconclusive, but at least the benefit derived from treatment of young animals with pGH results in a sustained benefit to growth velocity and lean body mass.

Table 8. Effects of porcine growth hormone administration (pGH) from 30 to 60 kg live weight on the rates of deposition of water, protein, fat and ash and the fat: protein ratio in the carcass of pigs.

pGH dose (ug/kg/d)	Live weight (kg)	Water	Accretion rates,g/d: Protein	Fat	Ash	Fat:Protein
(Treated)						
0	30-60	311	98	164	18.3	1.67
100		529	153	100	28.0	.65
SEM		53	16	27	3.7	.39
Significance of contrast, P<:						
0 pGH vs 100 pGH		.01	.01	.05	.05	.05
(Withdrawal)						
0 (0)	60-90	229	91	329	16.7	4.30
100 (0)		314	121	358	24.9	2.90
SEM		31	11	44	7.2	.72
Significance of contrast, P<:						
0 pGH vs 100 pGH		.01	.01	.50	.05	.01
(Overall)						
0	30-90	253	97	233	17.5	2.43
100		347	131	226	27.2	1.74
SEM		30	8	37	4.6	.43
Significance of contrast, P<:						
0 pGH vs 100 pGH		.01	.01	.75	.01	0.1

Conclusions

Recombinant DNA technology has made available sufficient quantities of somatotropin which could vastly alter the development pattern of livestock through amplification of genetic potential favoring the accretion of lean tissue and reducing the extent of fat deposition. Application of this technology in the swine industry should negate certain advantages in production practices of European countries thereby making North American swine production more competitive in the world marketplace. Hindering application at this time is the development of a sustained release drug delivery system; however, demonstration of a sustained effect in the young animal following a 30 day treatment regime may facilitate development. As this technology affects meat processing practices, competition among species with respect to market share for consumer selection, the impact on cereal grain utilization and similar economic issues are beyond the scope of this report. Biologically, the effects of ST on reproductive performance, immune system function, progress in classical animal breeding practices, etc. are all researchable questions awaiting.

References

Agricultural Statistics (Eds. L.D. Jewell and E. Johnson), 1987. United States Government Printing Office, Washington, DC 20402.

Bauman, D.E., Eisemann, J.H., and Currie, W.B. 1982. Hormonal effects on partitioning of nutrients for tissue growth: Role of growth hormone and prolactin. Fed. Proc. 41:2548.

Boyd, R.D., Bauman, D.E., Beerman, D.H., DeNeergard, A.F., Souza, L., and Butler, W.R., 1986. Titration of the porcine growth hormone dose which maximizes growth performance and lean deposition in swine. J. Anim. Sci. 63 (Suppl. 1) :218.

Campbell, R.G., Taverner, M.R., and Curic, D.M., 1985a. Effects of sex and energy intake between 48 and 90 kg live weight on protein deposition in growing pigs. Anim. Prod. 40:497.

Campbell, R.G., and Taverner, M.R. 1985b. Effects of strain and sex on protein and energy metabolism in growing pigs. In: P.W. Moe, H.F. Tyrrell and P.J. Reynolds (Eds.), p. 78. Energy metabolism of farm animals. Europ. Assoc. Anim. Prod., Publ. 32, Rowman and Littlefield, USA.

Campbell, R.G., and Taverner, M.R., 1988a. Genotype and sex effects on the responsiveness of growing pigs to exogenous porcine growth hormone (pGH) administration. J. Anim. Sci. 66 (Suppl 1) : 257.

Campbell, R.G., and Taverner, M.R., 1988b. Genotype and sex effects on the relationship between energy intake and protein deposition in growing pigs. J. Anim. Sci. 66:676.

Chung, C.S., Etherton, T.D. and Wiggins, J.P., 1985. Stimulation of swine growth by porcine growth hormone. J. Anim. Sci. 60: 118.

Davey, R.J., Morgan, D.P., and Kincaid, C.M., 1969. Response of swine selected for high and low fatness to a difference in dietary energy intake. J. Anim. Sci. 28: 197.

Easter, R.A., 1987. Nutritional requirements and repartitioning agents. Proc. Univ. IL Pork Industry Conf., p. 193.

Etherton, T.D., Wiggins, J.P., Evock, C.M., Chung, C.S., Rebhun, J.F., Walton, P.E. and Steele, N.C., 1987. Stimulation of swine growth performance by porcine growth hormone: determination of the dose-response relationship. J. Anim. Sci. 64:433.

Etherton, T.D., Evock, C.M., Chung, C.S., Walton, P.E., Sillence, M.N., Magri, K.A. and Ivy, R.E., 1986. Stimulation of pig growth performance by long-term treatment with pituitary porcine growth hormone (pGH) and a recombinant pGH. J. Anim. Sci. 63 (Suppl. 1) :219.

Hammer, R.E., Pursel, V.G., Rexroad, C.E., Jr., Wall, R.J., Bolt, D.J., Ebert, C.M., Palmiter, R.D., and Brinster, R.L., 1985. Production of transgenic rabbits, sheep and pigs by microinjection. Nature 315:680.

Hammond, J.A., 1952. Physiological limits to intensive production in animals. Brit. Agric. Bull. 4:222.

Giles, D.D. 1942. An experiment to determine the effect of growth hormone of the anterior lobe of the pituitary gland on swine. Amer. J. Vet. Res. 3:77.

Greenspan, F.S., Li, C.H., Simpson, M.E., and Evans, H.M., 1949. Bio-assay of hypophyseal growth hormone; the tibia test. Endocrinol. 45:455.

Kraft, L.A., Haines, D.R., and DeLay, R.L., 1986. The effects of daily injections of recombinant porcine growth hormone (rpGH) on growth, feed efficiency, carcass composition and selected metabolic and hormonal parameters in finishing swine. J. Anim. Sci. 63 (Suppl 1) : 218.

Li, C.H., Simpson, M.E., and Evans, H.M., 1948. The giantism produced in normal rats by injection of the pituitary growth hormone. III. Main chemical components of the body. Growth 12:39.

Machlin, L.J. 1972. Effect of porcine growth hormone on growth and carcass composition of the pig. J. Anim. Sci. 35:794.

Shields, R.G., Mahan, D.C., and Graham, P.L., 1983. Changes in swine body composition from birth to 145 kg. J. Anim. Sci. 57:43.

Turman, E.J., and Andrews, F.N., 1955. Some effects of purified anterior pituitary growth hormone on swine. J. Anim. Sci. 14: 7.

Walker, D.G., Simpson, M.E., Ashling, C.W. and Evans, H.M., 1950. Growth and differentiation in the rat following hypophysectomy at 6 days of age. Anat. Record 106 : 539.

Walton, P.E. and Etherton, T.D., 1986. Antagonism of insulin action in cultured pig adipose tissue by pituitary and recombinant porcine GH: potentiation by hydrocortisone. Endocrinology 118:2577.

Walton, P.E., Etherton, T.D., and Chung, C.S., 1987. Exogenous pituitary and recombinant growth hormones induce insulin and insulin-like growth factor 1 resistance in pig adipose tissue. Dom. Anim. Endocrinol. 4(3): 183.

Whittemore, C.T., 1983. Development of recommended energy and protein allowances for growing pigs. Agric. Sys. 11:159.

Wolfrom, G.W., Ivy, R.E., and Baldwin, C.D., 1986. Effect of native porcine growth hormone (npGH) injected intramuscularly in barrows. J. Anim. Sci. 63 (Suppl. 1):219.

USE OF RECOMBINANT PORCINE SOMATOTROPIN (rPST) IN EUROPE; RESEARCH EXPERIENCE AND PERSPECTIVES.

Vernon R. Fowler[1] and Egbert Kanis[2]

[1]*Rowett Research Institute and School of Agriculture, University of Aberdeen, Scotland*
[2]*Wageningen Agricultural University, The Netherlands*

Summary

European pig production is carried out within a distinctive agricultural, social and scientific environment. For many years there has been an intensive effort to breed for pigs which are both efficient in their use of feed and which can conform to very demanding grading standards set by the processor. A major issue is whether or not the use of recombinant porcine somatotropin (rPST) results in significant improvements in efficiency under all the conditions of production which prevail in Europe.

Experiments with rPST using European breeds at different centres in The Netherlands, West Germany and in the United Kingdom (Scotland) have all showed clearly that it was possible to achieve very considerable improvements from using rPST both in terms of growth rate and feed efficiency and particularly in the leanness of the carcass. The most dramatic increases were in the rate of deposition of the lean tissue and in daily nitrogen retention. This was true over all weight ranges varying between 35 to 140 kg depending on the period of administration and on dose rate. In the Scottish work, where treatments were applied between 35 and 95 kg liveweight, the dose was at the high rate of 7 mg per day of rPST and where protein was supplied at 190 g per kg in the diet, daily gains of the treated group were 20% above that of the control and the N content of the carcass was increased by over 10%. The Dutch work on N-balances with restricted feeding indicated increases in daily weight gain of over 10%, in daily protein gain of about 30% and decreases in daily fat deposition of about 10%, even in the Pietrain breed. In general, the effect of rPST was to reduce voluntary feed intake by about 5% but in the Dutch experiment with ad libitum feeding there was a major exception to this in the case of Pietrain and cross-bred pigs growing from 100 to 140 kg liveweight which increased their intake by about 8%.

The protein concentration in the diet was important for the full expression of the effects of rPST administration on protein deposition. There is clearly an immense opportunity for modelling exercises which will determine the best combinations of genotype, diet, slaughter weight and rPST dose rate to obtain the best advantage from this new and exciting technology.

Keywords: somatotropin, swine, carcass quality, growth rate, feed efficiency, Europe.

Introduction

There have been several reports from the United States indicating a very positive response by pigs to injections of both natural and recombinantly derived PST (Boyd et al., 1985; Etherton et al., 1986; Kraft et al., 1986). A major issue is whether or not the use of rPST results in significant improvements in efficiency under all the conditions of production which prevail in Europe. European pig production is carried out within a distinctive agricultural, market, social and scientific environment. For many years there has been an intensive effort to breed for pigs which are both

efficient in their use of feed and which can conform to very demanding grading standards set by the processor. These pigs normally receive high-quality, protein-rich diets throughout the growing period and typical marketing weights range between 85 kg liveweight at the lower end to about 125 kg at the upper end of the spectrum.

Among the favoured European genotypes in some European countries are pigs of the Pietrain type either bred pure or as cross-breds. This type is noted for its extreme leaness, sensitivity to stress and its compact appearance. These attributes are now believed to be mainly the result of a particular metabolism associated with a relatively simple gene known as the 'halothane sensitivity gene', because of the tendency of pigs which are homozygous for this trait to exhibit a characteristic rigour of the muscles and malignant hyperthermia when the anaesthetic substance halothane is administered. The extreme attributes of the Pietrain breed contrast markedly with those of the Duroc breed which is widely used in the United States and which tends to be rather fatter and, in a relative sense, stress resistant. The characteristic meat producing pigs of North West Europe tend to be based on hybrids or crosses of pigs of the Large White (Yorkshire) and Landrace types together with a varying degree of Pietrain blood depending on the market demand.

The experiments described below include representatives of these genotypes and relate to pigs grown on typical European diets under European conditions of husbandry. The main studies reported relate to work by Kanis and Van der Wal (1988) in The Netherlands, Fowler et al. (1988) in Scotland and reference is also made to work from the Federal Republic of Germany by Ellendorff et al. (1988). All the studies were conducted using rPST provided by Pitman-Moore, Inc. Terre Haute, USA. Much of this work has not yet been published in full scientific form, and the results given in this paper should be treated as provisional.

Experimental background

Many of the European experiments have been conducted using the same basic methods of administration of rPST, namely daily subcutaneous injection of a fixed dose over the relevant experimental period either in the shoulder or over the ham. In the Dutch experiments a fixed dose of 4 mg per day was administered over the entire liveweight range of 60 to 140 kg. In the Scottish experiments there were three dose rates 1.75 mg, 3.5 mg and 7.0 mg per day administered to pigs which were much lighter at the start than those in the other experiments (30 kg) and which continued until the pigs weighed 95 kg liveweight. In the West German experiments, a fixed dose of 5 mg rPST was used over the weight range 50 to 105 kg (70 days from 50 kg).

The breeding of the animals in the Dutch experiment was a comparison of purebred Pietrain and purebred Duroc with a typical cross between Dutch Yorkshire and Dutch Landrace. In the West German experiment, Pietrain were again used but in this case the second breed was the German Large White (Deutsche Edelschwein). In the Scottish experiment, the pigs were the product of a breeding company (National Pig Development) and were the result of crossing a Large White boar with a Large White x Landrace female. Feeding was close to ad libitum in all experiments although in the Scottish experiment a scale of feeding was used, intended to be just below appetite. Diets were typically based on cereals, barley and wheat supplemented with protein-rich materials including extracted soya-bean and fishmeal. In the Dutch and West German trials the concentration of protein in the fresh diet was about 190 g per kg but in the Scottish trial two protein concentrations were compared, 165 g per kg and 190 g per kg. In terms of the sex of the experimental animals the Dutch and Scottish experiments included females and castrated males but the West German experiment was based only on females.

Results

It is impossible to give a comprehensive listing of all the results without writing three or more papers. However it is possible to draw together some of the main features.

Growth rate

The response of growth rate differed between the centres. In the Dutch and Scottish experiments there were major increases in growth rate resulting from the treatment but in the West German experiments this was not demonstrated and in fact in the case of the Large White breed there was a slight reduction (see Table 1).

Feed gain ratio

Liveweight feed conversion was markedly improved in the Scottish and Dutch Experiments each kg of gain requiring about 10% less feed with the Pietrain on the West German experiment showing the least response (see Table 2).

Voluntary feed intake

In general, the effect of rPST was to reduce voluntary feed intake by approximately 4 to 12%, but there was a major exception to this in the case of Pietrain and cross-bred pigs growing from 100 to 140 kg liveweight in the Dutch experiment which actually increased their intake by about 8%, (see Table 3).

Carcass leaness

Without exception the effect of rPST increased in a most dramatic way the leaness of the carcass this being very sensitive to actual dose of rPST (see Table 4). The greatest increases were of the order of 15% and this was independent of the degree of leaness in the first instance.

Rate of gain of protein and lipid

A most impressive feature of rPST is the increase that it effected in the daily rate of protein deposition. This is illustrated by the data of Kanis and van der Wal from their metabolic experiments (see Table 5). The increases are virtually 25 % for the treated versus the control animals and there are corresponding reductions in the rate of deposition of the lipid, although the proportional change is not as great.

Chemical composition

The chemical composition of the carcass reflects the greater leaness and reduced fat of the carcasses and also shows that in general the normal proportions between protein, ash and water content are maintained. The data given in Table 6 are from the Scottish series of experiments and show consistent responses to the rPST dose rate in terms of increasing protein in the carcass for the high dietary protein treatment (190 g/kg) but a tendency to plateau for the low protein diet (165 g/kg). The same but opposite tendency is apparent in the concentration of lipid in the carcass. The ratio of water to protein and of ash to protein was unaffected by the rPST treatments suggesting that the physiological relationships between these components of the lean body remained completely normal.

Physical proportions

It is interesting to note that in so far as it was possible to determine the relationships between the physical entities of the body it appeared that rPST did not have any major effect in changing the proportions of the components of the fat-free body (see Table 7).

Fitness and health

In none of the experiments was any detrimental effect reported of the use of rPST found in terms of health or fitness. Ellendorff et al. (1988) examined the major endocrine glands of treated and untreated pigs including pituitary, thyroid, adrenals and ovaries and found no differences except in the case of the adrenals of the Pietrain breed for which organ the animals receiving rPST had an increase in size over the control of about 24%.

Eating quality

Kanis and van der Wal (1988) examined the meat quality parameters including tenderness, odour, taste, fat content and drip loss. Of the whole range of quality measures only meat colour showed a difference although this did not approach significance, see Table 8. However, in the work of Ellendorff et al. (1988) a difference was found in the amount of lipid in dry matter of the longissimus dorsi, the change being about a reduction of one third for both the German Large White and the German Pietrain. However, the amount of fat in the control animals was only about 3% of the dry matter, and it is unlikely that such a change would have a material effect on the eating quality.

Discussion

The effect of the use of rPST in pigs typical of the European breeds and under conditions of management and husbandry typical of North West Europe was dramatic. It not only increased the lean content of pigs considered to be already genetically lean, but also always increased the growth rate of the lean tissue and reduced that of fatty tissues. These improvements were usually accompanied by a reduction in daily feed intake and an improvement in feed gain ratio. At the higher weights, that is from 100 to 140 kg liveweight, greater growth rates were achieved in lean animals by an actual increase in the daily feed intake.

From this experience it appears that rPST is extraordinarily effective at increasing the rate of deposition of lean tissue or daily protein accretion rate. This appears mainly to have been achieved by diverting some of the metabolizable energy which would otherwise have been deposited as lipid towards protein deposition. However, when energy for protein deposition becomes otherwise limiting, pigs treated with rPST exhibit an increase in feed intake. This is particularly interesting in view of the fact that these pigs may actually have been selected over recent years in such a way that their appetite potential has been genetically reduced.

From the one experiment in which dose rate was incorporated as a factor, it appeared that dose rate is extremely important in determining the extent of the effect. Indeed, when 7 mg per day of rPST was administered to pigs from a light weight, that is 30 kg, the rate of fat deposition was so reduced that in some cases there was barely any visible fat over the eye muscle (longissimus dorsi) when the pigs were slaughtered at 95 kg liveweight.

The protein concentration in the diet appeared to be important for the full expression of the effects of rPST administration on protein deposition. There is clearly an immense opportunity for modelling exercises which will determine the best combinations of genotype, diet and slaughter-weight and rPST dose rate to obtain the best advantage from this new and exciting technology.

It appears that even for the sophisticated genotypes and diets used in North Western European pig production that the use of rPST could make an enormous impact on the efficiency of production and on the leaness of the carcass without detriment to the health of the animal or to the eating quality of the meat.

Table 1. Treatment means for daily liveweight gain for the Scottish (series 1), Dutch (series 2) and West German (series 3) experiments.
Breeds are designated as Large White x Landrace (LW/LR), Pietrain (PT), Duroc (DC), and Large White (LW).

Series No	Weight Range (kg)	Breed	Dose (mg/d)	Live-weight gain (kg/d)	% change
1	30-95	LW/LR	0.0	0.871	-
			1.75	0.938	+ 8.0
			3.50	0.966	+10.9
			7.00	0.974	+11.8
2	60-100	PT	0.0	0.952	-
			4.0	0.985	+ 3.5
		LW/LR	0.0	0.962	-
			4.0	1.019	+ 6.0
		DC	0.0	0.868	-
			4.0	0.902	+ 3.9
	100-140	PT	0.0	0.670	-
			4.0	0.882	+31.7
		F1	0.0	0.693	-
			4.0	0.883	+27.4
		DC	0.0	0.765	-
			4.0	0.786	+ 2.7
3	50-100	LW	0.0	0.901	-
			5.0	0.857	- 4.9
		PT	0.0	0.789	-
			5.0	0.797	+ 1.0

Table 2. Treatment means for feed/gain ratio for the Scottish (series 1), Dutch (series 2) and West German (series 3) experiments. Breeds are designated as Large White x Landrace (LW/LR), Pietrain (PT), Duroc (DC), and Large White (LW).

Series No	Weight Range (kg)	Breed	Dose (mg/d)	Feed/ gain	% change
1	30-95	LW/LR	0.0	2.51	-
			1.75	2.33	- 7.2
			3.50	2.25	-10.4
			7.00	2.22	-11.6
2	60-100	PT	0.0	3.18	-
			4.0	2.92	- 8.2
		LW/LR	0.0	3.02	-
			4.0	2.72	- 9.9
		DC	0.0	3.37	-
			4.0	3.13	- 7.2
	100-140	PT	0.0	4.71	-
			4.0	3.82	-19.0
		LW/LR	0.0	4.39	-
			4.0	3.70	-15.8
		DC	0.0	4.45	-
			4.0	4.16	- 6.5
3	50-100	LW	0.0	2.83	-
			5.0	2.50	-11.7
		PT	0.0	2.52	-
			5.0	2.44	- 3.2

Table 3. Treatment means for feed intake for the Scottish (series 1), note not true ad libitum, the Dutch (series 2) and West German (series 3) experiments. Breeds are designated as Large White x Landrace (LW/LR), Pietrain (PT), Duroc (DC), and Large White (LW).

Series No	Weight Range (kg)	Breed	Dose (mg/d)	Feed Intake (kg/d)	change
1	30-95	LW/LR	0.0	2.16	-
			1.75	2.18	-
			3.50	2.17	-
			7.00	2.15	-
2	60-100	PT	0.0	3.01	-
			4.0	2.85	- 5.2
		LW/LR	0.0	2.89	-
			4.0	2.77	- 4.2
		DC	0.0	2.93	-
			4.0	2.82	- 3.6
	100-140	PT	0.0	3.11	-
			4.0	3.36	+ 8.0
		LW/LR	0.0	2.99	-
			4.0	3.24	+ 8.3
		DC	0.0	3.39	-
			4.0	3.21	- 5.4
3	50-100	LW	0.0	2.02	-
			5.0	1.78	-11.9
		PT	0.0	1.80	-
			5.0	1.74	- 3.4

Table 4. Treatment means for feed/gain ratio for the Scottish (series 1), Dutch (series 2) and West Germain (series 3) experiments.
Breeds are designated as Large White x Landrace (LW/LR), Pietrain (PT), Duroc (DC), and Large White (LW), castrated males are designated (M*) and females as (F).

Series No	Weight Range (kg)	Breed (sex)	Dose (mg/d)	Lean %	% change
1	30-95	LW/LR			
		M*	0.0	54.9	-
		M*	7.0	63.6	+15.8
		F	0.0	59.6	-
		F	7.0	66.0	+10.7
2	60-100	PT	0.0	56.1	-
			4.0		+2.30
		LW/LR	0.0	57.8	-
			4.0	59.9	+3.70
		DC	0.0	52.7	-
			4.0	56.6	+ 7.4
	100-140	PT	0.0	52.2	-
			4.0	56.8	+ 8.8
		LW/LR	0.0	54.2	-
			4.0	58.5	+ 7.9
		DC	0.0	50.4	-
			4.0	55.1	+ 9.4
3	50-100	LW	0.0	49.4	-
			5.0	55.5	+12.3
		PT	0.0	55.4	-
			5.0	63.0	+13.7

Table 5. Treatment means for protein and lipid gain per d based on metabolism trials from the Dutch work of Kanis and van der Wal (series 2). The values given are the means of two experimental periods. Breeds are designated as Large White x Landrace (LW/LR), Pietrain (PT), Duroc (DC), and Large White (LW) with % change from control in brackets.

Series No	Weight Range (kg)	Breed (sex)	Dose (mg/d)	Protn (g/d)	Lipid (g/d)
2	60-100	PT	0.0	144	260
			4.0	187(+29.9)	243(-6.54)
		LW/LR	0.0	167	276
			4.0	211(+26.3)	213(-22.8)
		DC	0.0	116	265
			4.0	146(25.9)	220(-16.9)

Table 6. Treatment means for the chemical anniyses of the carcasses for the Scottish experiments (Fowler et al) series 1. The data are given as the means for castrates and females combined. The results are classified to give the full interaction between the rPST treatments and the protein concentration of the diet given between 30 and 95 kg liveweight.

	Diet Protein (g/kg)	rPST (g/d) 0.0	1.75	3.50	7.00	SED
Crude protein (g/kg)	165	177.3	184.9	195.9	191.7	
	190	185.4	194.2	203.2	206.0	3.13
Lipid (g/kg)	165	242.5	213.7	180.7	177.2	
	190	218.5	182.5	156.9	123.3	8.37
Water (g/kg)	165	548.0	569.8	588.6	597.4	
	190	564.1	590.6	603.5	635.2	7.63
Ash (g/kg)	165	32.2	31.6	34.8	33.8	
	190	32.1	32.7	36.4	35.6	1.50
Water/ protein	165	3.08	3.08	3.00	3.12	
	190	3.04	3.04	2.97	3.08	
Ash/ Protein	165	0.18	0.17	0.18	0.18	
	190	0.17	0.17	0.18	0.17	

Table 7. Treatment means for the dissection of the carcasses and ratios between major parts for the Scottish experiments (Fowler et al) series 1. The data are given separately for castrates and females.

	rPST (g/d)				
	0.0		7.0		
Sex	M	F	M	F	SED
Muscle %	54.9	59.6	63.6	66.0	2.24
Fat and skin %	33.5	29.2	23.9	22.1	1.92
Bone %	5.97	5.88	6.58	6.50	0.02
Bone as % muscle	10.9	9.9	10.9	9.9	
Longiss. Dorsi as % muscle	10.3	11.5	10.3	10.5	

Table 8. Treatment means for parameters of meat quality from pigs on series 2 (Kanis and van der Wal, 1988) and on fat in dry matter from Ellendorff et al. (1988), series 3.

	rPST (18)	Control (18)	Sig.
SERIES 2			
Tenderness	7.40	7.50	NS
Odour	7.73	7.80	NS
Taste	7.58	7.54	NS
Moisture %	73.81	73.69	NS
Fat %	2.17	2.05	NS
Protein %	23.27	23.09	NS
Drip loss %	4.41	4.39	NS
Cooking loss %	28.93	28.28	NS
Instron Shearforce	3.55	3.39	NS
Colour(Hunter)10a	5.13	5.85	(10%)
SERIES 3			
Large White			
% Fat in DM of			
Long. dorsl.	1.80	3.19	**
Pietrain			
% Fat in DM of			
Long. dorsl.	2.69	1.78	**

References

Boyd, R.D., M. Harkins, D.E. Bauman and W.R. Butler, 1985. Cornell Nutr, Conf. Feed Manufacturers. Nov. 1985; 11-19.

Ellendorff, F., E. Kallweit, E. Huster and D. Ekkels, 1988. Unpublished communication. Pitman-Moore Inc, Terre Haute. USA.

Etherton, T.D., C.M. Evock, C.S. Chung, P.E. Walton, M.N. Sillence, K.A. Nagri and R.E. Ivy, 1986. J, Anim. Sci. 63 (Suppl. 1),219, Physiol., Washington.

Fowler, V.R., M. Kay, H.M. Thikey, R.M. Livingstone, K. Pennie, and I.C. Hart, 1988. Unpublished communication. Pitman- Moore Inc, Terre Haute. USA.

Kanis, E. and P. van der Wal, 1988. Unpublished communication. Pitman- Moore Inc. Terre Haute. USA.

Kraft, L.A., D.R. Haines and R.L. Delay, 1986. J.Anim. Sci, 63 (Suppl, 1),218. Physiol., Washington.

PROSPECTS FOR USING PORCINE SOMATOTROPIN IN CHINESE PIGS

K.F. Fung[1] and S.Z. Qi[2]
[1]South China Agricultural University, Guangzhou, China
[2]Beijing Agricultural University, Beijing, China

Summary

Porcine somatotropin was administered to 44 Chinese Large Black-white and Landrace cross hogs in Guangdong Province. The average daily gain response was more prominent in F1 (+15.32%) than the Grading-up F2 (+11.26%). However the latter had much less backfat (-19.15%) and much more lean tissue (+17.00%) than the former (-10.54% and +9.77%, respectively) in response to PST treatment.

Porcine somatotropin was also administered to 48 Beijing Black finishing hogs in Beijing. The pigs fed 18% crude protein in diet had greater average daily gain, better feed efficiency and much more lean tissue than those fed 16% and 14% crude protein in response to PST treatment.

The results show that the Chinese breeds of hogs can be greatly improved in terms of greater gain, better feed utilization, less backfat and greater lean meat with PST treatment.

Keywords: somatotropin, swine, growth rate, feed efficiency, China.

Introduction

Pork is the most important meat for Chinese people so far. The total number of pigs is over 300 million in this country. However, China has a large population and the pork production, especially the lean meat, can not meet the needs of the people with their living level on the increase. The grain yield per capita in China is much lower than that in developed countries so they need to increase the feed efficiency and lean meat percentage of the Chinese pigs which are much lower than that in the American and European breeds. Of course, the Chinese breeds mature earlier and have higher fertility rate. It seems to be a good suggestion to enhance Chinese pig performance by administrating porcine somatotropin, besides by means of breeding and improvement. With this idea in mind, we have conducted experiments in Guangdong Province and Beijing.

Materials and methods

In Guangdong experiment, two groups of crossbreds between Chinese Black-white and Landrace were available. The first batch was the cross (F1), consisting of 45 barrows and gilts, with an initial average weight of about 30 kg; the second batch was Landrace Grading-up (F2), consisting od 46 castrated barrows and gilts, with an initial average weight of about 31 kg. The crude protein content of the diet was 16%. The PST group was administered intramuscularly 4 mg per day for 70 days. The amount of feed consumed was measured every day. The pigs were weighed every two weeks. All the pigs were slaughtered after 77 days of the experiment.

In Beijing experiments, three groups of Beijing Black finishing hogs were fed diets containing 14, 16 and 18% crude protein; there were 36, 36 and 24 castrated barrows and gilts in these groups.

The initial average weight was 67 kg. The PST hogs of each group were administrated intramuscularly 2 mg per day for 28 days. The pigs were weighed every week and slaughtered on 29th day.

All the carcasses were dissected according to a standard commercial dissection method.

Results

Experiment on Chinese Large Black-White and Landrace cross:

The average daily gain response was more prominent in F1 than that of the Grading-up F2, but the latter had much less backfat and much more lean tissue than the former (Table 1).

Table 1. Production performance and carcass quality of Chinese large Black-white and Landrace cross by treatment (PST; 4 mg for 70 days).

		PST	Control	Difference%
Group 1				
	Crossbreed (F1)	n= 22	n= 23	
	Average Daily Gain (g)	512	444	+15.32
	Feed Efficiency (kg/kg)	3.48	4.07	-14.50
	Backfat Thickness (cm)	2.77	3.10	-10.65
	Lean Meat Percentage	56.83	51.77	+ 9.77
Group 2				
	Grading-up (F2)	n=22	n=24	
	Average Daily Gain (g)	494	444	+11.26
	Feed Efficiency (kg/kg)	3.41	4.00	-14.75
	Backfat Thickness (cm)	2.28	2.82	-19.15
	Lean Meat Percentage	59.68	51.01	+17.00

Experiment on Beijing Black finishing pigs:

The pigs fed 18% crude protein level had greater average daily gain, better feed efficiency and much more lean tissue than those fed 16, 14% crude protein levels (Table 2).

Table 2. Production performance and carcass quality of Beijing Black finishing hogs by treatment (PST; 2 mg for 28 days).

		PST	Control	Difference%
Group 1				
	(14% crude protein)	n=18	n=18	
	Average Daily Gain (g)	940	817	+15.1
	Feed Efficiency (kg/kg)	3.70	4.35	- 15.0
	Backfat Thickness (cm)	2.38	2.70	- 11.9
	Lean Meat Percentage	56.3	52.8	+ 6.6
Group 2:				
	(16% crude protein)	n=18	n=18	
	Average Daily Gain (g)	1029	867	+18.7
	Feed Efficiency (kg/kg)	3.41	4.20	- 18.8
	Backfat Thickness (cm)	2.49	2.76	- 9.8
	Lean Meat Percentage	57.4	52.7	+ 8.9
Group 3				
	(18% crude protein)	n=12	n=12	
	Average Daily Gain (g)	1050	860	+22.1
	Feed Efficiency (kg/kg)	3.19	4.11	- 22.4
	Backfat Thickness (cm)	3.03	3.33	- 8.9
	Lean Meat Percentage	55.5	48.5	+14.4

Discussion

According to the experiments, the Chinese breed pigs which have a slower growth rate, less efficient feed utilization, more fatty tissue and less lean tissue are more responsive to porcine somatotropin.

From the results, it is worthwhile for Chinese breed pigs to use porcine somatotropin to increase daily gain, feed utilization and lean meat and to decrease backfat to meet the demands of marketing at home and abroad.

These studies have demonstrated the potential of PST to improve the performance and carcass composition of crosses of Chinese breeds with leaner Western breeds. The Chinese breeds are typically slow growing, inefficient converters of feed, fat, light muscled and early maturing. They are also very prolific and certain breeds are known for sweet-tasting meat.

The Chinese are very interested in improving pigs in their country to reduce the need for imported feed sources and to improve the public diet by reducing fat intake. Many Western countries are interested in improving the reproductive efficiency of the typical Western breeds.

It has been shown that PST administration to a Chinese Western crossbreed (Beijing Blacks) improves performance and reduces fat thickness if dietary protein is adequate. Many countries are interested in utilizing the Chinese breeds to take advantage of the prolificacy of these breeds. However, use of these breeds causes a proportional sacrifice in performance and carcass traits. This trial demonstrated that by using a grading-up F2, the maternal lines used to produce the commercial pigs were 1/2 Chinese and 1/2 Western breeds. In this way, great advantage of the reproductive ability of the Chines pigs was realized with only 1/4 of the terminal pigs being Chinese, thereby causing minimal decrease in the level of performance and carcass measures. Use of PST in these F2 pigs during the growing-finishing phase caused a restoration in these traits up to the levels generally seen with crossbred Western pigs.

This set of trials proved that PST has positive effects on crosses of Chinese and Western breeds to obtain reproductive improvements without sacrificing performance and carcass measures.

DIRECT MODIFICATION OF THE LIVESTOCK GENOME

Thomas E. Wagner, Ph.D. Director

Edison Animal Biotechnology Center, Ohio University Athens, Ohio 45701 U.S.A.

Summary

Current methods for introducing genes into the germline of laboratory and livestock animals are reviewed. These methods include direct gene transfer by pronuclear microinjection or of fertilized eggs, infection of embryos by retroviral vectors, and the production of animals from totipotent embryonal stem cells grown in continuous culture. Although transgenic livestock (pigs) have, to date, only been produced by pronuclear microinjection, an embryonal stem cell line from porcine embryonic cells is described for use in the production of transgenic or clonal swine. The phenotypic characteristics of transgenic swine expressing growth hormone are discussed in detail including the positive characteristics of 50% or greater reductions in body fat and 30% or greater increases in feed efficiency and the negative effects of increased structural difficulties and stress susceptibility. It is suggested that the negative effects of growth hormone expression in transgenic pigs may be overcome by controlling the time of expression of growth hormone to only a portion of the life of these animals. With this goal in mind chimeric genes containing the P-enolpyruvate carboxykinase (PEPCK) promoter ligated to the structural gene for bovine growth hormone (bGH) were introduced into the germlines of mice and pigs. Results confirm that growth hormone expression in these animals does not occur during embryonic development and may be controlled by diet. Diets high in carbohydrate reduced the concentration of bGH in mice to 5% of basal levels and refeeding a diet high in protein but devoid of carbohydrate resulted in a 20-fold increase in serum bGH within one week. Studies of the control of bGH expression by diet are in progress in the pig, but PEPCK/bGH transgenic pigs do not show the many of the disabilities of transgenic pigs expressing growth hormone under the control of a constitutive promoter.

Keywords: gene transfer, growth, swine, regulation promoter.

Introduction

Traditionally, improvement in livestock production has centered around breeding programs which take advantage of spontaneous mutations in the animal's genome. Selective breeding programs, because they do not require any knowledge of the physiological basis of the desired phenotype, can be successful without an understanding of the molecular basis of a trait. But, such approaches to animal improvement require decades or centuries to achieve their goals.

With an increased understanding of the physiological and molecular basis of performance traits in animal, new approaches to animal improvement are now possible. One very effective approach is the administration of a key physiological modifying intermediate, such as a hormone, to the growing animal. The administration of somatotropins to livestock is the subject of this symposium because of the dramatic improvement in livestock performance demonstrated as the result of somatotropin administration by many of those gathered here. But, modification of the genome of the animals to "deliver" somatotropins naturally within the permanent make-up of the animals might be an even more effective, convenient and acceptable means of livestock production

improvement. The emergence of transgenic animal technology has provided the means to attempt improvement of livestock by direct genome modification.

Contrary to common opinion, the ability to insert a genetic sequence into the germ line of animals is only one of several technological hurdles necessary to overcome prior to producing useful and practical transgenic livestock. For most applications it is necessary to not only express the transgene within the animal but to regulate the expression to specific target tissues and during the life cycle of the animal. Such exquisite control of transgene expression has not yet been achieved in the laboratory animals let alone livestock, but some important progress towards this goal has been achieved. In the ensuing text a review of the present state of the science of transgenic animals is presented. This presentation is divided into three sections: (1) gene transfer technology, (2) control of tissue specific expression and (3) external regulation of transgene expression.

Gene transfer technology in animals

Transgenic animals may be produced by the introduction of discrete genetic sequences into the permanent chromosomal composition of animals by three different methods including pronuclear microinjection of one cell fertilized embryos, infection of embryos by viral vectors and the production of germline chimeras from embryonal stem (ES) cells containing added genes. Since a thorough review of these methods has recently been published by the author (Strojek and Wagner, 1988), the important features of these procedures are reprinted here.

The term "transgenic" was introduced originally by Gordon and Ruddle (1988) for mice which had integrated a foreign gene into all somatic tissues examined. This had been achieved by injecting these genes into the pronuclei of fertilized mouse ova. Since it became evident later (Wagner et al., 1981) that the offspring of these mice can inherit the foreign genes in a Mendelian fashion, the word transgenic is now commonly used to refer to a stable germ line integration of foreign genes. At present three different approaches have been reported which succeed in the establishment of transgenic mouse lines. These methods include pronuclear injection of DNA, infection of embryonal stages with recombinant viral vectors and the production of germline chimeras which consist partially of totipotent, genetically transformed, cell lines.

Pronuclear Injection

Several groups (Wagner et al., 1981; Gordon et al., 1980; Wagner, Stewart and Mintz, (1981); and Constantini and Lacy, 1981) were involved in the establishment of this method of gene transfer showing that by using this technique integration of the introduced foreign gene into all somatic and also into the germ cells of the developing animal can be achieved. In order to achieve optimal results, approximately 1 pl of a DNA suspension containing 200 to 2000 linearized copies of the foreign gene is injected into either pronucleus of fertilized mouse eggs (Brinster et al., 1985). After overnight cultivation cleaved eggs (50% to 75%) are transferred to the oviducts of foster mothers. Of these 10% to 25% usually develop to term and about 15% to 37% of the born young inherit the injected genes, which leads to an overall efficiency rate of 1% to 4% based on the total number of zygotes manipulated.

Provided the introduced genes are integrated into the genomic DNA before the zygote enters cleavage, all embryonal cells will contain the same integration site and copy number of the foreign gene. Integration after the first cleavage will give rise to chimeric animals, which consist of at least two genetically different cell populations. According to Wilkie, Brinster and Palmiter, (1986) the latter seems to be true in at least 30% of the mice born after microinjection of DNA.

Infection of Embryos by Viral Vectors

Infection of blastocysts by SV40 (Jaenisch and Mintz, 1974) was the first evidence that foreign genes could be integrated into the genome of embryonal cells and lead to their stable integration

into somatic tissue. Jeanisch (1976) also observed that the M-MuLV provirus was not only retained by somatic cells after embryonal infection but was also transmitted to the offspring of the resulting mature mice.

Viral infection of the preimplantation embryo is naturally prevented by the existence of the zona pellucida. This barrier can be overcome by either enzymatic digestion of the zona, so that 2-cell to morula stages can be infected (Jaenisch, Fan and Croker, 1975; Rubenstein, Nicholas and Jacob, 1986) or direct microinjection of virus particles into the blastocoel cavity (Jaenisch and Mintz, 1974). This procedure has been used successfully to introduce proviruses into the germ line of mice. However, the resulting embryos generally are mosaic, as different integration events can take place in a variable number of embryonal cells (Jaenisch et al., 1981).

To transfer foreign genes into the germ line of mice, recombinant retroviral vectors can be used which contain the gene of interest. Since recombinant retroviruses generally are replication incompetent, they require the presence of helper virus for propagation. Stuhlmann et al. (1984) have thus infected day-9 mouse fetuses with recombinant and helper virus simultaneously and observed subsequent integration and expression in the resulting offspring. However, their results suggested, that the superinfection with helper virus in these mice had interfered with the spread of the recombinant virus and therefore limited the number of transformed somatic cells.
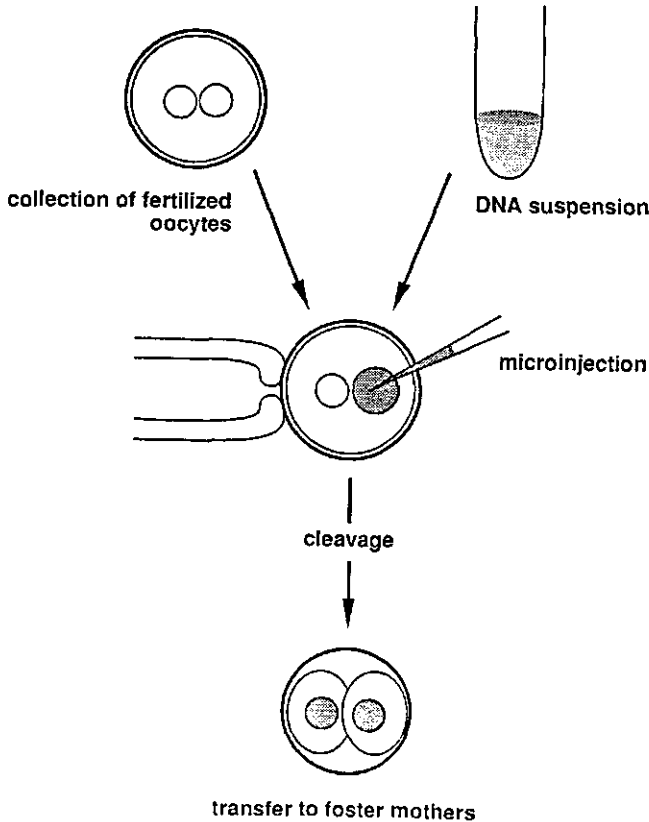

Figure 1. Pronuclear Injection of DNA.

(Reprinted, with permission, from Genetic Engineering, Principles and Methods, Vol. 10, Edited by Jane K. Setlow)

As separation of recombinant and helper virus yet cannot be achieved, an alternative propagation method using psi-2 cells (Mann, Mulligan and Baltimore, 1983) can be chosen if viremia from the helper virus is to be avoided in the resulting animals. Psi-2 cell lines have incorporated a retroviral genome which cannot be packaged into virus particles itself because of a mutation in its psi-region, but it delivers all the information needed for the propagation of recombinant virus with an intact psi-region to the cell. Consequently, the yield of recombinant virus will be lower in these cell lines, but is not accompanied by the production of helper virus.

Van der Putten et al. (1985) and Rubenstein, Nicholas and Jacob (1986) have infected pre-implantation mouse embryos with recombinant replication-incompetent retrovirus without the use of helper virus. 197 denuded 8-cell stages cultivated over psi-2 monolayers for 16 hours and subsequently transferred to foster mothers gave rise to one animal which had incorporated the recombinant provirus including the foreign gene and transmitted it to its offspring (Van der Putten et al., 1985). Rubenstein, Nicholas and Jacob (1986) co-cultivated 278 4 -cell-stage mouse embryos over psi-2 cells and obtained 76 (30%) live fetuses after transfer, of which one contained the recombinant provirus.
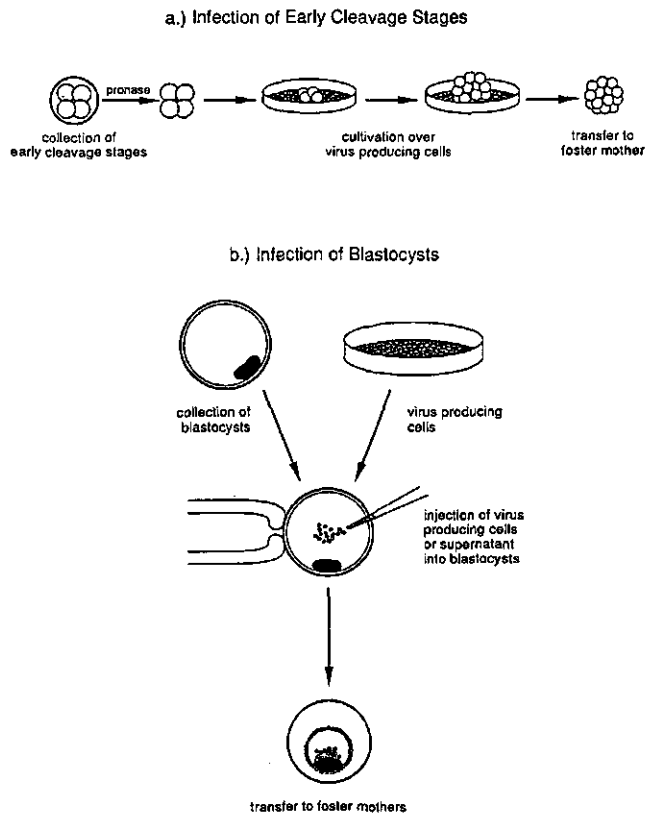
a.) Infection of Early Cleavage Stages

b.) Infection of Blastocysts

Figure 2. Infection of embryos with viral vectors.
(Reprinted, with permission, from **Genetic Engineering, Principles and Methods,** Vol. 10, **Edited by Jane K. Setlow**)

Production of Germline Chimeras

Chimeras can be produced either by aggregating two embryos or by injecting embryonal cells into expanded blastocysts, a procedure that results in the formation of individuals which consist of two or more genetically different cell lines (McLaren, 1976). When totipotent embryonal cell lines, which can be grown in culture for many generations, are genetically transformed before using them for chimera formation, this technique offers another route of producing transgenic animals, provided that the transformed cells will participate in the formation of germ cells.

The first embryonal cell line used for this purpose were murine embryonal teratocarcinoma (EC-) cells (Watanabe, Dewey and Mintz, 1987). However, these cells appeared to have the disadvantage of showing a tendency to loose their euploidy during the in-vitro cultivation process and therefore loose their totipotency, especially to contribute to the germ line. Also the development of abnormal fetuses was observed in EC-cell derived chimeras (Rossant and McBurney, 1982). More stable results can be obtained with embryonal stem ES-cells (Evans and Kaufman, 1981), which can be isolated from in vitro attached mouse blastocysts and grown in culture for many passages. After microinjection of EK-cells into expanded mouse blastocysts, Bradley et al. (1984) obtained an average birth rate of 70%; about 50% of the born young proved to be chimeric, of which 20% also showed germ line chimerism. Stewart, Vanek and Wagner, (1985) aggregated 8-cell-stage mouse embryos with ES-cells and received birth rates of 36%, 20% of the pups being chimeric. The successful us of genetically transformed ES-cells (Stewart, Vanek and Wagner, 1985; Robertson et al., 1986) led to the expression of the transferred genes within somatic tissues of the chimeric animals. Robertson et al. (1986) injected 10 to 12 ES-cells, which had been repeatedly exposed to psi-2 cells for transfection and selected for transformation, into expanded mouse blastocysts. Out of 21 mice born after transfer 20 proved to be chimeric, of which two were reported to have transgenic offspring. According to Evans (1987), 20% to 30% germ line chimerism can be achieved by this method.

A very critical step in this approach of producing transgenic animals is the successful transformation of the ES-cells. There are several possibilities to introduce foreign genes into the genomes of these cells with variable degrees of efficiency and technical equipment and skill required. The calcium-phosphate-precipitation method, which is comparatively simple, yields only very few transformants (frequency 10^{-6} to 10^{-7}), but can be used if large numbers of totipotent cells are available (Pellicer et al., 1980; Lovell-Badge, 1987; Lovell-Badge et al., 1985).

One alternative method to transform EC- of ES-cells more efficiently is the use of recombinant retroviruses (Stewart, Vanek and Wagner, 1985; Robertson et al., 1986; Rubenstein, Nicholas and Jacob, 1984). Rubenstein, Nicholas and Jacob (1984) infected EC-cells with psi-2 cell propagated recombinant retrovirus and demonstrated that 1 of 250 EC-cells had incorporated the retrovirus without observing any further multiplication of the virus in these cells. The efficiency of this retrovirus-mediated transformation method can be further increased depending on the infectivity and the titer of the recombinant virus as well as on the time of exposure (Robertson et al, 1986).

If retroviral infection cannot be established for some reason, microinjection of DNA into the nuclei of totipotent embryonal cells offers a third most effective but cumbersome method of gene transfer with a frequency of 10^{-2} to 1 (Lovell-Badge, 1987).

Control of tissue specific expression

Most transgenic animals produced to date or planned for agricultural use utilize fusion genes composed of genetic regulatory regions from one or more genes fused to the structural gene coding for the protein product desired to be delivered to the resulting transgenic animal. One of the purposes of the regulatory regions of these fusion genes is to direct expression of the transgene product to a specific tissue or group of tissues within the animal. Tissue specific expression of a constructed fusion gene was first demonstrated by Ornitz and coworkers (1985) who linked the rat

elastase regulatory region to the human growth hormone structural gene and produced transgenic mice expressing growth hormone exclusively in the pancreas. Since then, much transgenic research has focused on the development of fusion genes which contain the information necessary for tissue specific expression patterns. Although eukaryotic gene regulation, especially in mammals, remains unclear in many respects, in particular when the involvement of cell specific trans-acting factors is considered, some cis-acting elements have been found to provide tissue specific expression in transgenic mice when fused to structural genes. These elements, termed tissues specific enhancers, are discrete DNA sequences which, apparently, interact with some protein factor in specific tissues to "open" or activate the promoter of the associated fusion gene. In the absence of this factor, in non-target tissues, these sequences may block or repress the action or the promoter. Some examples in which gene expression was strictly directed into promoter specific tissues in transgenic animals are listed in Table 1.

Table 1. Promoter Specific Expression of Foreign Genes in Transgenic Mice

Promoter	Structural Gene	Reference
elastase I (rat)	elastase I (rat)	Swift et al., 1984
elastase I (rat)	growth hormone (human)	Ornitz et al., 1985
myosin-L-chain (rat)	myosin-L-chain (rat)	Shani, 1985
beta-globin (human)	beta-globin (human)	Townes et al., 1985
beta-globin (mouse)	beta-globin (human)	Chada et al., 1985
insulin II (rat)	SV40 T antigen	Hanahan, 1975
alpha-a-crystallin (mouse)	CAT (prokaryotic)	Overbeek et al., 1985
alpha-l-collagen (mouse)	CAT (prokaryotic)	Khillan et al., 1986
insulin (human)	insulin (human)	Bucchini et al., 1986 Selden et al., 1986
skeletal muscle actin (rat)	epsilon-globin (human)	Shani, 1986
whey acidic protein (mouse)	Ha-ras oncogene (human)	Andres et al., 1987
delta-crystalling (chicken)	delta-crystallin (chicken)	Kondoh et al., 1987
alpha-l-antitrypsin (human)	alpha-l-antitrypsin (human)	Sifers et al., 1987
pancreatic amylase (mouse)	pancreatic amylase (mouse)	Osborn et al., 1987

External regulation of transgene expression

Often, for livestock applications, it is not sufficient to regulate the expression of the transgene to a specific tissue or set of tissues since the continued expression of the transgene is detrimental to the animal. An excellent example of this problem is provided by growth hormone transgenic pigs. While pigs injected with growth hormone for discrete periods of their growth phase remain healthy and differ significantly from untreated pigs only in performance traits, which are improved (Chung, Etherton and Wiggins, 1985; Etherton et al., 1986), transgenic swine expressing growth hormone

continuously in several tissues throughout the animals life cycle display gross abnormalities (Pursel, 1987; Hammer et al., 1986). On this basis, it seems likely that external regulation of a growth hormone transgene in swine, and, perhaps, other livestock species, allowing expression of the gene only during the preferred period, would result in improved and highly useful animals for agriculture. An experiment involving the external regulation of a growth hormone transgene in mice and pigs, performed in our laboratory recently, serves as a good example of the value of external regulation of transgene expression.

a.) Aggregation of Cleavage Stages with ES-Cells
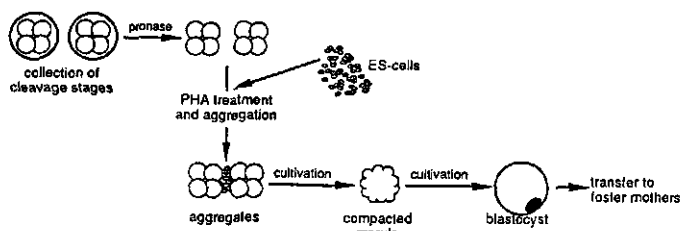
b.) Injection of ES-cells into Blastocysts
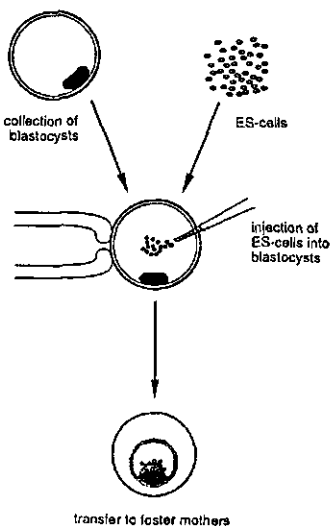
Figure 3.Production of chimeras with transformed totipotent cells.

(Reprinted, with permission, from **Genetic Engineering, Principles and Methods,** Vol. 10, Edited by Jane K. Setlow)

The gene for the cytosolic form of the gluconeogenic enzyme, P-enolpyruvate carboxykinase (GTP) E.C.4.1.1.32 (PEPCK) in most mammalian species is expressed primarily in the liver and kidney cortex (Machlin, 1972; Johnsson, Hart and Butler-Hogg, 1985). This enzyme is generally regarded as catalyzing the pace setting step in hepatic gluconeogenesis (Eisemann et al., 1986). In all mammalian species, PEPCK is absent during fetal development and appears initially at birth (McKeith, 1987; Pursel, 1987) when the transcription of the gene is markedly stimulated by the

rapid fall in the concentration of blood glucose in the neonate (Hammer et al., 1986). The rate of synthesis of the enzyme is regulated by hormones such as glucagon (acting via cAMP), glucocorticoids and thyroxine, which increase its synthesis and by insulin which markedly suppresses the synthesis of the enzyme (Nordlie and Lardy, 1963; Hanson and Mehlman, 1976; Rognstad, 1979). The major point of regulation of the expression of the PEPCK gene is at the level of gene transcription, which is rapidly altered by the hormones mentioned above (Ballard and Hanson, 1967; Yeung and Oliver, 1968). The gene for the enzyme has been isolated (Girard, Bol and Asson, 1972), the cDNA sequence (Tilghman et al., 1974; Gunn et al., 1975) and the promoter-regulatory region characterized by a systematic series of deletions through the first 400 BP of the 5' flanking DNA (Tilghman et al., 1976, Lamers, Hanson and Meisner, 1982). This segment of DNA contains a cAMP regulatory element at -80 to -91, two putative glucocorticoid regulatory elements and an insulin responsive region (Lamers, Hanson and Meisner, 1982). This region of DNA contains multiple binding domains for specific proteins which control the complex pattern of expression characteristic of the PEPCK gene (Granner et al., 1983).

Recently, we reported that 450 bp of the promoter-regulatory region of the PEPCK gene can drive the specific expression of the bGH structural gene in the liver and kidney of transgenic mice (Yoo-Warren et al., 1983). A series of mice were produced in these experiments, which contained serum bGH levels ranging from a low of 5 ng/ml to more than 2000 ng/ml. Mice with high rates of bGH production were often double the weight of their littermates which did not contain the transgene. Furthermore, expression of the chimeric PEPCK/bGH gene was regulated by diet and by hormones in a manner predicted from our previous studies on the expression of the endogenous PEPCK gene in rat liver (Beale et al., 1985). Feeding animals a diet high in carbohydrate for one week caused a 90% reduction in the concentration of bGH in the serum, suggesting that the regulation of the chimeric PEPCK/bGH gene is sensitive to insulin. Furthermore, when the same animals were re-fed a diet high in protein devoid of carbohydrate, the concentration of bGH in their protein devoid of carbohydrate, the concentration of bGH in their blood was induced by 30-fold in a week. The administration of Bt2cAMP to transgenic mice cause a 2-3 fold induction of bGH in the serum within 90 min. The animals all appear healthy and are reproductively active. More recently, the total absence of bGH messenger RNA in any tissue of these transgenic mice during all stages of embryonic development and before birth has been confirmed by sensitive Northern hybridization analysis.

Thus, the PEPCK promoter-regulatory region seems to be an excellent vehicle for acutely regulating the tissue specific expression of linked structural genes, when introduced into the germ line of animals by microinjection into the male nucleus of the one cell embryo. Through the use of the native PEPCK promoter-regulatory region or specific modifications of this region allowing absolute regulation of any structural gene fused adjacent to these sequences, it may be possible to generate transgenic animals which will not express their transgene product until they are fed a diet devoid of carbohydrate. These animals might then harbor "dormant" transgenes which otherwise might be lethal, debilitating or restrictive to reproduction. Such animals might be of real value as research tools.

The success with the mouse system regulated by the PEPCK promoter-regulatory region suggested its potential value in transgenic livestock applications as well. In order to produce transgenic swine with a phenotype mimicking the performance traits of swine injected with the growth hormone protein, a linear fragment containing the PEPCK-bGH gene (Yoo-Warren et al., 1983) was injected into the pronuclei of fertilized swine eggs and over 100 swine were produced.

The approximate number of integrated PEPCK-bGH gene sequences in these animals was determined by dot hybridization and positive animals were demonstrated to contain the integrated sequences with copy numbers ranging from 1 to 200 copies per cell. Over 20 transgenic animals showed significant levels of bovine growth hormone protein in their circulating serum, with concentrations ranging from 5 ng/ml to 200 ng/ml, as determined by radioimmune and ELISA assays. These animals showed remarkable improvements in performance traits including a 30% increase in the efficiency of feed utilization and a greater than 65% decrease in back fat, while

remaining healthy and free from any infirmities well beyond market weight. They also have been proven to be reproductively normal.

These experiments demonstrate that, when appropriately regulated, genes transferred into the germline of agricultural animals can have a profound and positive effect on animal performance and the economics of animal husbandry. During the last several years, studies in mice have proven that transgene expression may be regulated as to the time and tissue of choice. Application of these principles, through the use of the PEPCK promoter/regulatory element, has resulted in the production of lines of transgenic swine with increased economic efficiency (feed:gain ratios) which produce a leaner meat product. In economics of swine husbandry, animals like these could have a significant positive influence on the health of the consumer of pork products, since the U.S. National Academy of Sciences has recently reported that the consumption of excessive animal fat is the most significant contributor to diet-related disease in the U.S. and probably many other countries (Cook et al, 1986).

The growth hormone transgenic swine serve as an example of the potential of transgenic livestock in agriculture. Applications of the technology to increase disease resistance and enhance prolificacy in a wide variety of livestock, in addition to enhancing growth characteristics are underway in several laboratories throughout the world. The ability to externally regulate the transgene in transgenic livestock using systems like the PEPCK regulatory region enhances the potential of producing useful and practical transgenic livestock.

Future prospectives

If the technology to introduce and appropriately regulate transgenes in livestock becomes perfected in the near future, it will have a major impact upon animal breeding. With transgenics it should be possible to select animals with native genomic traits which are more supportive of transgenic effects yielding an animal superior to both an unselected transgenic and a "classically" bred animal. The combination of transgenic technology and established selective breeding methods appears to offer unique opportunities for the animal breeder and suggests a resurgence of basic research in animal breeding.

References

Andres, A.-C., Schonenberger, C.-A., Groner,B., Hennighausen, L.,LeMeur, M. and Gerlinger, P., 1987. Proc. Nat. Acad. Sci. U.S.A. 84, 1299-1303.

Ballard, F.J. and Hanson, R.W., 1967. Biochem. J. 104, 866-872.

Beale, E.G., Chrapkiewicg, N.B., Scoble, H.A., Metz, R.J., Wuick, D.P., Nobble, R.L., Donalson, J.E., Beimann, K. and Granner, D.K., 1985. J. Biol. Chem. 260, 10749-10760.

Bradley, A., Evans, M., Kaufman, M.H. and Robertson, E., 1984. Nature 309, 255-256.

Brinster, R.L., Chen, H.Y., Trumbauer, M.E., Yagle, M.K. and Palmiter, R.D., 1985. Proc. Nat. Acad. Sci. U.S.A. 82, 4438- 4442.

Buchini, D., Ripoche, M.A., Stinnakre, M.G., Desbois, P., Lores, P., Monthioux, E., Absil, J., Lepesant, J.-A., Pictet, R. and Jami, J., 1986. proc. Natl. Acad. Sci. U.S.A. 83, 2511-2515.

Chada, K., Magram, J., Raphael, K., Radice, G., Lacy, E. and Constantini, F., 1985. Nature 314, 377-380.

Chung, C.S., Etherton, T.D. and Wiggins, J.P., 1985. J. Animal Science 60, 118-130.

Costantini, F. and Lacy, E., 1981. Nature 294, 92-94.

Cook, J.S., Weldon, S.L., Garcia-Ruiz, J.P., Hod, Y. and Nanson, R.W., 1986. Proc. Natl. Acad. Sci. U.S.A. 83, 7583- 7587.

Eisemann, J.H., Tyrrell, H.F., Hammond, A.C., Reynold, P.J., Bauman, D.E., Haaland, G.L., McMurtry, J. and Varga, G.A., 1986. J. Nutrition 116, 157-163.

Etherton, T.D, Wiggins, J.P., Chung, C.S., Evock, C.M., Rebhun, J.F. and Walton, P.E., 1986. J. Animal Science 63, 1389-1399.

Evans, M.J., 1987. 3rd Internat. Symp. Cell. Endocrinol., Lake Placid.

Evans, M.J. and Kaufman, M.H., 1981. Nature 292, 154-156.

Girard, J., Bol, D. and Asson, R., 1972. Hormone and Metab. Res. 4, 168-170. NY.

Gordon, J.W. and Ruddle, F.H., 1981. Science 214, 1244-1246.

Gordon, J.W., Scangos, G.A., Plotkin, D.J., Barbosa, J.A. and Ruddle, F.H., 1980. Proc. Natl. Acad. Sci. U.S.A. 77, 7380-7384.

Granner, D., Andreone, T., Sasaki, K. and Beale, E., 1983. Nature 305, 549-551.

Gunn, J.B., Tilghman, S.M., Hanson, R.W.,Reshef, L. and Ballard, F.J., 1975. Biochemistry 14, 2350-2357.

Hammer, R.E., Pursel, V.G., Rexroad, Jr., C.E., Wall, R.J., Bolt, D.J., Palmiter, R.D. and Brinster, R.L., 1986. J. Animal Science 86, 269-278.

Hanahan, D., 1975. Nature 315, 115-122.

Hanson, R.W. and Mehlman, M.H., 1976. *Gluconeogenesis: Its Regulation in Mammalian Species*, John Wiley and sons, New York.

Jaenisch, R., 1976. Proc. Nat. Acad. Sci. U.S.A. 73, 1260-1264.

Jaenisch, R., Fan, H. and Croker, B., 1975. Proc. Nat. Acad. Sci. U.S.A. 72, 4008-4012.

Jaenisch, R., Jahner, D., Nobis, P., Simon, I., Lohler, J., Harbers, K. and Grotkopp, D., 1981. cell 24, 519-529.

Jaenisch, R. and Mintz, B., 1974. Proc. Nat. Acad. Sci. U.S.A. 71, 1250-1254.

Johnsson, I.D., Hart, I.C. and Butler-Hogg, B.W., 1985. Animal Production 41, 207-217.

Khillan, J.S., Schmidt, A., Overbeek, P.A., Crombrugghe, B. de and Westphal, H., 1986. Proc. Natl. Acad. Sci. U.S.A., 83, 725-729.

Kondoh, H., Katoh, K. Takahashi, Y., Fujisawa, H., Yokoyama, M., Kimura, S., Katsuk, M., Saito, M., Nomura, T., Hiramoto, Y. and Okada, T.S., 1987. Dev. Biol. 120, 177-185.

Lamers, W.H., Hanson, R.W. and Meisner, H.M., 1982. Proc. Natl. Acad. Sci. U.S.A. 79, 5137-5141.

Lovell-Badge, R.H., 1987. in Teratocarcinomas and Embryonic Stem Cells - A Practical approach (Robertson, E.J., ed., 153-182, IRL Press, Oxford.

Lovell-Badge, R.H., Bygrave, A.E., Bradley, A., Robertson, E. Evans, M.J. and Cheah, K.S.E., 1985. Cold Spring Harbor Symp. Quant. Biol. 50, 707-711.

Machlin, L.J., 1972. J. Animal Science 35, 794-799.

Mann, R., Mulligan, R.C. and Baltimore, D., 1983. cell 33, 153-159.

McKeith, F. in *The Repartitioning Revolution: Impact of Somatotropin and Beta Adrenergic Agonists on Future Pork Production*, Proceedings of the Pork Industry Conference, 69-83 (Univ. of Illinois, Urbana-Champaign, 1987.

McLaren, A., 1976. Mammalian Chimeras, Cambridge University Press, England.

Nordlie, R.C. and Lardy, H.A., 1963. J. Biol. Chem. 258, 2259-2263.

Ornitz, D.M., Palmiter, R.D., Hammer, R.E., Brinster, R.L., Swift, G.H. and MacDonald, R.J., 1985. Nature 313, 600-602.

Osborn, L., Rosenberg, M.P., Keller, S.A. and Meisler, M.H.,, 1987. Mol. Cell. Biol. 7, 326-334.

Overbeek, P.A., Chepelinsky, A.B., Khillan, J.S.,Piatigorsky, J. and Westphal, H., 1985. Proc. Natl. Acad. Sci. U.S.A. 82, 7815-7819.

Pellicer, A., Robins, D., Wold, B., Sweet, R., Jackson,J., Lowy, Roberts, J.M., Sim, G.K., Silverstein, S. and Axel, R., 1980. Science 209, 1414-1427

Pursel, V. in *The Repartitioning Revolution: Impact of Somatotropin and Beta Adrenergic Agonists on Future Pork Production,* Proceedings of the Pork Industry Conference, 12-18 (Univ. of Illinois, Urbana-Champaign, 1987.

Van der Putten, H., Botteri, F.M., Miller, A.D., Rosenfeld, M.G., Fan, H., Evans, R.M. and Verma, I.M., 1985. Proc. Nat. Acad. Sci. U.S.A.

Robertson, E., Bradley, A., Kuehn, M. and Evans, M., 1986. Nature 323, 445-448. 82, 6148-6152.

Rognstad, R., 1979. J. Biol. Chem. 254, 1875-1878.

Rossant, J. and McBurney, M.W., 1982. J. Embryol. Exp. Morph. 70, 99-112.

Rubenstein, J.L.R., Nicholas, J.F. and Jacob, F., 1984. Proc. Nat.

Rubenstein, J.L.R., Nicholas, J.F., and Jacob, F., 1986. Prod. Nat Acad. Sci. U.S.A. 83, 366-368. Acad. Sci. U.S.A., 7137-7140.

Selden, R.F., Skoskiewicz, M.J., Howie, K.B., Russell, P.S. and Goodman, H.M., 1986. Nature 321, 525-528.

Sifers, R.N., Carlson, J.A., Clift, S .M., DeMayo, F.J., Bullock, D.W. and Woo, S.L.C., 1987. Nucl. Acids res. 15, 1459-1475.

Shani, M., 1985. Nature 314, 283-286.

Shani, M., 1986. Nol. cell. Biol. 6, 2624-2631.

Stewart, C.L., Vanek, M. and Wagner, E.F., 1985. Embo J. 4, 3701-3709.

Strojek, R.M. and Wagner, T.E., 1988. Genetic Engineering, Principles and Methods 10, 221-246.

Stuhlmann, H., Cone, R., Mulligan, R.C. and Jaenisch, P., 1984. proc. Nat. Acad. Sci. U.S.A. 81, 7151-7155.

Swift, G.H., Hammer, R.E., MacDonald, R.J. and Brinster, R.L., 1984. Cell 38, 639-646.

Tilghman, S.M., Gunn, J.M., Fisher, L.M., Hanson, R.W., Reshef, L. 54.Townes, T.M., Lingrel, J.B., Chen, H.Y., Brinster, R.L. and Palmiter, R.D., 1985. Nature.314, 1715-1723 and Ballard, F.J. 1975. J. Biol. Chem. 250, 3322-3329.

Tilghman, S.M., Hanson,R.W., Reshef, L., Hopgood, M.F. and Ballard, F.J., 1974. Proc. Natl. Acad. Sci., U.S.A. 71, 1304.

Wagner, T.E., Hoppe, P.C., Jollick, J.D., Scholl D.R., Hodinka, R.J. and Gault, J.B., 1981. Proc. Natl. Acad. Sci. U.S.A. 78, 6376-6380.

Wagner, E.F., Stewart, T.A. and Mintz B., 1981. Proc. Nat. Acad. Sci. U.S.A. 78, 5016-5020.

Watanabe, T., Dewey, M.J. and Mintz, B., 1987. Proc. Nat. Acad. Sci. U.S.A. 75, 5113-5117

Wilkie, T.M., Brinster, R.L. and Palmiter, R.D., 1986. Dev. Biol. 118, 9-18.

Yeung, D. and Oliver, I.T., 1968. Biochem. J. 108, 325-331.

Yoo-Warren, H., Momahan, J.E., Short, J. Meisner, H.M., Samols, D. and Nanson, R.W., 1983. Proc. Natl. Acad. Sci. U.S.A. 80, 3656-3660.

SOMATOTROPIN RELATED TECHNOLOGIES: IMPLICATIONS FOR PIG BREEDING

Egbert Kanis

Wageningen Agricultural University, Department of Animal Breeding, P.O. Box 338, 6700 AH Wageningen, The Netherlands

Summary

The use of present and future biotechnological techniques for control of growth and body composition will have important implications for pig breeding programs. This can be expected from somatotropin related technologies in particular, because of the marked positive effects of somatotropin on feed conversion ratio and body composition. In this paper the implications of porcine somatotropin (PST) administration and the use of animals which are transgenic for somatotropin genes are considered.

Administration of PST on a large scale may have indirect consequences for selection intensity and genetic response. Breeding goal traits and their economic values have to be re-evaluated. In case of interactions between genotype and PST administration it is recommended to administer PST to nucleus animals during performance tests. Genetic and phenotypic parameters (heritabilities and correlations) should be re-estimated.

PST can open new possibilities for introduction of very prolific (Chinese) breeds as dam line in the breeding program. Negative impact of Chinese genotypes on carcass composition can be counteracted by PST administration. PST will increase the optimum slaughter weight and so decrease the number of pigs to be produced per year if the total pork production is fixed. As a consequence fewer commercial sows are needed and production costs will decrease.

Successful transfer of the somatotropin gene into the germ line of pigs will eventually have implications for growth and body composition similar to PST administration. In addition, however, the use of transgenic pigs will have enormous implications for the breeding strategy in the nucleus. Variation between the produced founder transgenics is expected to be high and many animals will have to be culled because of negative characteristics. The remaining transgenics should be utilized for breeding very intensively, giving problems of small population sizes. The optimum breeding strategy depends on whether homozygosity is desired in the commercial end product and whether introduction of other foreign genes can be continued successfully in lines that are already transgenic for a somatotropin gene.

It is concluded that development and introduction of transgenics in the nucleus of a pig breeding program is very capital and research intensive. This can only be successful by combining the efforts in joint ventures of breeding organizations.

Keywords: somatotropin, transgenics, pig breeding, biotechnology.

Introduction

Animal improvement by human beings has already a long history. As symbolized in Figure 1, (after Skjervold, 1976) genetic improvement occurs partly in steps and partly as gradual progress. Starting as hunters, man selected some of the animal species for domestication. During many centuries these species have been gradually changed and improved by means of selection and

adaptation to the environment and care that man offered his animals. Different breeds and strains emerged because of geographical isolation and different selection directions. Crossbreeding created new ways for improvement by utilization of heterosis. Some examples of inter-species crossing are known, such as horse and donkey but, fitting into the definition of a species, their progeny is not fertile. At present it is possible to transfer single genes from one species to another (Palmiter et al., 1982; Hammer et al., 1985). Some of the resulting transgenic animals are fertile and some are not (Pursel, 1987). It is conceivable that it will be possible and worthwhile in future to combine several kinds of favourable genes into one new species. In the last 50 years most of the genetic improvement came and now still comes from intensive selection of better genotypes in purebred lines. Developments in artificial insemination and embryo handling increase selection intensity and contribute strongly to that improvement.
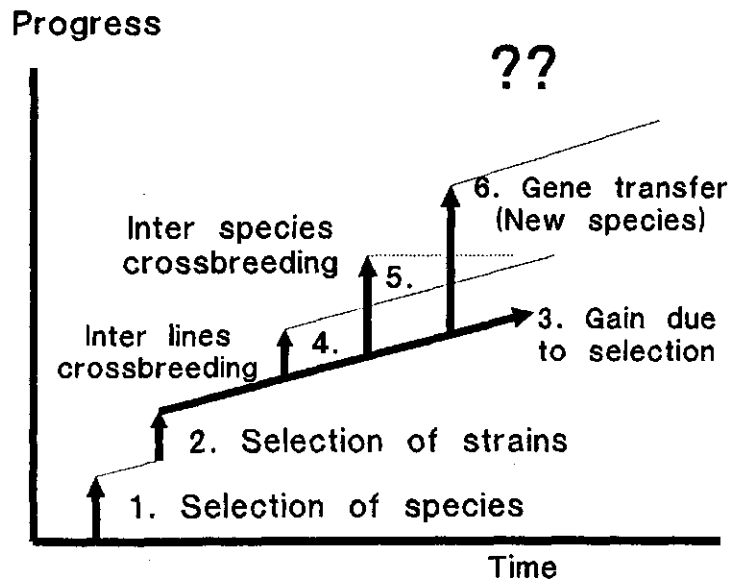

Figure 1. Schematic representation of genetic progress with different methods, after Skjervold (1976). Length of arrows is not related to relative progress.

Genetic values for traits which are controlled by many genes, such as growth, feed conversion ratio and slaughter quality can normally not be measured because of the inability to identify all single genes and gene combinations in question. Therefore, estimation of breeding values and selection is based on phenotypic information from the potential breeding animals themselves and from relatives. Smith (1984) showed that the rate of genetic change is in the range of 1 to 3 % per year for most economic traits. The accuracy of selection increases by the use of more phenotypic information. However, with present selection methods it is inevitable that apart from favourable genes also a proportion of unfavourable genes is carried over to the next generation.

By means of biotechnology it is now possible to change specific single genes or gene products. One of the genes that can play a major role in further improvement of production traits in pigs is the somatotropin gene. Together with somatotropin releasing factor, somatomedins and somatostatin, somatotropin has a large impact on growth and body composition. The somatotropin gene has been cloned and transferred into bacteria and higher animal species, including swine. In the first case bacteria are activated to produce recombinant porcine somatotropin (PST) which can be administered to pigs. In the second case transgenic pigs produce the extra somatotropin themselves.

Although several other related biotechnologies for control of growth are available (Van der Wal, 1988), this contribution is focussed on administration of PST and on use of animals which are transgenic for the somatotropin gene. Particularly concerning the administration of PST a lot of experimental data are available about effects on production performance. Transgenic pigs are a relatively new phenomenon and there is not a clear picture yet about effects on different aspects of production.

For both technologies literature on implications for breeders and breeding programs is scarce. Concerning the impact of repartitioning agents on genetic improvement programs a review has been presented at the Pork Industry Conference in Illinois by McLaren (1987). Literature about implications of the use of transgenic animals (transgenics) in pig breeding programs was not found, although work by Smith et al. (1987) concerning use of transferred genes (transgenes) in livestock in general has many applications in swine. The purpose of this contribution is to consider the possible implications for genetic improvement of administration of PST and use of transgenic pigs in swine production.

Administration of PST

Effects of daily PST administration on production performance of fattening pigs are described by many authors (e.g. Chung et al., 1985; Etherton et al., 1987; Campbell et al., 1988). In general an increase in growth and carcass meat content and a decrease in feed intake, feed conversion ratio and carcass fat content are found in animals treated from 60 to about 100 kg live weight. There is evidence that effects are smaller in leaner animals (Hüster et al., 1988; Kanis et al., 1988a) and larger in animals treated till higher weights (Kanis et al., 1988a). Data from Boyd (1987) show that milk production of lactating sows and growth of nursing piglets can be significantly improved by daily treatment of lactating sows with PST.

Present constraints for use of PST in practice are the facts that it is not yet approved and that no practical method for administration is available at the moment. Till now most results concerning PST are based on daily intra-muscular injections. However, in intensive pig production systems as in West-European countries, only one or two administrations per animal during the fattening period can be considered as practicable. If PST is approved and if a practical and effective method of administration is available at an acceptable price, then PST will have a substantial effect on total pig production.

In this part of the paper implications of administration of PST are discussed for:

- selection and genetic response,
- possibilities for hyper-prolitie breeds,
- slaughter weights.

Implications for selection and genetic response

Modern pig breeding programs have a more or less pyramidal structure (Figure 2) with a relatively small number of nucleus breeders on top who sell purebred animals or semen to multipliers that produce crossbred parents. From these parents crossbred piglets are produced by commercial producers who sell these piglets to the commercial fattening farms where they are fattened. Sometimes two layers (for example multiplier sows and fattening pigs) can be found on one farm. It should be realized that the bottom layer consists of the end products whose financial returns should balance all costs made in the total pyramid.

It has been proved that genetic improvement in all layers of the pyramid (and so in the bottom layers of commercial producers) fully depends on the genetic improvement in the nucleus. (Bichard, 1971). The genetic lag (or time lag) between the lower layers of the pyramid and the nucleus depends on efficiency of the dissemination of genetic superiority from the nucleus through the pyramid.
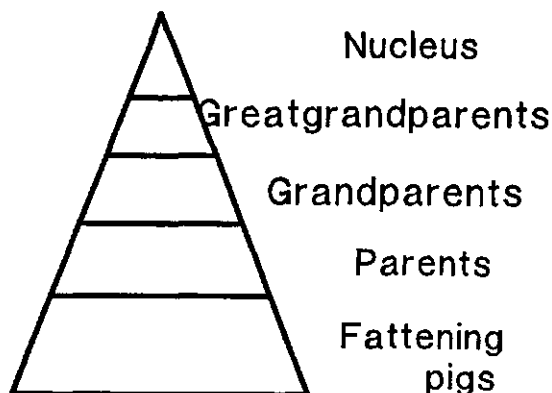
Nucleus
Greatgrandparents
Grandparents
Parents
Fattening
pigs

figure 2. Production structure in pig breeding programs.

Genetic response to selection in a nucleus line can be predicted by

$$R = (i\, r_{IH}\sigma_H) / L$$

where R = predicted genetic response per year,
    i = selection intensity,
   r_{IH} = selection accuracy,
   σ_H = standard deviation of the breeding goal or aggregate genotype,
    L = generation interval in years.

Administration of PST to fattening pigs does not create a genetic effect in itself, but may have indirect consequences for each of these four parameters or for the genetic lag between nucleus and fattening pigs.

Selection intensity and genetic lag

Use of PST in fattening pigs will not directly influence the selection intensity for replacement animals in a nucleus of fixed size. However, because of faster growth of fattening pigs, more slaughter pigs can be produced per year with fixed fattening facilities. Therefore, more commercial sows are needed and particularly in the dam lines, more nucleus females must be assigned for replacement of sows in lower layers of the pyramid. These extra sows will on average have a lower genetic superiority and therefore an increasing effect on the genetic lag between nucleus and fattening pigs.

Use of PST in lactating commercial sows might result in shorter intervals between successive farrowings. Assuming a fixed nucleus size, no change in number of farrowings per sow and sufficient fattening facilities, this results in more commercial sows needed per year and an increasing genetic lag.

The opposite happens if the amount of pork to be produced per year is fixed. Because of higher meat percentage per pig or a possibly higher slaughter weight with use of PST, the same amount of pork can be produced by fewer sows and slaughter pigs. With a fixed size of the nucleus this results in a shorter genetic lag. It should be realized, however, that eventually a decreasing number of slaughter pigs may also have a decreasing effect on the size of the nucleus dam lines. This will then result in lower total production costs.

Selection accuracy

The accuracy of selection depends on heritabilities, genetic and phenotypic correlations of the traits involved and on the amount of own performance data and information from relatives. It is unknown whether administration of PST has influence on heritabilities and correlations. For

instance, if PST is able to neutralize certain negative environmental effects, as is sometimes thought from antibiotics and feed additives, this may reduce phenotypic variation and thus increase heritabilities and selection accuracies.

Use of PST in fattening pigs may cause genotype by environment interaction if the nucleus animals are not selected in a PST environment. This results in a lower selection accuracy because the breeding goal should be defined at the level of commercial fattening pigs (Merks, 1988). There fore, if PST would be generally used, it is recommended to administer PST during performance test in the nucleus in order to create an environment similar to that in fattening farms. In addition, because of faster growth in the nucleus more animals can be tested and selection intensity might increase. Another way to cope with this type of genotype by environment interaction is to base selection on information from PST treated relatives.

It is not known whether administration of PST has impact on puberty and fertility of potential breeding animals. This is also relevant to commercial producers who practice rotational crossbreeding and select female replacements from the finishing pens (McLaren, 1987). Data from McLaren (1987) show that weights of ovaries and uteri of PST-treated gilts are significantly increased. Functional effects of these higher weights are unknown.

In case of selection based on "on the farm testing", as is carried out in Dutch pig herdbooks to select females, the farmer can apply preferential treatment by administering PST to some animals only. If it is not recorded which animals are treated, then an unbiased estimation of breeding values is impossible and PST treated animals will be overestimated. If recording of PST treatment (and the doses used) is reliable, which is impossible to check, then corrections for these environmental effects could be carried out. For bovine somatotropin the potential impact on dairy sire evaluation has been simulated by Burnside and Meyer (1988).

Aggregate genotype

Use of PST may have important implications for the traits to be incorporated in the aggregate genotype (breeding goal) and the relative economic weight of each trait. Because PST has a decreasing effect on appetite, feed intake capacity will become of greater economic importance, whereas lean percentage will become less important because of its increased level. Furthermore, meat quality traits may get higher economic values because of lower intra-muscular fat contents (Beermann et al., 1988; McKeith et al., 1988).

Although genetic differences for response to PST treatment may exist, it is probably not advisable to select for PST responsiveness in cases PST is used on a large scale. Kanis et al. (1988a) showed that, with respect to carcass composition, fatter breeds respond more to PST administration than leaner breeds. It is likely that also within breeds, animals with the highest response to PST have the highest genetic potential for fat production. Moreover, the response to PST administration in terms of improvement of production traits is hard to measure in individual animals.

Generation interval

Impact on generation intervals depends on effects of PST on age at puberty in young breeding stock and on intervals between subsequent farrowings in case lactating nucleus sows are treated. Moreover, a higher slaughter weight in commercial fattening pigs, if treated with PST (see part c, below) could ask for performance tests of nucleus animals till higher weights. However, because performance test will normally be finished before puberty is reached, it is not expected that PST has much influence on average generation intervals.

Quantification of the potential implications above is difficult because of the many unknowns. Heritabilities, genetic correlations and genotype x environment interactions should be estimated in datasets of a large size with an appropriate genetic structure. Adaptations that are needed for optimization of breeding programs with use of PST can be sufficiently quantified only after introduction of PST on a large scale. Simulation studies may give some extra insight in the complications for breeding. It is foreseen that use of PST may change the ranking of breeding organizations for their final products because of different responses. Furthermore, efficiency of selection may be temporary decreased because of the use of unadapted genetic, phenotypic and

economic parameters. At this moment no great long term implications of the use of PST for genetic improvement are expected.

Possibilities for hyper-prolific breeds

Commercial fattening pigs are often produced as three- or four-breed crossbreds from specialized sire and dam lines. One of the main advantages of crossbreeding is utilization of heterosis which can be subdivided into genetic heterosis due to increased heterozygosity and sire-dam heterosis (Moav, 1966). Genetic heterosis is assumed to be positively correlated with the genetic distance between breeds. Genetic heterosis can be expected for production traits if the fattening pig is a crossbred, and for maternal traits such as litter size at weaning, if the dam is a crossbred. Sire-dam heterosis can be utilized by mating females with excellent fertility to males with good fattening and slaughter qualities. Relative to the average of both parental genotypes sire-dam heterosis will result in more piglets weaned of average production performance, giving a higher total economic merit.

Currently, the use of hyper-prolific Chinese breeds in pig breeding programs is considered. Females of the Chinese Meishan breed produce three to four weaned piglets more per litter than French Landrace females (Sellier and Legault, 1986). However, daily gain and feed conversion ratio of Meishan pigs are unfavourable and the carcasses are very fat. Crossbreeding to European breeds may partly remove these negative characteristics. However, according to Gueblez et al. (1987) the increased productivity of various types of crossbred Chinese sows is insufficient to compensate for the poorer carcass merit of the offspring.

Results from purebred Meishan fattening pigs treated with PST indicate that improvement in carcass composition is larger than in leaner breeds. (Kanis et al., 1988b). Particularly in cases of unacceptable carcass conformation, administration of PST to crossbred Chinese fattening pigs will improve carcass conformation so much that such a crossbreeding system becomes economically attractive.

Possibilities for higher slaughter weight

Results by Kanis et al. (1988a) show that with administration of PST from 60 kg live weight onwards, the response in carcass lean percentage in animals slaughtered at 140 kg was about double the response in animals slaughtered at 100 kg. Averaged over three genotypes, PST-treated animals had 4.4 and 8.7 % more carcass meat at 100 and 140 kg than control animals. The response for daily gain and feed conversion ratio was also much higher in the weight range from 100 to 140 kg than from 60 to 100 kg. Present work (unpublished) on growth curves indicates that PST-treated animals have a more persistent growth and that deposition of extra fat is delayed. Although, over the full range from 100 to 140 kg feed conversion ratio in treated animals is too high from an economic standpoint, PST makes it possible to slaughter animals at higher weights than the usual 100 kg, without excessive production of fat. Assuming a fixed amount of pork to be produced per year, this can then be done with less growing pigs and less sows at lower production prices. On the other hand, higher slaughter weights may require investments for adaptation of slaughter houses and subsequent meat processing chains. Computer simulation can help to determine the optimum slaughter weight from the viewpoint of production costs, costs of slaughtering and processing, production of manure and a shorter genetic lag between nucleus and commercial fattening pigs.

In the points above it is assumed that PST is used as a routine in all situations where it can be of economic advantage. We should be aware, however, of a trend for an increasing consumers' interest for "naturally" produced pork. It may well be that eventually two categories of production systems and breeding programs can exist, with and without use of advanced (bio)technologies.

Transgenic pigs

Literature

Palmiter et al. (1982) were probably the first who published results on transgenic animals carrying extra somatotropin genes. Mice with the structural gene for rat somatotropin and the mouse metallothionein (MT) gene as promoter had a dramatically increased growth rate compared to littermate control mice. At present, an increasing number of publications is available on different farm animals, being transgenic for somatotropin genes from different species, fused to different promoter genes (e.g. Hammer et al., 1985; Wagner, 1988). A number of criteria (Kräusslich, 1986) and limitations (Renard and Babinet, 1987) for useful gene transfer in farm animals have been mentioned in the literature. Land and Wilmut (1987) stated that the favourable effect of a particular gene should be at least 10% to make transfection useful.

Pursel (1987) defined a long-term research goal for insertion of the somatotropin gene into swine DNA as: "to produce transgenic boars that will transmit a controllable somatotropin gene into the genome of their progeny". Specific goals that must be achieved in sequential order to successfully achieve the long-term goal are: 1. Microinjection of a gene into the pronucleus; 2. Integration of somatotropin genes into the pig genome; 3. Expression of the integrated somatotropin gene; 4. Transmission of somatotropin genes to progeny; 5. Regulation of the integrated somatotropin gene.

Recent research has clearly demonstrated that it is possible to achieve goals 1 to 4, however, several abnormalities in transgenic pigs have been observed (Pursel, 1987). It was concluded that tight control over the level of somatotropin production is essential to obtain only the positive effects of transferred somatotropin genes on growth performance. Wagner (1988) states that the Phosphoenolpyruvate carboxikinase (PEPCK) promoter offers great possibilities for external regulation (via the carbohydrate content of the diet) of transgene expression. Moreover, in contrast to for example the widely used MT promoter, the PEPCK promotor is only active after birth and primarily in the liver and kidney cortex. Pigs transgenic for PEPCK/BST (bovine somatotropin) showed remarkable improvements in performance traits, remained healthy and free from any infirmities well beyond market weight and have been proven to be reproductively normal (Wagner, 1988).

It can be concluded from the literature that the five specific goals presented by Pursel (1987) and given above are at least partly achieved on an experimental scale. However, the technology is at present far from perfect and a lot of problems have to be solved. Nevertheless, substantial progress is still being made and it can be anticipated that within a few years the long-term goal is achieved and that transgenic boars (and sows) become available with controllable somatotropin genes. With present techniques it is not possible to control the number of copies and the site of integration of the transferred gene in the genome of the receptor embryos. This may be a source of variation in expression of the transferred gene between transgenic animals and may also influence other characteristics. The question then is how to make optimal use of these animals in pig breeding programs. This question has been dealt with for livestock in general by Smith et al. (1987). In this paper their approach will be followed and applied to somatotropin transgenics in pig breeding.

Breeding goal

The aim of a breeding program with pigs that are transgenic for somatotropin is to produce commercial fattening pigs that are all transgenic for the somatotropin gene and have, therefore, a higher economic merit. It is assumed here that the general structure of breeding programs is maintained and that crossbreeding is still more economical than purebreeding.

At this moment it is not clear whether it is desirable to produce fattening pigs that are homozygous for the extra somatotropin genes. If so, then both sire and dam lines should preferably be homozygous for the transgene. If not, then it is enough to have homozygous sire lines only. The number of copies seems not to be strongly related to the somatotropin level in the blood (Rexroad

et al., 1987). Therefore, it is assumed here that there is not much difference between homozygous and heterozygous animals and that heterozygosity for the transgene is sufficient in commercial fattening pigs. The specific goals then are to maintain and select one or more homozygous transgenic nucleus sire lines with better performance than the existing lines and to keep the genetic lag between nucleus and commercial as short as possible.

If the developed transgenic founder pigs do not belong to a high performance sire line, then backcrossing to the existent sire lines with selection for the transgene may be considered. This process of introgression is similar to introduction of major genes as the Booroola gene in sheep or the gene for halothane insensitivity in swine (e.g. Smith, 1985). However, this is not likely to be an efficient procedure, because it should be possible to directly produce transgenic animals from existing high performing sire lines. Moreover, during introgression a new and better transgene may become available and the whole process should start again. Therefore, to make optimum use of new developments it should be possible to transfer better genes into animals that are already transgenic for another gene.

Homozygous or heterozygous breeding stock

It is assumed now that transgenic founder pigs are offsprings from the best parents of the sire lines and that they are heterozygous for the transgene (carry one copy or a tandem array of copies on one chromosome). Heterozygous animals will transmit the transgene to half of their progeny, whereas homozygous animals transmit it to all progeny. Therefore, if the transgene has a large effect on economic merit, the fastest genetic response can be obtained by making a homozygous line (Smith et al., 1987). With avoiding too much inbreeding this will take at least three generations during which time little selection for production traits can be done. This should be compared with the normal selection response of about two percent per year in pigs (Smith, 1984).

For example in a three-way cross with a generation interval of one year, the economic merit of the transgenic should be at least six percent higher than of normal animals to make homozygosity worthwhile. In that case after three years, fattening pigs from heterozygous sires have on average a three percent higher merit because of transgenity plus six percent because of normal selection in sire and dam lines. After three years, fattening pigs from homozygous sires have six percent higher merit because of transgenity plus three percent because of selection in dam lines only. General formulas are given in Table 1.

In a four-way cross a crossbred boar is used as sire of the commercial fattening pigs. Assuming that 25% of the crossbred male offsprings from two heterozygous sire lines carries transgenes from both lines (called homozygous) and can be separated from the 50% heterozygous animals, then only these homozygous boars should be used as sire to the fattening pigs. This means that extra parental animals are needed to produce the required number of crossbred boars, which reduces selection intensity. If homozygous animals can not be separated from heterozygous animals, then it may be considered to produce first homozygous sire lines in order to get 100% homozygous crossbred boars. In that case the transgene should increase economic merit by at least twelve percent to get better fattening pigs from homozygous (after four years) than from heterozygous purebred sire lines (Table 1). In both examples an extra benefit from using heterozygous sire lines, compared with waiting for homozygous sires, is that the first transgenic fattening pigs are produced much earlier.

Table 1. Dissemination of genetic progress with use of heterzygous vs. homozygous nucleus animals. Normal genetic progress is g % per generation and effect of the transgene is t. Generation 0 are the founder transgenics in the nucleus.

Generation:	Genetic level of growing pigs				
	0	1	2	3	4
Situation I: three way cross (A sire x BC dam)					
Direct use of heterozygous A sires and selection in line A, B and C	0	a+.50t	2a+.50t	3a+.50t	4a+.50t
Use of homozygous A sires, no selection in A during three generations	0	.50a	a	1.50a+t	2.50a+t
Situation II: four way cross (AB sire x CD dam)					
Direct use of heterozygous A and B sires and of homo- and heterozygous AB sires	0	a	2a+.67t	3a+.67t	4a+.67t
Use of homozygous A and B sires, no selection in A and B during three generations	0	.50a	a	1.50a	2a+t

Selection within transgenic lines

Transgenic pigs have to be multiplied by selection and pure breeding, to develop a transgenic breeding pool or line (Smith et al., 1987). It could remain open for new transgenic animals, carrying the same or other transgenes. By means of normal testing and selection procedures the favourable transgenes will be fixed, while others will be gradually eliminated. The chance of fixing a transgene by selection for a quantitative trait depends on the effective population size, the selection intensity, the effect of the transgene and the initial transgene frequency (Smith et al., 1987). To increase the chance of fixation, laboratory tests with DNA probes should be used during the first generations of development.

Although the five conditions given by Pursel (1987) have been met on an experimental scale and transgenic animals can be produced in reasonable numbers, it should be realized that many of the heterozygous and homozygous transgenics may not be useful as breeding stock in a pig breeding program. All transgenic animals should be tested and evaluated thoroughly on a large number of different traits before they can be used for breeding. Those traits are not only the normal production and reproduction traits, but concern for example also the requirements for housing, feeding and hygienic measures. Probably a second selection step is required where selection of transgenics is based on progeny performance. This has an increasing effect on the generation interval and so on the benefits of transgenics relative to normal selection. Particularly from the newly produced transgenics probably many individuals have to be culled. The number of culled animals may even increase if transfer of genes is continued for several different genes, because it may be expected that in "multi-transgenic" animals it is more difficult to find suitable breeding animals than in "uni-transgenic" animals.

The relatively few remaining animals should be used for breeding very intensively. This means that techniques as artificial insemination, multiple ovulation and embryo transfer, embryo splitting, embryo sexing and freezing of embryos and semen will become more important parts of nucleus breeding. However, concentration on a few transgenic breeding animals implies small effective population sizes and risks of inbreeding depression. This should be controlled by production of a sufficient number of founder transgenics from different families and a gradual increase of the size of the line. Until a sufficient size has been reached use of an adequate number of sires per year,

combined with a good selection strategy will avoid the negative effects of inbreeding to a large extent (De Roo, 1988).

Organization

Successful production and introduction of transgenic animals into a pig breeding program will be very capital and research intensive. Considerable investments are necessary and these can only be afforded by large firms. Therefore breeding companies and other organizations involved in biotechnology should cooperate in joint ventures. A strong control of the flow of financial returns from the bottom of the production pyramid to the nucleus will be necessary.

Introduction of transgenes will lead to an increase in the number of (experimental) selection lines because the standard lines will not be replaced immediately. Furthermore, new lines may be developed that are transgenic for different genes.

Conclusions

For administration of PST as well as for the use of animals which are transgenic for the somatotropin gene, many questions have still to be answered before implications for pig breeding can be quantified.

Concerning PST administration a major problem is that new genetic and phenotypic parameters have to be estimated, which can only be done after introduction of PST. Breeding goal traits and economic values should also be re-evaluated.

PST offers new possibilities to introduce prolific Chinese breeds in the breeding program. Administration to commercial fattening pigs, partly from Chinese origin, will counteract the poor carcass quality and the extra fecundity can be fully utilized.

The optimum slaughter weight will increase with use of PST, although the extent depends on a number of economic factors.

If transfer of somatotropin genes is completely successful (microinjection, integration, expression, transmission and regulation), and all commercial fattening pigs carry these extra genes, then the implications for the breeding program may be similar to implications of PST administration. However, many other questions have to be answered first.

It is not known whether for optimum impact on production traits heterozygosity for the transgene is sufficient or that homozygosity should be aimed at. In the latter case all breeds that contribute to the commercial end product should carry the gene, preferably in a homozygous form.

Another problem is the presumed variation between the produced (founder) transgenics. All animals should be tested for a lot of traits and only a few will be acceptable. Problems with small population sizes will arise.

The optimum breeding strategy in the nucleus further depends on the economic merit of the transgene. This is not quantified yet and it may change when better structural genes are isolated and transferred, or when better promoters become available. An important point is whether and when genes can be transferred into animals which are already transgenic for another gene.

Independent of the specific solutions to these problems it is quite clear that production of excellent transgenic animals is very much capital and research intensive. Everything should be done to utilize these animals for breeding as intensive as justified. This will lead to re-organizing of nucleus breeding and to more cooperation and joint ventures of breeding companies.

References

Beermann, D.H., G. Armbruster, R.D. Boyd, R.D. Roneker, and K.D. Fagin, 1988. Comparison of the effect of two recombinant forms of porcine somatotropin (pST) on pork composition and palatability. Abstr. 153, J. An. Sc. 66 (suppl. 1): 281.

Bichard, M., 1971. Dissemination of genetic improvement through a livestock industry. Animal Production 13:401-411.

Boyd, D., 1987. The effect and practical implications of recombinant porcine growth hormone on lactation performance of sows. In: Proc. Pork Industry Conference, Univ. of Illinois, pp. 126-135.

Burnside, E.B. and K. Meyer, 1988. Potential impact of bovine somatotropin on dairy sire evaluation. J. Dairy Sci. 71:2210-2219.

Campbell, R.G., N.C. Steele, T.J. Caperna, J.P. McMurtry, M.B. Solomon, and A.D. Mitchell, 1988. Interrelationships between energy intake and exogenous porcine growth hormone administration on the performance, body composition, and protein and energy metabolism of growing pigs weighing 25 to 55 kg live weight. J. Anim. Sc. 66:1643-1655.

Chung, C.S., T.D. Etherton and J.P. Wiggins, 1985. Stimulation of swine growth by porcine growth hormone. J. Anim. Sc. 60:118-130.

De Roo, G., 1988. Studies on breeding schemes in a closed pig population. Ph.D Thesis, Wageningen Agricultural University, pp. 163.

Etherton, T.D., J.P. Wiggins, C.M. Evock, C.S. Chung, J.F. Rebhun, P.E. Walton and N.C. Steele, 1987. Stimulation of pig growth performance by porcine growth hormone: determination of the dose-response relationship. J. Anim. Sc. 64:433-443.

Gueblez, R., L. Bruel and C. Legault, 1987. Evaluation des croisements Sino-Europeens en conditions de terrain en France. Journees Recherche de Porcine en France 19:25-32.

Hammer, R.E., V.G. Pursel, C.E. Rexroad Jr., R.J. Wall, D.J. Bolt, K.M. Ebert, R.D. Palmiter, and R.L. Brinster, 1985. Production of transgenic rabbits, sheep and pigs by microinjection. Nature 315:680-683.

Hüster, E., D. Ekkel, E. Kallweit, R.E. Ivy, and F. Ellendorf, 1988. The use of recombinant porcine growth hormone to influence growth and body composition in pigs. Acta Endocrinol. 117 (Suppl. 287):74 (Abstr.).

Kanis, E., K.H. De Greef, W. Van der Hel, J. Huisman, R.D. Politiek, M.W.A. Verstegen, P. Van der Wal and E.J. Van Weerden, 1988a. Interactions of recombinant porcine somatotropin (rPST) treatment with genotype and slaughter weight for production traits of growing pigs. Abstr. 189, J. An. Sc. 66 (suppl. 1):296.

Kanis, E., H.A.M. Van der Steen, P.N. De Groot and G.J. Nieuwhof, 1988b. Effects of rPST on growth and carcass quality of Chinese Meishan pigs. In: Proc. Int. seminar on the science of porcine somatotropin, Terre Haute, USA, pp. 208-217.

Kräusslich, H., 1986. Criteria for useful gene transfer. In: Proc. 3rd World Congress on Genetics applied to Livestock Production XII: 22-31.

Land, R.B. and I. Wilmut, 1987. Gene transfer and animal breeding. Theriogenology 27:169-179.

McKeith, F.K., P.J. Bechtel, J. Novakofski, D.G. McLaren, R.A. Easter, R.W. Jones and D.L. Ingle, 1988. Effect of porcine somatotropin on composition of boneless retail cuts from pigs. Abstr. 156, J. An. Sc. 66 (suppl. 1):282.

McLaren, D., 1987. The impact of repartitioning agents on genetic improvement programs. In: Proc. Pork Industry Conference, Univ. of Illinois, pp. 93-104.

Merks, J.W.M., 1988. Genotype x environment interactions in pig breeding programmes. Ph.D. Thesis Wageningen Agricultural University, Wageningen.

Moav, R., 1966. Specialized sire and dam lines. I. Economic evaluation of crossbreds. Animal Production 8:193-202.

Palmiter, R.D., R.L. Brinster, R.E. Hammer, M.E. Trumbauer, M.G. Rosenfeld, N.C. Birnberg and R.M. Evans, 1982. Dramatic growth of mice that develop from eggs microinjected with methallothionein-growth hormone fusion genes. Nature 300:611-615.

Pursel, V., 1987. Potential for inserting the somatotropin gene into the swine DNA: long term goals and implications. In: Proc. Pork Industry Conference, Univ. of Illinois, pp. 12-18.

Renard, J.P. and C. Babinet, 1987. Genetic engineering in farm animals: the lessons from the genetic mouse model. Theriogenology 27:181-200.

Rexroad Jr., C.E., V.G. Pursel, R.E. Hammer, D.J. Bolt, K.F. Miller, K.E. Mayo, R.D. Palmiter and R.L. Brinster, 1987. Gene insertion: Role and limitations of technique in farm animals as a key to growth. In: G.L. Steffens and T.S. Rumsey (eds.), Biomechanisms regulating growth and development. Kluwer Ac. Publ., Dordrecht. pp. 87-97.

Sellier, P. and C. Legault, 1986. The Chinese prolific breeds of pigs: examples of extreme genetic stocks. In: C. Smith, J.W.B. King and J.C. McKay (eds.): Exploiting new technologies in animal breeding. Genetic developments. Oxford University Press, Oxford. pp. 153-162.

Skjervold, H., 1976. Genetic improvement of salmonids for fish culture. In: E.H. Huisman (ed.): Aspects of fish culture and fish breeding. Miscellaneous papers 13, Landbouwhogeschool, Wageningen, pp. 7-27.

Smith, C., 1984. Rates of genetic change in farm livestock. Research and Development in Agriculture 1, 79-85.

Smith, C., 1985. Utilization of major genes. In: R.B. Land and D.W. Robinson (ed.), Genetics of reproduction in sheep. Butterworths, London, pp.151-158.

Smith, C., T.H.E. Meuwissen and J.P. Gibson, 1987. On the use of transgenes in livestock improvement. An. Br. Abstr. 55 (1):1-10.

Van der Wal, P., 1988. Regulatory and public acceptance on biotechnology for control of growth and product quality in swine. This symposium.

Wagner, T.E., 1988. Direct modification of the livestock genome. This symposium.

IMPLICATIONS OF SOMATOTROPIN TO THE PORK PROCESSING INDUSTRY

F.K. McKeith, P.J. Bechtel and J. Novakofski
University of Illinois, Urbana, IL U.S.A

Summary

The pork processing industry includes slaughter and dressing, fabrication into fresh meat cuts, cured meats and sausage manufacture. Our studies have shown that somatotropin will reduce fat and increase muscle in finishing pigs. These large changes in composition may affect some or all of the different segments of the pork industry. Potential problems associated with the slaughter and dressing procedure include increased by-product mass, difficulty in removing the skin, changes in the carcass chilling rate and changes in cooler shrinkage. Potential problems associated with fabrication into wholesale cuts or joints include difficulty in cutting the soft pliable lean tissue, separation of muscles or muscle groups when retail cuts are prepared and difficulty in removing the skin from cuts without exposing the muscle surface. The increased lean content will affect water content and may require altered handling procedures to achieve desired composition end points and shelf live. The cured meat processor will be concerned with changes in the composition and thickness of the belly for bacon (particularly for the USA market). Also, the protein extraction properties of meat for boneless ham production will need to be reevaluated. Sausage makers will be concerned with the potential changes in meat properties, such as pigment concentration, moisture to protein ratio, water binding, pH, myofibrillar protein concentration, and the composition of the fat.

Considerable information is available concerning the growth and composition of pigs treated with somatotropin; however, limited information is available concerning their processing attributes. The limited data available have not indicated problems with the slaughter and dressing procedures for somatotropin treated pigs. Only a very limited number of pigs have been slaughtered commercially in high speed operations. Fabrication properties of the carcass have been evaluated by several research groups and advantages in cutting yield and composition of the cuts have been reported. Incidence of potential slaughter problems such as an increased incidence of PSE have not been documented. Curing and sausage problems have not been addressed directly; however, the questions of pH, meat color, fat content, moisture to protein ratios and belly characteristics have been evaluated and few problems noted. One exception is belly thickness, which is direct correlated to backfat thickness.

Although the use of somatotropin will require changes to be adopted by both the producer and processor, we do not believe it will cause insurmountable difficulties and problems can be handled with existing technology.

Keywords: somatotropin, cutting yield, processing, cured meats.

Introduction

The composition of pigs has changed dramatically during the past four decades. Pigs are leaner and more muscular today due to improvements in genetics, management and nutrition. The improvements in composition are consistent with changes in consumer demand. Contemporary consumers are reducing animal fats and increasing the use of lipids from plant sources. In addition,

consumers are trying to reduce the caloric density of their diet by reducing lipids in the foods that they consume. Thus, consumers are demanding less fat in fresh and processed pork meats.

Per capita consumption of pork in the United States has been relatively static in the past 50 years. The estimated market direction of boneless skinless pork in the United States is presented in Table 1. Approximately 25% of the pork is consumed fresh (85% of the loin and 30% of the blade boston) and the remaining 75% of the pork is consumed as a cured or processed meat.

Table 1. Estimated market direction of boneless, skinless pork.

	Soft tissue Wt.to prod. (Bil.Lbs)	Percent fresh	Billions of Lbs.	Percent processed	Billions of Lbs.
Leg	2.8627	8	.2290	92	2.6337
Loin	2.2870	85	1.9440	15	.3430
Blade (Boston)	.9536	30	.2861	70	.6675
Arm Picnic	1.0989	5	.0550	95	1.0439
Spare Ribs	.3420	100	.3420	-	. -
Neck Bones	.1228	100	.1228	-	. -
Belly	2.2576	-		100	2.2576
Trimmings	1.1518	-		100	1.1518
Jowls	.3387	-		100	.3387
Fat Tissue	.4275	-		100	.4275
Total	11.8426		2.9789		8.8637

Consumers are eating more meals away from the home and purchasing more meals that are precooked and/or prepared quickly at home. Consumer surveys are indicating large increases in the number of people who have a active lifestyle and do not want or have the time to prepare meals at home (Burke Marketing, 1987). The same surveys indicate an increase in the awareness of consumers to nutritional quality of food. The demand for lean pork that is easy/convenient to prepare is increasing and the survival of the pork industry may depend on the development and adoption of technologies that will result in pork and pork products that meet consumer demand.

The use of somatotropin has been shown to have dramatic effects on the composition of pork (Machlin, 1972; Etherton et al., 1986; Etherton et al., 1987; Steel et al., 1987). Carcass fat content may be reduced as much as 50 % (Beermann et al., 1988). The use of somatotropin will allow producers to achieve consumer demand very rapidly for pork low in fat. However, limited information is available regarding the processing properties of fresh and processed pork manufactured from somatotropin treated swine. The purpose of this report is to evaluate the current literature for information on the slaughter and dressing, fabrication into fresh meat cuts, cured meat processing and sausage manufacture.

Overview of the Processing industry

Slaughter and dressing is the first step in the processing scheme. Changes associated with somatotropin treatment that may affect these procedures include: increases in by-product volume, decreases in dressing percentage, difficulty in skin removal, changes in the rate of chilling and/or cooler shrinkage. By-product volume is increased significantly for pigs treated with various levels of somatotropin. Liver weights increased up to 33%, heart weights increased 21% and kidneys increased 39% (table 2). The increase in by-product volume does not reflect a problem other than developing uses and/or markets for 30% more by- products. The increase in by-product volume is also reflected in the dressing percentage of the animals.

Table 2. By-product yield of somatotropin treated pigs.

Trait	Dosage level (mg/day)			
	0	3	6	9
Liver wt. (g)	1517.5	1814.8	1994.8	2057.5
Heart wt. (g)	295.5	339.2	366.1	376.3
Kidney wt. (g)	344.5	426.1	473.8	487.6
Stomach wt. (g)	590.3	617.6	644.9	672.2
Leaf fat wt. (g)	1415.0	902.7	747.1	636.4

Numerous studies have reported decreases in dressing percentage up to 3. 5% (Baile et al., 1983; Machlin, 1972; Grebner et al., 1987). Dressing percentage will be a concern of processors in the United States, particularly if pigs are purchased live by the processor. The value of the animal is not truly reflected by carcass weight, however, the concept of value of the tissues obtained from the carcass has not been readily adapted at this time. Limited information is available regarding any potential problems associated with the slaughter/skinning, chilling rates and/or cooler shrinkage of animals processed in a commercial processing facility. Carcass fatness has been shown to affect rate of chilling in other species (Smith et al., 1977). Barton-Gade et al. (1987) reported that fast chilling can cause cold shortening in pigs with slow post-mortem glycolysis; however, the carcasses from most somatotropin treated pigs would normally have sufficient fat to protect against cold induced shortening.

Fabrication of the carcass into wholesale cuts/joints is the next step in processing pork carcasses. Fabrication of carcasses that are very lean has resulted in some concerns by processing plants. The limited amounts of subcutaneous fat will limit the speed and ability of existing equipment to remove fat and skin from some cuts (the use of a loin knife to remove the subcutaneous fat and skin from the pork loin is difficult when backfat thickness is less than 1.8 cm). Exposure of the lean surface will increase dehydration and/or purge loss in wholesale cuts packaged for distribution.

Table 3. Effect of somatotropin on the carcass yield and composition of major wholesale cuts*.

		Control (kg)	(%)	Treated (kg)	(%)
Side wt.	Ham	34.56		33.79	
Wholesale cuts	Ham	9.24	26.7	9.36	27.7
	Loin	8.49	24.6	8.28	24.5
	Belly	5.39	15.6	5.03	14.9
	Shoulder	7.36	21.3	7.22	21.4
Trimmed wholesale Cuts	Ham	8.21	23.8	8.51	25.2
	Loin	6.75	19.5	7.07	20.9
	Picnic shoulder	3.85	11.1	3.84	11.4
	Boston butt	2.58	7.5	2.75	8.1
Boneless trimmed wholesale cuts	Ham	6.16	17.8	6.57	19.4
	Water (%)	68.34		71.67	
	Lipid (%)	12.48		8.96	
	Loin	4.50	13.0	4.99	14.8
	Water (%)	56.74		66.95	
	Lipid (%)	27.18		14.05	
	Boston butt	2.43	7.0	2.55	7.5
	Water (%)	62.70		70.92	
	Lipid (%)	20.99		10.00	
	Picnic shoulder	2.94	8.5	2.89	8.6
	Water (%)	67.35		71.67	
	Lipid (%)	15.00		9.34	

*McKeith et al., 1988.

Retail cuts prepared from carcasses with less than 1.2 cm of P2 fat tend to have increased muscle separation when the retail cut is packaged for sale (Wood et al., 1988). In addition, the carcasses and wholesale cuts tend to be more pliable for handling since there is a limited amount of fat to aid in cut firmness. Carcass cutting yields are higher (up to 1.8% for trimmed boneless cuts) for most cuts (Tables 3, 4 and 5) and the composition of the cuts is much more desirable (up to 50% reductions in fat content) for the somatotropin treated carcasses.

Table 4. Carcass cutting yields of carcasses treated with somatotropin.*

| | Slaughter weight | | | | | |
| | 100 Kg | | | 140 Kg | | |
	Control	Treated (% +)		Control	Treated (% +)	
Loin	6.93	+2.5	NS	9.61	+7.0	***
Ham	8.74	+4.3	*	11.79	+9.1	***
Shoulder	4.45	+5.6	***	6.10	+8.6	***
Belly	5.24	-3.5	*	7.68	-2.9	NS

*Kanis et al., 1988.

Intramuscular fat content of the longissimus and semitendinosus muscle were significantly reduced with somatotropin treatment (Grebner et al., 1987).

Table 5. Carcass cutting yields of pigs treated with human growth hormone releasing factor*.

		Control	Human GRF	
Ham	Muscle	5.35	6.05	P<.05
	Fat	2.65	1.94	P<.05
	Bone	.92	1.03	P<.05
Loin	Musle	4.83	5.67	P<.05
	Fat	4.28	2.96	P<.05
	Bone	1.27	1.48	P<.05
Shoulder	Muscle	5.69	6.61	P<.05
	Fat	2.70	2.34	
	Bone	1.36	1.72	P<.05
Flank	Muscle & fat	6.59	6.12	
	Bone	.47	.54	

*Pomnier et al., 1988.

Reductions in all of the major fat depots (internal, subcutaneous, intermuscular and intramuscular) were observed. The role of intramuscular fat content in cooked pork palatability appears to be related to the acceptability of pork (Devol et al., 1988). However, Wood et al. (1988) reported that intramuscular fat content did not have an effect on meat palatability. Grebner et al. (1987), reported reduction in intramuscular fat content from 3.5% to 2.3% with somatotropin treatment (Table 6).

Table 6. Carcass and muscle composition of somatotropin treated pigs.[*]

Trait	Dosage level (mg/day)			
	0	3	6	9
Longissimus				
Moisture	73.04	74.15	74.03	72.68
Lipid	3.54	2.61	2.33	2.70
Semitendinosus				
Moisture	71.93	74.19	74.61	74.92
Lipid	7.29	4.96	3.97	4.29
Carcass				
Moisture	51.91	57.93	61.32	62.07
Lipid	29.87	21.82	17.59	17.19

[*] Grebner et al., 1987.

Cured meat processors will obtain cuts that are leaner (Tables 3, 4 and 5) and these cuts will have similar processing yields and color properties (Table 7). Prusa and others (1988) evaluated the processing, visual and sensory properties of boneless hams, Canadian style bacon and traditional bacon. Results of their study indicated that few differences observed between control and treated products and that somatotropin had no detrimental effects on the processing characteristics of muscle. Warner-Bratzler shear force values of boneless hams were evaluated and no statistical differences were observed (Prusa et al., 1988). The lack of texture differences indicate that the products bound together effectively and no problems with muscle binding were mentioned in their report.

Table 7. Processing properties of cured meat.[*]

	Somatotropin level (mg/day)		
	0	3.33	6.67
Yields			
Belly	86.3	84.8	84.3
Canadian style			
bacon	83.8	84.8	86.2
Boneless ham	77.6	77.2	76.6
Ham color (4 wks storage)			
L	47.1	46.9	47.7
a	9.0	9.2	9.3
b	4.1	4.4	4.7
Ham composition			
Moisture	68.3	68.1	67.6
Fat	3.6	4.3	4.6
Protein	22.0	22.2	22.7
Warner-Bratzler			
shear force	1.0	1.2	1.4

[*] Prusa et al., 1988.

One of the concerns that processors in the United States will have will involve belly thickness and suitability of the belly for bacon production. The effect of belly thickness on the processing charac- teristics and acceptability of bacon was evaluated at the University of Illinois. Bellies were obtained from a group of pigs treated with somatotropin and controls and evaluated based on belly thickness. Bellies were characterized and processing traits were characterized as well as visual evaluation of the cooked products (Table 8). Raw average belly thickness ranged from 2.1 cm to 3.3 cm and the composition of the bellies ranged from 22.95 % fat to 42.51 % fat. Differences were observed in visual slice integrity, fat to lean ratio and overall appearance of the products; however, no sensory differences were observed.

Sausage manufacture involves a major proportion of the pork produced annually. Reducing fat content in carcasses will result in reduced fat in much of the trim utilized for sausage production. Reducing fat in sausage products will be perceived positively by consumers; however, the acceptability of reduced fat sausage has been evaluated and the textural properties of the sausage become less desirable using traditional processing techniques.

Table 8. Belly characteristics and processing yields*.

Trait	Mean	Maximum	Minimum	Probability of a linear effect
Physical characteristics				
Green weight (kg)	4.71	6.03	3.74	.002
Raw average thickness (cm)	2.78	3.30	2.14	.001
Cooked average thickness(cm)	3.25	4.13	2.29	.001
Processing yield (%)	98.5	104.1	95.7	.001
Chemical characteristics				
Moisture (%)	53.71	69.11	45.77	.003
Fat (%)	32.85	42.51	22.95	.001
Visual traits				
Slice integrity	8.87	12.06	4.90	.008
Fat to lean ratio	9.32	12.75	6.18	.001
Overall appearance	8.23	10.90	3.50	.001

* University of Illinois unpublished data.

Valvano (1983) reported acceptable low fat sausage can be manufactured using some different processing techniques and Foegeding and Ramsey (1986) evaluated the use of carrageenan in low fat emulsion products. Research currently being conducted in our laboratory indicates that acceptable emulsified sausage products may be manufactured using less than 15% fat. Little or no information has been compiled on the functional properties of the muscle tissue or the composition of the lipids.

Conclusions

Numerous concerns were brought out in the discussion of the processing characteristics of somatotropin treated pork. Many of the potential concerns have been addressed and few differences or problems have been documented. Currently available technology should answer of alleviate any potential problems that arise.

References

Baile, C.A., M.A. Della-Fera & C.L. McLaughlin, 1983. Performance and carcass quality of swine injected daily with bacterially-synthesized human growth hormone. Growth 47:225-236.

Barton-Gade, P.A., C. Bejerholm & U. Borup, 1987. Proc. 33rd Internatl. Congress of Meat Science & Technology, Helsinki, Finland, Vol. 1, 181-184.

Beermann, D.H., R.D. Boyd, G. Arnbruster, A.F. Deneergard, K. Roneker, T.D. Bartley & K.D. Fain, 1988. Dose response effect of native and recombinant porcine somatotropin (pST) on growth performance, composition of gain and pork quality. Proc. 34th Internatl. Congress of Meat Science & Technology, Brisbane, Australia, Vol. 2, 601-602.

Breidenstein, B.C. & J.C. Williams, 1985. Contribution of red meat to the U.S. diet. National Live Stock and Meat Board, Chicago, IL USA.

Burke Marketing Research, 1987. Consumer climate for meat. National Live Stock and Meat Board, Chicago, IL USA.

DeVol, D.L., F.K. McKeith, P.J. Bechtel, J. Novakofski, R.D. Shanks & R.D. Carr, 1988. Variation in the composition and palatability traits and relationship between muscle characteristics and palatability in a random sample of pork carcasses. J. Animal Science 66:385.

Etherton, T.D., J.P. Wiggins, C.M. Evock, C.S. Chung, J.F. Rebhun, P.E. Walton & N.C. Steele, 1987. Stimulation of pig growth performance by porcine growth hormone: determination of the dose-response rela- tionship. J. Animal Science 64:433-443.

Etherton, T.D., J.P. Wiggins, C.S. Chung, C.M. Evock, J.F. Rebhun & P.E. Walton, 1986. Stimulation of pig growth performance by porcine growth hormone and growth hormone-re leasing factor. J. Animal Science 63: 1389-1399.

Foegeding, E.A. & S.R. Ramsey, 1986. Effects of gums on low-fat meat batters. J. Food Science 51:33.

Grebner, G.L., F.K. McKeith, J. Novakofski, R.A. Easter, D.G. McLaren, K. Brenner, P.J. Bechtel, R.W. Jones & R.H. Dalrymple, 1987. Carcass characteristics of pigs injected with different levels of natural porcine somatotropin (PST) from 57 to 103 kg weight. J. Animal Science 65:245 (u str).

Kanis, E., W. Van der Hel, J. Huisman, G.J. Nieuwhof, R.D. Politiek, M.N.A. Verstegen, P. Van der Wal & E.J. Van Weerden, 1988. Effect of recombinant porcine somatotropin (rPST) treatment on carcass charac- teristics and organ weights of growing pigs. J. Animal Science 66:280 (Abstr).

Machlin, L.J., 1972. Effect of porcine growth hormone on growth and carcass composition of the pig. J. Animal Science 35:794-800.

McKeith, F.K., P.J. Bechtel, J. Novakofski, D.G. McLaren, R.A. Easter, R.W. Jones & D.L. Ingle, 1988. Effect of porcine somatotropin on composition of boneless retail cuts from pigs. Annual Meeting of the American Society of Animal Science.

Pomnier, S., P. Dubreul, P. Gandreau, G. Pelletier, C. Farmer, D. Petitclerc, H. Lapierre, Y. Couture & T. Mowles, 1988. Effect of a potent analog of human growth hormone releasing factor (hGRF) on the carcass composition of pigs. J. Animal Science 66:295 (Abstr).

Prusa, K.J., J.G. Sebranek & J.A. Love, 1988. Processing and quality characteristics of Canadian style bacon, boneless ham and bacon from pigs treated with porcine somatotropin. J. Food Science (submitted).

Smith, G.C., T.R. Dutson, R.L. Hostetler & Z.L. Carpenter, 1976. Fatness, rate of chilling and tenderness of lamb. J. Food Science 41:748.

Steele, N.C., R.G. Campbell & T.J. Caperna, 1987. Update of porcine growth hormone research: practical and biological implications. Cornell Nutrition Conference, October 27, 1987.

Valvane, R.A, 1983. The effects of preblending and lowered fat content on processed meats. M.S. Thesis. University of Nebraska, Lincoln, NE.

Wood, J.D., M. Enser & Moncraff, 1988a. Effects of carcass fatness and sex on the composition and quality of pig meat. Proc. 34th Inter- national Congress of Meat Science & Technology, Brisbane, Australia, Vol. 2, 562.

Wood, J.D., 1988b. Influence of the Duroc breed on pig meat quality. Proc. 34th Internatl. Congress of Meat Science & Technology, Brisbane, Australia, Vol. 2, 571-572.

EFFECT ON REQUIREMENTS AND WELL BEING
OF THE TARGET ANIMAL

Physiological mode of action

Nutrient and management requirements

Health and immune response

Side effects

Effects on reproduction and lactation

MECHANISMS BY WHICH PORCINE GROWTH HORMONE (pGH) AND INSULIN-LIKE GROWTH FACTORS (IGFs) REGULATE PIG GROWTH PERFORMANCE: APPROACHES FROM THE pGH AND IGF RECEPTORS TO THE WHOLE ANIMAL

T.D. Etherton

Department of Dairy and Animal Science, University Park, PA 16802 U.S.A.

Summary

Porcine GH is a naturally occurring protein hormone that has a wide array of biological effects in pigs. Treatment of growing pigs with porcine growth hormone (pGH) dramatically increases pig growth performance (the composite of average daily gain, feed efficiency and carcass composition). The biological actions of pGH can broadly be categorized as being either somatogenic or metabolic. In this chapter, I will discuss some mechanisms by which pGH affects growth and metabolism. The discussion will address: 1) the effects that pGH has on adipose tissue growth and metabolism, 2) the role that both pGH and insulin-like growth factor 1 (IGF-1) play in stimulating muscle growth, 3) the events that occur which lead to the hyperglycemia and hyperinsulinemia observed in pigs treated with pGH chronically, 4) the evidence which indicates that IGF-1 binding proteins (IGF-BPs) not only transport IGFs in the circulation but also modulate biological activity of IGFs and 5) the significance of the recently established amino acid sequence of cDNA clones that encode the human and rabbit GH receptors.

Although it is now clear that pGH alters nutrient partitioning in meat animals, the biological mechanisms by which this occurs are not clear. Little is known about how the pGH receptor generates chemical signals nor the identity of those molecules that mediate the intracellular biological effects of pGH. As our understanding of the interaction between pGH and its receptor increases it will likely be possible to establish the amino acid residues of pGH that bind to the pGH receptor. This information may make it possible to "design" analogs of pGH that may have enhanced biological activity. Thus, the effects we have seen of treating pigs with exogenous pGH to date may represent only the first step in a series of advances that lead to economical and effective ways to manipulate meat animal growth performance.

Keywords: growth hormone, insuline-like growth-factor, receptors, physiological mechanisms, swine.

Introduction

An exciting era is evolving in animal agriculture. Numerous studies have shown that treating pigs with exogenous pituitary pGH dramatically increases pig growth performance (Chung et al., 1985; Boyd et al., 1986; Etherton et al., 1986, 1987b; Campbell et al., 1988). Recently, it has also been established that recombinant pGH mimics the effects of pituitary GH (Evock et al., 1988). The magnitude of response in these studies has varied somewhat primarily because of differences in experimental design (e.g., initial pig weight, length of study, breed, sex, dose of pGH used and differences in diet). Despite these differences, however, it has become apparent that pGH increases average daily gain approximately 10 to 20%, improves feed efficiency 15 to 35%, decreases

adipose tissue mass and lipid accretion rates by as much as 50 to 80% and concurrently increases protein deposition by as much as 50%.

These responses have sparked interest in developing a rpGH-based growth promotant for the pork industry world-wide. In addition to the economic benefits realized by the producer who integrates pGH into their production scheme, the other benefit of this new biotechnology will be to provide a leaner product for the consumer. In fact, the greatest benefit of this technology to society may be the ability to produce pork that is considerably leaner. This will be of particular interest to individuals concerned about the relationship between the consumption of saturated fatty acids and coronary heart disease. In the U.S.A, the present dietary recommendations are that consumption of saturated fatty acids be reduced to less that 10% of total calories. Thus, treating pigs with pGH provides an effective means of safely producing leaner, more nutritious pork that will enable consumers to include pork in their diet and still achieve the dietary recommendations.

History of pGH

Evans and co-workers first demonstrated the presence of a substance in the anterior pituitary that increased the growth rate of rats (Evans and Long, 1922a,b; Evans and Simpson, 1931). Lee and Schaffer (1934) subsequently established that pair-fed rats injected with an alkaline extract of bovine pituitaries not only gained more weight but the composition of the gain contained proportionally more muscle and less adipose tissue. It was not until 1951 that Raben and Weatermeyer (1951) described a method for the isolation of pGH. Because the preparation was quite heterogenous a complete chemical characterization was not presented. Subsequently, Papkoff et al. (1962) published a procedure for the preparation of pGH from freshly frozen pig pituitaries and reported that pGH had a molecular weight of 41,600 (ascertained by sedimentation velocity). With advances in protein chemistry and separation techniques further improvements in pGH purification were achieved (Chen et al., 1970). In the latter paper, a molecular weight of 22,000 was assigned to pGH. Also in 1970, Mills et al. (1970) presented the first partial amino acid sequence data for pGH. The complete amino acid sequence was not established until 1983 when Seeburg et al. (1983) deduced the sequence from a cloned cDNA for pGH.

Porcine GH is a 191 amino acid protein that shares a high degree of homology with bovine growth hormone (bGH) (see Figure 1). There are 18 positions between pGH and bGH that have different amino acids whereas there are 59 residues that differ between pGH and human GH (hGH). Recently, the three-dimensional structure of recombinant pGH has been reported (Abdel-Meguid et al., 1987). In the future it should be possible to use structural studies such as this in conjunction with recombinant DNA technology to identify the amino acid residues that are involved in binding of pGH to its receptor. If this is achieved, it may be possible to design recombinant pGH analogs that have a greater biological activity.

The awareness that the pituitary produces substances that play an important role in the growth process prompted animal scientists to treat pigs with pituitary preparations of GH. The early studies (Giles, 1942; Turman and Andrews, 1955; Henricson and Ullberg, 1960) were inconclusive with respect to the effects of these pituitary preparations on growth performance of pigs. These negative findings were due to the purity of the GH preparations. In 1972, Machlin (1972) established that treating pigs with pituitary pGH significantly improved weight gain and feed efficiency. At that time commercialization of a pGH-based product was not practical because of the availability of pig pituitaries and the cost of pGH purification. The emergence of molecular biology and the means to produce large quantities of biologically active recombinant proteins has resolved this issue.

```
                 10         20         30         40         50
     pGH  AFPAMPLSSL FANAVLRAQH LHQLAADTYK EFERAYIPEG QRYS-IQNAQA
     bGH  AFPAMSLSGL FANAVLRAQH LHQLAADTFK EFERTYIPEG QRYS-IQNTQV
     hGH  AFPTIPLSRL FDNAMLRAHR LHQLAFDTYQ EFEEAYIPKE QKYSFLQNPQT

                 60         70         80         90         100
     pGH  AFCFSETIPA PTGKDEAQQR SDVELLRFSL LLIQSWLGPV QFLSRVFTNS
     bGH  AFCFSETIPA PTGKNEAQQK SDLELLRISL LLIQSWLGPL QFLSRVFTNS
     hGH  SLCFSESIPT PSNREETQQK SNLELLRISL LLIQSWLEPV QFLRSVFANS

                 110        120        130        140        150
     pGH  LVFGTSDR-VY EKLKDLEEGI QALMRELEDG SPRAGQILKQ TYDKFDTNLR
     bGH  LVFGTSDR-VY EKLKDLEEGI LALMRELEDK TPRAGQILKQ TYDKFDTNMR
     hGH  LVYGASDSNVY DLLKDLEEGI QTLMGRLEDG SPRTGQIFKQ TYSKFDTNSH

                 160        170        180        190
     pGH  SDDALLKNYG LLSCFKKDLH KAETYLRVMK CRRFVESSCA F
     bGH  SDDALLKNYG LLSCFAKDLH KTETYLRVMK CRRFGEASCA F
     hGH  NDDALLKNYG LLYCFAKDMD KVETFLRIVQ CR-SVEGSCG F
```

Figure 1. Amino Acid sequence for pGH (Seeburg et al., 1983), bGH and hGH (Miller and Eberhardt, 1983). Amino acids highlighted differ from residues in pGH. A=Ala; C=Cys; D=Asp; E=Glu; F=Phe; G=Gly; H=His; I=Ile; K=Lys; L=Leu; M=Met; N=Asn; P=Pro; Q=Gln; R=Arg; S=Ser; T=Thr; Y=Tyr; V=Val; W=Trp.

Metabolic effects of pGH

Adipose tissue

It is clear that pGH induces numerous metabolic effects that influence the partitioning of nutrients among various body tissues. The precipitous decrease in adipose tissue accretion rate is one important metabolic effect of pGH. The effects of pGH on adipose tissue metabolism are important because they: 1) establish the rate of adipose tissue accretion and, therefore, the extent to which pGH affects carcass composition, 2) play a key role in accounting for the effects that pGH has on feed efficiency and 3) likely play a role in the decrease observed in feed intake of pGH-treated pigs.

Accretion of adipose tissue is a function of the relative rates of triglyceride synthesis and degradation (lipolysis). For pGH to decrease growth rate of adipose tissue it is clear that lipid synthesis must decrease, lipolysis increase or a combination of both occur. We have found that pGH affects lipid synthetic events on two levels: 1) there is a striking decrease in glucose utilization by porcine adipocytes and 2) the stimulatory effects of insulin on glucose metabolism are blunted. With respect to the effects of pGH on lipolysis, there is evidence which suggests that pGH potentiates the effects of lipolytic hormones (Boyd and Bauman, 1988). In the latter study, an epinephrine challenge caused a greater rise in plasma free fatty acid (FFA) concentration in pigs treated chronically with pGH than controls. There is no information which resolves whether pGH affects FFA turnover in vivo. Although pGH appears to affect mobilization of FFAs it is likely that the primary effect of pGH on adipose tissue accretion is mediated via changes in triglyceride synthesis when pigs are fed ad libitum.

Considerable evidence exists to support the hypothesis that pGH affects glucose utilization and insulin sensitivity of porcine adipocytes. We have found that treating pigs with pGH for 7 d (70 µg/kg body weight) reduces fatty acid synthesis 50 to 70% (Walton et al., 1987) and that this is paralleled by a decline in activity of several lipogenic enzymes (glucose-6-phosphate dehydrogenase, 6-phosphogluconate dehydrogenase, malic enzyme and fatty acid synthase; Magri,

1988). The extent to which pGH affects lipogenic enzyme activity is illustrated by the observation that fatty acid synthase activity is abolished after 7 d of pGH treatment. In addition to directly affecting glucose utilization, pGH also markedly decreases the stimulatory effects of insulin on lipogenesis and glucose transport (Walton et al., 1987; Magri, 1988). These effects of pGH are intrinsic properties since they are mimicked by recombinant pGH.

To determine whether the effects of pGH are direct we have developed techniques for culturing porcine adipose tissue in defined medium that maintains lipogenic capacity for 48 h (Walton and Etherton, 1986; Walton et al., 1986; Walton and Etherton, 1987). These experiments have shown that pGH blunts the ability of insulin to maintain lipogenic capacity in a dose-dependent manner. Similar findings have been reported for ovine and bovine adipose tissue (Vernon et al., 1982; Etherton et al., 1987a). Based on these observations, it is evident that the effects of pGH on adipose tissue are direct and not the result of IGF-1 (discussed later). Furthermore, the effects of pGH in culture are not observed in short- term incubations (2 h), but rather are only observed after chronic exposure of the tissue to pGH. This suggests that pGH acts to inhibit glucose utilization by changing the mass of key lipogenic enzymes, second messengers or glucose transporters.

There is considerable evidence (with rodents) to indicate that GH exerts an insulin-like effect in adipose tissue. This is only seen in adipose tissue from GH-deficient animals such as hypophysectomized rats or rats treated with antiserum to GH (Goodman and Coiro, 1981; Schwartz, 1980; Gause et al., 1983). This effect is not seen in the presence of GH (Eden et al., 1982). Thus, under normal physiological circumstances (when GH is present) pGH has no insulin-like effects on adipose tissue accretion. Given this perspective, it is not clear why studies are conducted looking at the insulin-like effects of GH in adipose tissue when this does not occur in any meaningful physiological setting. This becomes particularly apparent when one considers the catabolic effects that pGH has on adipose tissue accretion which unquestionably is not an insulin-like effect.

It can be speculated that the reduction in insulin sensitivity and responsiveness of porcine adipocytes may due to a pGH-dependent decrease in binding of insulin to the insulin receptor. To address this, we have quantified insulin binding to adipocytes from pigs treated chronically with pGH in which insulin sensitivity is blunted. We have found that insulin binding is unaffected by pGH (Magri, 1988). In addition, we have determined that insulin receptor tyrosine kinase activity is not affected by pGH in porcine adipocytes (Magri, 1988). Our interpretation of these findings is that pGH blocks insulin action at a site somewhere other than recognition of insulin by the receptor or phosphorylation of some critical intracellular protein involved in the cascade of events associated with the generation of chemical signals that mediate the intracellular effects of insulin. Nothing is known about the level at which this blockade occurs.

Insulin sensitivity and glucose kinetics

Numerous studies have shown that treating pigs with exogenous pGH increases plasma glucose and insulin concentrations (Etherton et al., 1987b; Evock et al., 1988). In addition, other studies using a euglycemic clamp technique have shown that pGH reduces uptake of glucose in response to insulin infusion in pigs chronically treated with the hormone (28 d) (see Boyd and Bauman, 1988). Recently, we have found that glucose and insulin tolerance tests are impaired in pigs treated chronically with pGH (Gopinath and Etherton, 1989a,b). This effect is not seen in pigs treated acutely with pGH. We have also found that hepatic glucose output is significantly increased by pGH treatment. Thus, the increase in circulating plasma glucose concentration in pGH-treated pigs is due to an increase in hepatic glucose output and a concurrent impairment in glucose clearance. The increase in hepatic glucose output appears to be associated with a reduction in the insulin sensitivity of liver (Gopinath and Etherton, 1989b).

There are several issues that need to be resolved about the effects that pGH has on carbohydrate metabolism. The first is what is the significance of an increase in both plasma glucose and insulin in a physiological state where changes in growth rate and nutrient partitioning occur? This leads to the second question which is: what is the fate of the glucose in plasma? Based on some estimates

we have made (Etherton, 1989), a significant quantity of glucose (±20 to 40% of glucose cleared per day) is diverted away from deposition as lipid in adipose tissue. It is not clear where the glucose diverted away from adipose tissue goes. Given the marked increase in muscle protein deposition it seems likely that the requirement for ATP in muscle is increased. To meet this increased need for ATP it would appear that plasma glucose or FFA (due to changes in lipolysis) utilization by muscle would have to be increased in pGH-treated pigs. It has not been established whether indeed this happens.

There are data which indirectly support the idea that amino acid flux from muscle to liver is perturbed by pGH. In all the studies we have done one of the most consistent findings is that pGH treatment decreases blood urea nitrogen concentration. This suggests that hepatic amino acid degradation is reduced and infers that delivery of amino acids from peripheral tissues to the liver is also reduced. It remains to be established whether this change in delivery of amino acids to the liver is a function of changes in amino acid uptake by muscle, release or both. Studies with hypophysectomized rats (Albertson-Wikland, 1980) and normal rats (Schwartz, 1982) have shown that GH stimulates protein synthesis in diaphragm muscle. There is some basis to suggest that the IGFs also play a role in protein synthesis and degradation. IGF-1 has been shown to stimulate protein synthesis in the soleus and extensor digitorum longus muscles of rats (Monier et al., 1983). Ballard et al. (1986) found that both IGF-1 and IGF-2 stimulated protein synthesis and inhibited protein degradation in rat L6 myoblasts. In vivo studies looking at the effects of pGH on protein synthesis and degradation in pigs are needed to resolve the contribution that changes in protein synthesis and/or degradation make to alterations in muscle protein deposition rates.

The repeated observations that plasma insulin concentrations are higher and that insulin tolerance tests are impaired in pGH-treated pigs indicate that there is a significant impairment in insulin sensitivity in vivo. The role that this state of insulin insensitivity plays in pGH- treated pigs is not known.

Somatogenic effects of pGH: The role of the IGFs

Administration of GH to animals stimulates chondrogenesis and satellite cell proliferation (for reviews see Isaksson et al., 1987 and Allen, 1988). Both of these responses are an important component of the anabolic effects that GH has because of the rate-limiting role chondrocyte proliferation plays in regulating long bone growth and the similar role that satellite cell proliferation plays in regulating postnatal muscle growth. In 1941, Kibrick et al. (1941) found that epiphyseal plate width of hypophysectomized rats increased after treatment with GH. This finding formed the basis for a bioassay of long-standing for GH. It was subsequently established that GH increased the rate of sulfate incorporation into chondroitin sulfate proteoglycans of cartilage (Murphy et al., 1956). This finding prompted Salmon and Daughaday (1957) to determine if GH stimulated sulfate uptake in vitro in cartilage from hypophysectomized rats. They found that GH did not directly stimulate sulfate incorporation whereas serum from GH-treated rats stimulated sulfate incorporation. This observation led to the somatomedin hypothesis which states that GH stimulates somatic growth indirectly via circulating sulfation factors. We now know these sulfation factors as insulin-like growth factor 1 (IGF-1) and insulin-like growth factor 2 (IGF-2). IGF-1 is a single chain peptide of 70 amino acids (M_r = 7649) whereas IGF-2 has 68 amino acids (M_r =1 7471) (Rinderknecht and Humbel, 1978a,b). IGF-1 is regulated by GH whereas IGF-2 is less GH dependent. We have found that treating pigs with exogenous pGH does increase IGF-2 (C.M. Evock and T.D. Etherton, unpublished data), however, the response is less than that observed for IGF-1.

The somatomedin hypothesis of GH action implies that GH stimulates longitudinal bone growth by increasing the concentration of circulating IGF-1 in plasma. Over the past six years, however, information has been published which demonstrates that administration of GH locally at the epiphyseal plate also stimulates bone growth in hypophysectomized rats (Isaksson et al., 1982; Russell and Spencer, 1985; Isgaard et al., 1986a,b). Other evidence such as the finding of specific

binding sites for GH on chondrocytes from rabbit ear and epiphyseal growth plate (Eden et al., 1983) and the observation that GH stimulates DNA and proteoglycan synthesis in cultured chondrocytes (Madsen et al., 1983, 1985) are incompatible with the effects of GH being mediated solely by circulating IGF-1. These findings imply that GH may stimulate local production of IGF-1 and that locally produced IGF-1 plays an important role in mediating the somatogenic effects of GH. Recently, Isgaard et al. (1988). reported that treating hypophysectomized rats with GH increased IGF-1 mRNA abundance in rat rib growth cartilage in a dose-dependent manner. These findings are significant because they not only indicate that IGF-1 acts in an endocrine manner but also acts as a paracrine or autocrine growth factor and that local production of IGF-1 is under GH regulation. The finding that IGF-1 mRNA is also present in a variety of rat tissues (Murphy et al., 1987) indicates that a number of other tissues expresses the IGF-1 gene.

The awareness that the somatogenic effects of GH are mediated by IGF-1 has led to experiments to determine whether administration of exogenous IGF-1 increases growth rate. This approach has been facilitated by the availability of recombinant human IGF-1 (which has the same sequence as pig IGF-1; Tavakkol et al., 1988). There have been no studies reported in which pigs have been treated for more than 3 days with IGF-1. Nonetheless, studies with hypophysectomized and normal rats have shown that exogenous IGF-1 increases growth (see Table 1 for a summary). We have considered the possibility that treating pigs with exogenous IGF-1 might be alternative means of increasing pig growth performance. Several observations, however, suggest that while IGF-1 may increase growth rate in pigs (which remains to be established), IGF-1 treatment will not be comparable to the effects seen with pGH. This is because the metabolic effects of pGH in adipose tissue will not be mimicked by IGF-1 (specifically, the effects of pGH on glucose uptake, metabolism and insulin sensitivity). It is our contention that the metabolic effects of pGH play an integral role in regulating the rate of adipose tissue accretion and, hence, are an important determinant in establishing the changes in carcass composition and feed efficiency.

Insulin-like growth factor binding proteins and receptors

It has been known for some time that IGF-1 in human plasma circulates bound to insulin-like growth factor binding proteins (IGF-BPs) (Hintz, 1974; Megyesi et al., 1975; Hintz and Liu, 1977). In pigs, we have found that there is also no detectable free IGF-1 in the circulation (Walton, 1988). Approximately 70 to 80% of the immunoreactive IGF-1 is bound to a 150 kDa IGF-BP complex, with the remainder associated with a 40 kDa ^{125}I-IGF-1 IGF-BP (Walton, 1988). When porcine serum is incubated with ^{125}I-IGF-1 and then fractionated over a FPLC sizing column little is bound to the 150 kDa IGF-BP (which is pGH-dependent), approximately 40% is bound to a smaller IGF-BP (ca. 40 kDa and not regulated by pGH) and the remainder is free. Thus, the high molecular weight IGF-BP is saturated with endogenous IGF-1 and is the major IGF-1 transport protein in porcine serum. Evidence which corroborates the finding that porcine IGF-BPs are highly occupied with endogenous IGF-1 in vivo comes from studies in which pigs have been treated with exogenous IGF-1 (Walton et al., 1988b). In this study, recombinant human IGF-1 (either 4 or 8 mg/day) was administered daily (as a single intra-arterial injection) for three consecutive days, blood samples were taken frequently and IGF-1 clearance determined. IGF-1 was cleared quite rapidly ($t^1/2$= ca. 6 min). In addition, administration of free IGF-1 caused hypoglycemia. The temporal profile of the elevation in serum IGF-1 following administration of exogenous IGF-1 differs markedly from that observed after pGH treatment where serum IGF-1 concentrations are elevated for 2 to 12 hours (Sillence and Etherton, 1987). The rapid clearance of exogenous IGF-1 ia apparently a function of the available binding sites for IGF-1 on the IGF-BPs. When the IGF-BPs are highly occupied with endogenous IGF-1 little exogenous IGF-1 binds and the ability of the IGF-BPs to inhibit clearance of IGF- 1 is lost.

Table 1. Studies to assess the effects of exogenous IGFs.

1   Schoenle et al. (1982). IGF-1 infused continuously via sc implanted minipumps, increased body weight gain, tibial epiphyseal width and costal cartilage mitogenesis in hypophysectomized rats.

2. Schoenle et al. (1985). IGF-1 administered as above increased tibial epiphyseal width and costal cartilage mitogenesis in hypox rats.

3. Russell and Spencer (1985), Isgaard et al. (1986). IGF-1 injections directly into the tibial epiphyseal plate stimulated cartilage growth in hypophysectomized rats.

4. Hizuja et al. (1986). IGF-1 via sc implanted minipump increased body weight gain, body length and tibial epiphyseal width in normal rats.

5. Van Buul-Offers et al. (1986). IGF-1 injections increased body weight and length in Snell dwarf mice.

6. Skottner et al. (1987). IGF-1 by iv bolus injection caused a dose-dependent decrease in blood glucose and an increase in disappearance rates of labeled aminoisobutyric acid from the circulation of hypophysectomized rats. IGF-1 given by continuous iv or sc infusion or by sc injection increased body clear weight gain and long bone growth only when given continuously at the highest dose.

To gain insight into the physiology of the IGF-BPs several of these proteins have been purified. An acid-stable subunit of the 150 kDa IGF- BP that is GH-dependent has been purified from rat serum, human plasma and porcine serum (see Figure 2). In pigs, this protein had a molecular weight of 45 kDa under reducing conditions and shares homology with acid- stable IGF-BPs purified from rat serum and human plasma (see Figure 2). In addition to the binding proteins found in serum, ca 30 kDa IGF-BPs have also been purified from human amniotic fluid (Drop et al., 1984; Povoa et al., 1984), placenta (Koistenen et al., 1986) and conditioned medium of HEP G2 hepatoma cells (Povoa et al., 1985). The IGF-BP originally isolated from human placenta has been shown to be synthesized in secretory endometrium (Rutanen et al., 1986) and decidua (Rutanen et al., 1985) but not in the placenta (Rutanen et al., 1985). The IGF-BP isolated from amniotic fluid is identical to the IGF-BP secreted by HEP G2 hepatoma cells (Povoa et al., 1985). There is evidence that antibodies raised against the amniotic fluid IGF-BP cross-react with the small serum IGF-BP in humans that is not GH-dependent which suggests that these are similar if not identical proteins (Baxter and Cowell, 1987).

```
                      2    4    6    8    10   12   14

Pig Serum        G-K-G-A-V-G-A-G-P-V-V-R-

Rat Serum        G-A-G-A-V-G-A-G-P-V-V-R-C-E-P-

Human Plasma     G-A-S-S-A-G-L-G-P-V-V-R-C-E-P-
```

Figure 2. N-terminal amino acid sequence of IGF-BPs purified from pig serum (Walton et al., 1988a), rat serum (Baxter and Martin, 1987) and human plasma (Baxter et al., 1986). Amino acids highlighted differ from residues in porcine IGF-BP. Amino acid code is presented in Figure 1.

Polyclonal antiserum raised against the acid-stable IGF-BP recognizes the 150 kDa IGF-BP in porcine serum (Walton and Etherton, 1988). This finding indicates that we purified a component of the large complex (150 kDa IGF-BP) and this protein is a heterogenous complex of subunit proteins. An RIA established for this IGF-BP in porcine serum has been used to ascertain whether pGH affects circulating IGF-BP concentrations (Walton and Etherton, 1988). When pigs are treated with pGH acutely (10 to 1000 g/kg BW) serum IGF-BP concentration is unaffected. Chronic treatment with pGH, however, increases IGF-BP concentration significantly (Walton and Etherton, 1988). In the studies we have done, it takes approximately two days for pGH to increase IGF-BP

concentration. The rise in IGF-BP concentration is paralleled by an increase in serum IGF-1 concentration. Hypophysectomy reduces IGF-BP concentration by 60 to 70%. When pigs are treated with daily intra-arterial injections of IGF-1 for three days there is no increase in IGF-BP concentration (Walton and Etherton, 1988). This suggests that IGF-BP concentration is not under IGF-1 regulation. Studies are needed, however, to establish whether chronic infusion of IGF-1 affects IGF-BP concentration in domestic animals. It is possible that because exogenous IGF-1 was cleared so rapidly (see above) plasma levels were not elevated for a sufficient length of time to answer the question of whether exogenous IGF-1 affects IGF-BP synthesis and secretion.

Recently, Baxter (1988) suggested that the human 150 kDa IGF-BP is comprised of an acid-stable IGF-binding subunit (analogous to the porcine acid-stable IGF-BP) with a M_r of 53 and a 100-110 kDa acid-labile subunit. This would suggest that there is only one binding subunit for IGF-1 in this complex. What is not clear is that when porcine serum is subjected to ligand blotting that six IGF-BPs are observed (McCusker et al., 1988). It may turn out that the use of gel chromatography and FPLC to determine of the distribution of ^{125}I-IGF-1 in pig serum does not resolve heterogenous forms of ca. 150 kDa IGF-BP that exist. It is also important to realize that simply evaluating chromatographic profiles of ^{125}I-IGF-1 specific binding to serum proteins as means of identifying IGF-BPs is constrained by the availability of unoccupied binding sites (i.e., if all the sites are occupied with endogenous IGF-1 then no exogenous IGF-1 will bind and the IGF-BP not recognized).

The observation that the GH-dependent IGF-BP concentration is not affected by exogenous IGF-1 suggests that IGF-1 treatment may not be as effective as treating pigs with pGH. Other studies provide evidence to support this assertion. Since adipose tissue plays such an important role in the adaptive response to exogenous pGH we asked whether this may be mediated by the elevation in IGF-1. In vitro, IGF-1 is an insulin mimic in porcine adipose tissue and stimulates both lipogenesis and glucose oxidation (Walton et al., 1987; Walton et al., 1988c). This effect is inhibited by physiological concentrations of the purified acid- stable IGF-BP (Walton et al., 1988c). This is a specific effect of IGF-BP because insulin action is not blocked by addition of the binding protein. In summary, it appears that IGF-1 does not mediate the effects that pGH has on adipose tissue metabolism because: 1) the effects of free IGF-1 are insulin-like whereas the effects of pGH both in vivo and in vitro are to antagonize insulin action in adipose tissue and decrease adipose tissue growth rate; 2) the IGF-BPs block the insulin-like effects of free IGF-1; and 3) there is no detectable free IGF-1 in porcine serum. Even if free IGF-1 were present in adipose tissue it appears that the insulin-like effects would be blunted in pGH-treated pigs because pGH decreases adipose tissue sensitivity and responsiveness to free IGF-1 (Walton et al., 1987).

IGF-BP cDNAs

As noted above, the IGFs bind to IGF-BPs in serum in addition to the type 1 and 2 IGF receptors (discussed later) on target cells. In addition to merely acting as binding proteins, it is apparent the IGF- BPs affect IGF-1 removal from blood and act to modulate bioactivity of IGF-1. Based on the finding that a small molecular weight IGF-BP is present in the secretory endometrium and decidua together with the observation that the 150 kDa IGF-BP is present in a variety of biological fluids in pigs (follicular fluid, amniotic fluid, allantoic fluid, colostrum and milk) (Walton and Etherton, 1988) indicate that the IGF- BPs are produced locally. To determine whether IGF-BPs are produced locally studies have been undertaken to clone the IGF-BP cDNAs and then use these as probes to determine if IGF-BP mRNA can be detected in various tissues. To date, there have been no studies with tissues from domestic animals.

Initial efforts to determine whether IGF-BP genes are being expressed by peripheral tissues have focused on cloning the small M_r IGF-BP secreted by HEP G2 cells and found in amniotic fluid. Studies have been conducted in which the IGF-BP from HEP G2 cells (Lee et al., 1988), human placenta (Brinkman et al., 1988; Grundmann et al., 1988) and human decidua (Brewer et al, 1988; Julkunen et al., 1988) have been cloned. The amino acid sequence deduced from the cDNA clones indicates that the IGF-BP produced by HEP G2 cells and the human placenta/decidua are identical

(Brinkman et a., 1988; Grundmann et al., 1988, Lee et a., 1988, Julkunen et al., 1988). There is one residue difference in the sequence reported by Grundmann et al. (1988) and Lee et al. (1988) versus the sequence reported by Brinkman et al. (1988) and Julkunen et al. (1988); however, for practical purposes these two proteins are identical. In contrast, the deduced amino acid sequence reported by Brewer et al. differs markedly from the sequences reported for the other IGF-BPs. It is interesting to note that sequence reported by Brewer et al. (1988) is similar to the other clone in that the first 30 amino acids at the NH_2 terminus are identical, the next 15 amino acids are different, the sequence for residues 45-144 of the open reading frame are the same, however, they are off register by one residue when compared with the sequences reported for the other IGF-BP clones. The remainder of the sequence reported by Brewer et al. (1988) is off register by two residues. The meaning of this is not clear at this time. The availability of cDNAs will enable studies to be conducted to establish what tissues synthesize which IGF-BPs and whether GH regulates transcript abundance. The limited information available indicates that the transcript for the small IGF-BP is detected only in human liver, secretory endometrium and late-pregnancy decidua (Julkunen et al., 1988).

IGF-1 receptors

Three types of cell surface receptors bind IGF-1: the insulin receptor and the IGF type 1 and 2 receptors. The type 1 and 2 IGF receptors and the insulin receptor exhibit different binding affinities for insulin and the IGFs. The insulin and type 1 receptors bind IGF-1 and 2 as well as insulin. The relative affinities of the insulin receptor for these ligands is in the order insulin >= IGF-2 >= IGF-1, whereas for the type 1 IGF receptor it is IGF-1 >= IGF-2 >= insulin (Nissley and Rechler, 1984; Rechler and Nissley, 1985). Type 2 receptors have a greater affinity for IGF-2 and do not bind insulin or IGF-1 (Rosenfield et al., 1987).

Growth hormone receptors

Because the biological effects of pGH are initiated at the level of the receptor in target cells there has been considerable interest in looking at the effects of pGH treatment on binding to the receptor, the structure of the pGH receptor and the means by which the receptor generates chemical signals that mediate the many diverse biological effects of the hormone. Unfortunately, there is little information in the literature about the pGH receptor. This paucity of information about the signalling systems used by the GH receptor is also true for other species. There is, however, some information about the structure of the GH receptor. The most definitive information is the recently published amino acid sequences for the hGH and rabbit GH receptors (Leung et al., 1987). Both rabbit and human GH receptor clones contain an open reading frame of 638 amino acids which includes an 18 amino acid membrane signal sequence. Thus, the mature form of the receptor is 620 amino acids with an M_r of 70 kDa. This is much smaller than the 130 kDa molecular weight determined by SDS-gel electrophoresis. The difference is likely the result of glycosylation and the presence of covalently bound ubiquitin (Leung et al., 1987). Cloning of the GH receptor from porcine and bovine tissues will permit studies to be conducted in the future to clarify the effects of exogenous GH on GH receptor mRNA abundance. In studies we have conducted, treating pigs with pGH caused an up-regulation of GH binding to porcine liver microsomes. It is not known whether this is the result of differences in pGH receptor mRNA or reflects other changes (such as translational regulatory events).

The amino acid sequence data presented by Leung et al. (1987) indicate that the soluble GH binding protein found in rabbit serum also has the same sequence as the extracellular domain of the receptor. This suggests that the protein could be released by proteolysis of the receptor near the transmembrane domain.

Conclusion

A remarkable era has occurred in animal agriculture over the past eight years. The emergence of recombinant DNA technology has provided sufficient quantities of previously scarce proteins to enable scientists to test hypotheses not previously addressed. Based on our progress to date, it is reasonable to speculate that as we gain a better understanding of the GH receptor and the mechanisms by which GH mediates its biological effects it will be possible to develop second generation approaches that provide either more potent GH analogs or alternative methods to increase GH biopotency. Irrespective of when this happens the progress made to date has shown that treating pigs with exogenous pGH markedly enhances pig growth performance.

References

Abdel-Meguid, S.S., H.S. Shieh, W.W. Smith, H.E. Dayringer, B.N. Violand and L.A. Bentle, 1987. Three-dimensional structure of a genetically engineered variant of porcine growth hormone. Proc. Natl. Acad. Sci. USA. 84:6434-6437.

Albertsson-Wikland, K., S. Eden and 0. Isaksson, 1980. Analysis of early responses to growth hormone on amino acid transport and protein synthesis in diaphragms of young normal rats. Endocrinology 106:291- 297.

Allen, R.E., 1988. Muscle cell growth and development. In: Designing foods. Technical options for the marketplace. National Academy Press, Washington, D.C. p. 142-162.

Ballard, F.J., L.C. Read, G.L. Francis, C.J. Bagley and J.C. Wallace, 1986. Binding properties and biological potencies of insulin-like growth factors in L6 myoblasts. Biochem. J. 233:223-230.

Baxter, R.C., 1988. Characterization of the acid-labile subunit of the growth hormone-dependent insulin-like growth factor binding protein complex. J. Clin. Endocrinol. Metab. 67 :265-272.

Baxter, R.C. and C.T. Cowell, 1987. Diurnal rhythm of growth hormone-independent binding protein for insulin-like growth factors in human plasma. J. Clin. Endocrinol. Metab. 65:432-440.

Baxter, R.C. and J.L. Martin, 1987. Binding proteins for insulin-like growth factors in adult rat serum. Comparison with other human and rat binding proteins. Biochem. Biophys. Res. Commun. 147 :408-415.

Baxter, R.C., J.L. Martin, M.I. Tyler and M.E.H. Howden, 1986. Growth hormone - dependent insulin-like growth factor (IGF) binding protein from human plasma differs from other human IGF binding proteins. Biochem. Biophys. Res. Commun. 139:1256-1261.

Boyd, R.D. and D.E. Bauman, 1988. Mechanisms of action for somatotropin in growth. In : D.R. Campion, G.J. Hausman and R.J. Martin (Ed.): Current concepts of animal growth regulation. Plenum Publishing Corp., New York. (In Press).

Boyd, R.D., D.E. Bauman, D.H. Beermann, A.F. De Neergaard, L. Souza and W.R. Butler, 1986. Titration of the porcine growth hormone dose which maximizes growth performance and lean deposition in swine. J. Anim. Sci. 63 :218.

Brewer, M.T., G.L. Stetler, C.H. Squires, R.C. Thompson, W.H. Busby and D.R. Clemmons, 1988. Cloning, characterization and expression of a human insulin-like growth factor binding protein. Biochem. Biophys. Res. Commun. 12:1289-1297.

Brinkman, A., C. Groffen, D.J. Kortleve, A. Geurts van Kessel and S.L.S. Drop, 1988. Isolation and characterization of a cDNA encoding the low molecular weight insulin-like growth factor binding protein (IBP- 1). EMBO J. 7:2417-2423.

Campbell, R.G., N.C. Steele, T.J. Caperna, J.P. McMurtry, M.B. Solomon and A.D. Mitchell, 1988. Interrelationships between energy intake and exogenous porcine growth hormone

administration on the performance, body composition and protein and energy metabolism of growing pigs weighing 25 to 55 kilograms body weight. J. Anim. Sci. 66 : 1643-1655.

Chen, H.C., A.E. Wilhelmi and S.C. Howard, 1970. Purification and characteristics of porcine growth hormone. J. Biol. Chem. 245:3402- 3406.

Chung, C.S., T.D. Etherton and J.P. Wiggins, 1985. Stimulation of swine growth by porcine growth hormone. J. Anim. Sci. 60: 118-130.

Drop, S.L.S., D.J. Kortleve and H.J. Guda, 1984. Isolation of a somatomedin-binding protein from preterm amniotic fluid. Development of a radioimmunoassay. J. Clin. Endocrinol. Metab. 59 :899-907.

Eden, S., 0. Isaksson, K. Madsen and U. Friberg, 1983. Specific binding of growth hormone to isolated chondrocytes from rabbit ear and epiphyseal plate. Endocrinology 112:1127-1129.

Eden, S., J. Schwartz and J.L. Kostyo, 1982. Effects of preincubation on the ability of rat adipocytes to bind and respond to growth hormone. Endocrinology 111:1505-1512.

Etherton, T.D., 1989. The mechanisms by which porcine growth hormone improves pig growth performance. In: R.B. Heap and C.G. Prosser (Ed.): Biotechnology in growth regulation. Butterworths, London (In Press).

Etherton, T.D., J.P. Wiggins, C.S. Chung, C.M. Evock, J.F. Rebhun and P.E. Walton, 1986. Stimulation of pig growth performance by porcine growth hormone and growth hormone-releasing factor. J. Anim. Sci. 63 1389-1399.

Etherton, T.D., C.M. Evock and R.S. Kensinger, 1987a. Native and recombinant bovine growth hormone antagonize insulin action in cultured bovine adipose tissue. Endocrinology 121 : 699-703.

Etherton, T.D., J.P. Wiggins, C.M. Evock, C.S. Chung, J.F. Rebhun, P.E. Walton and N.C. Steele, 1987b. Stimulation of pig growth performance by porcine growth hormone : Determination of the dose-response relationship. J. Anim. Sci. 64:433-443.

Evans, H.M. and J.A. Long, 1922a. Characteristic effects upon growth, oestrus and ovulation induced by the intraperitoneal administration of fresh anterior hypophyseal substance. Anat. Rec. 23 : 19.

Evans, H.M. and J.A. Long, 1922b. Characteristic effects upon growth, oestrus and ovulation induced by the intraperitoneal administration of fresh anterior hypophyseal substance. Proc. Natl. Acad. Sci. USA 8 38-39.

Evans, H.M and M.E. Simpson, 1931. Hormones of the anterior hypohysis. Amer. J. Physiol. 98 : 511-546.

Evock, C.M., T.D. Etherton, C.S. Chung and R.E. Ivy, 1988. Pituitary porcine growth hormone (pGH) and a recombinant pGH analog stimulate Pig growth performance in a similar manner. J. Anim. Sci. 66 : 1928- 1941.

Gause, L, S. Eden, J.O. Jansson and 0. Isaksson, 1983. Effects of in vivo administration of antiserum to rat growth hormone on body growth and insulin responsiveness in adipose tissue. Endocrinology 112 : 1559- 1566.

Giles, D.D., 1942. An experiment to determine the effect of the growth hormone of the anterior lobe of the pituitary gland on swine. Am. J. Vet. Res. 3 : 77-85.

Goodman, H.M. and V. Coiro, 1981. Induction of sensitivity to the insulin-like action of growth hormone in normal rat adipose tissue. Endocrinology 108 : 113-119.

Gopinath, R. and T.D. Etherton, 1989a. Effects of porcine growth hormone on glucose metabolism of pigs. I. Acute and chronic effects on plasma glucose and insulin status. J. Anim. Sci. (In Press).

Gopinath, R. and T.D. Etherton, 1989b. Effects of porcine growth hormone on glucose metabolism of pigs. 2. Glucose tolerance, peripheral tissue insulin sensitivity and glucose kinetics. J. Anim. Sci. (In Press).

R. Grundmann, U., C. Nerlich, H. Bohn and T. Rein, 1988. Cloning of cDNA encoding human placental protein 12 (PPl2) binding protein for IGF 1 and somatomedin. Nucleic Acid Res. 16:8711.

Henricson, B. and S. Ullberg, 1960. Effects of pig growth hormone on pigs. J. Anim. Sci. 19:1002-1008.

Hintz, R.L. and F. Liu, 1977. Demonstration of specific plasma binding sites for somatomedin. J. Clin. Endocrinol. Metabol. 45:988-995.

Hintz, R.L., E.M. Orsini and M.G. Van Camp, 1974. Demonstration of reversible binding of somatomedins to plasma proteins. Endocrinology 94(Suppl.l) :A71.

Hizuka, N., K. Takano, K. Shizume, K. Asakawa, M. Miyakawa, I. Tanaka and R. Horikawa, 1986. Insulin-like growth factor I stimulates growth in normal growing rats. Eur. J. Pharmacol. 125 : 143-146.

Isaksson, O., J.O. Jansson and I.A. Gause, 1982. Growth hormone stimulates longitudinal bone growth directly. Science 216 : 1237-1239.

Isaksson, O., A. Lindahl and J. Isgaard, 1987. Mechanism of the stimulatory effect of growth hormone on longitudinal bone growth. Endocrine Rev. 8 :426-438.

Isgaard, J., C. Moller, O. Isaksson, A. Nilsson, L.S. Mathews and G. Norstedt, 1988. Regulation of insulin-like growth factor messenger ribonucleic acid in rat growth plate by growth hormone. Endocrinology 122:1515-1520.

Isgaard, J., A. Nilsson, A. Lindahl, J.O. Jansson and O. Isaksson, 1986. Effects of local administration of GH and IGF-1 on longitudinal bone growth in rats. Am. J. Physiol. 250 :E367-E372.

Julkunen, M., R. Koistinen, K. Aalto-Setala, M. Seppala, O.A. Janne and K. Kontula, 1988. Primary structure of human insulin-like growth factor-binding protein/placental protein 12 and tissue specific expresson of its mRNA. FEBS Lett. 236:295-302.

Kibrick, E.A., H. Becks, W. Marx and H.M. Evans, 1941. Effect of different dose levels of growth hormone on the tibia of young hypophysectomized female rats. Growth 5:437-447.

Koistinen, R., N. Kallkinen, M.J. Huhtala, M. Seppala, H. Bohn and E.M. Rutanen, 1986. Placental protein 12 is a decidual protein that binds somatomedin and has an indentical N-terminal amino acid sequence with somatomedin binding protein from human amniotic fluid. Endocrinology 118:1375-1378.

Lee, Y.L., R.L. Hintz, P.M. James, P.D.K. Lee, J.E. Shively and D.R. Powell, 1988. Insulin-like growth factor (IGF) binding protein complementary deoxyribonucleic acid from human HEP G2 hepatoma cells: Predicted protein sequence suggests an IGF banding protein domain different from those of the IGF-1 and IGF-2 receptors. Mol. Endocrinol. 2:405-411.

Lee, M.O. and N.K Schaffer, 1988. Anterior pituitary growth hormone and the composition of growth. J. Nutr. 7 : 337-363.

Leung, D.W., S.A. Spencer, G. Cachianes, R.G. Hammonds, C. Collins, W.J. Henzel, R. Barnard, M.J. Waters and W.I. Wood, 1987. Growth hormone receptor and serum binding protein: Purification, cloning and expression. Nature 330 : 537-543.

Machlin, 1972. Effect of porcine growth hormone on growth and carcass composition of the pig. J. Anim. Sci. 35 : 794-800.

Madsen, K., U. Friberg, P. Roos, S. Eden and O. Isaksson, 1983. Growth hormone stimulates the proliferation of cultured chondrocytes from rabbit ear and rat rib growth cartilage. Nature 304: 545-547.

Madsen, K., A.M. Makower, U. Friberg S. Eden and O. Isaksson, 1985. Effect of human growth hormone on proteoglycan synthesis in cultured rat chondrocytes. Acta Endocrinol. 108 : 338-242.

Magri, K.A., 1988. Effects of growth hormone on glucose transport, lipogenic enzyme activities, insulin receptor binding and tyrosine kinase activity in pig adipocytes. M.S. Thesis, The Pennsylvania state University.

McCusker, R.H., D.R. Campion and D.R. Clemmons, 1988. The insulin-like growth factor binding proteins of porcine sera; endocrine and nutritional regulation. J. Anim. Sci. 66(Suppl. 1) : 259.

Megyesi, K., C.R. Kahn, J. Roth and P. Gorden, 1975. Circulating NSILA-s in man: Preliminary studies of stimuli in vivo and of binding to plasma components. J. Clin. Endocrinol. Metab. 41 : 475-484.

Miller, W.L. and N.L. Eberhardt, 1983. Structure and evolution of the growth hormone gene family. Endocrine Rev. 4: 97-130.

Mills, J.B., S.C. Howard, S. Scapa and A.F. Wilhelmi, 1970. Cyanogen bromide cleavage and partial amino acid sequence of porcine growth hormone. J. Biol. Chem. 245: 3407-3415.

Monier, S., A. Le Cam and V.L. Marchand-Brustel, 1983. Insulin and insulin-like growth factor 1. Effects of protein synthesis in isolated muscles from lean and goldthiglucose-obese mice. Diabetes 32:392-397.

Murphy, L.J., G. Bell and H.G. Friesen, 1987. Tissue distribution of insulin-like growth factor 1 and 2 messenger ribonucleic acid in the rat. Endocrinology 120: 1279-1282.

Murphy, W.R., W.H. Daughaday and C. Hartnett, 1956. The effect of hypophysectomy and growth hormone on the incorporation of labeled sulfate into tibial epiphyseal and nasal cartilage of the rat. J. Lab. Clin. Med. 47: 715-722.

Nissley, S.P. and M.W. Rechler, 1984. Insulin-like growth factors: Biosynthesis, receptors, and carrier proteins. In: C.H. Li (ed.) : Hormonal proteins and peptides. Volume 12. Academic Press, Orlando.

Papkoff, H., C.H. Li a W.K. Liu, 1962. The isolation and characterization of growth hormone from porcine pituitaries. Arch. Biochem. Biophys. 96 : 216-225.

Povoa, G., G. Enberg, H. Jornvall and K. Hall, 1984. Isolation and characterization of a somatomedin-binding protein from mid-term human amniotic fluid. Eur. J. Biochem. 144: 199-204.

Povoa, G., M. Isaksson, H. Jornvall and K. Hall, 1985. The somatomedin- binding protein isolated from a human hepatoma cell line is identical to the human amniotic fluid somatomedin-binding protein. Biochem. Biophys. Res. Commun. 128 :1071-1078.

Raben, M.S. and V.W. Westermeyer, 1951. Recovery of growth hormone in purification of corticotropin. Proc. Soc. Exp. Med. Biol. Med. 78:550-551.

Rechler, M.W. and S.P. Nissley, 1985. The nature and regulation of the receptors for insulin-like growth factors. Ann. Rev. Physiol. 47 425-442.

Rinderknecht, E. and R.E. Humbel, 1978a. The amino acid sequences of human insulin-like growth factor 1 and its structural homology with proinsulin. J. Biol. Chem. 253:2769-2776.

Rinderknecht, E. and R.E. Humbel, 1978b. Primary structure of insulin- like growth factor 2. FEBS Lett. 89:283-286.

Rosenfeld, R.G., C.A. Conover, D. Hodges, P.D.K. Lee, P. Misra, R.L. Hintz and C.H. Li, 1987. Heterogeneity of insulin-like growth factor- I affinity for the insulin-like growth factor-2 receptor: comparison of natural, synthetic and recombinant DNA-derived insulin-like growth factor-I. Biochem. Biophys. Res. Commun. 143 : 199-205.

Russell, S.M. and E.M. Spencer, 1985. Local injections of human or rat growth hormone or of purified human somatomedin-C stimulate unilateral tibial epiphyseal growth. Endocrinology 116:2563-2567.

Rutanen, E-M., R. Koistinen, T. Wahlstrom, H. Bohn, T. Ranta and M. Seppala, 1985. Synthesis of placental protein 12 by human decidua. Endocrinology 116:1304-1309.

Rutanen, E-M., R. Koistinen, J. Sjorberg, M. Julkunen, T. Wahlstrom, H. Bohn and M. Seppala, 1986. Synthesis of placental protein 12 by human endometrium. Endocrinology 118:1067-1071.

Salmon, W.D. Jr. and W.H. Daughaday, 1957. A hormonally controlled serum factor which stimulates sulfate incorporation by cartilage in vitro. J. Lab. Clin. Med. 49:825-836.

Schoenle, E., J. Zapf, C. Hauri, T. Steiner and E.R. Froesch, 1985. Comparison of in vivo effects of insulin-like growth factors 1 and 2 and of growth hormone in hypophysectomized rats. Acta Endocrinol. 108:167-174.

Schoenle, E., J. Zapf, R.E. Humbel and E.R. Froesch, 1982. Insulin-like growth factor stimulates growth in hypophysectomized rata. Nature 296:252-253.

Schwartz, J., 1980. Enhanced sensitivity to insulin in rats treated with antibodies to rat growth hormone. Endocrinology 107:877-883.

Schwartz, J., 1982. Rapid modulation of protein synthesis in normal rats by specific neutralization and replacement of growth hormone. Endocrinology 111 :2087-2090.

Seeburg, P.H., S. Sias, J. Adelman, H.A. de Boer, J. Hayflick, P. Jhurani, D.V. Goeddel and J.L Heyneker, 1983. Efficient bacterial expression of bovine and porcine growth hormones. DNA 2:37-45.

Sillence, M.N. and T.D. Etherton, 1987. Determination of the temporal relationship between porcine growth hormone, serum IGF-1 and cortisol concentrations in pigs. J. Anim. Sci. 64:1019-1023.

Skottner, A., R.G. Clark, I .C.A.F. Robinson and L. Frykland, 1987. Recombinant human insulin-like growth factor: Testing the somatomedin hypothesis in hypophysectomized rats. J. Endocrinol. 112:123-132.

Tavakkol, A., F. A. Simmen and R. C. M. Simmen, 1988. Porcine insulin-lake growth factor-1 (pIGF-1): Complementary deoxyribonucleic acid cloning and uterine expression of measenger ribonucleic acid encoding evolutionarily conserved IGF-1 peptides. Mol. Endocrinol. 2:674-681.

Turman, E.J. and F.N. Andrews, 1955. Some effects of purified anterior pituitary growth hormone on swine. J. Anim. Sci. 14: 7-18.

Van Buul - Offers, S., Il Ueda and J. L. van den Brande, 1986. Biosynthetic Somatomedin C (SM-C/IGF-1) increases the length and weight of snell dwarf mice. Pediatr. Res. 20:825-827.

Vernon, R.G., 1982. Effects of growth hormone on fatty acid synthesis in sheep adipose tissue. Int. J. Biochem. 14:255-258.

Walton, P.E., 1988. Purification and characterization of porcine growth hormone-dependent insulin-like growth factor binding protein. Ph.D. Thesis, The Pennsylvania State University.

Walton, P.E., R.C. Baxter, B.D. Burleigh and T.D. Etherton, 1988a. Purification of the serum acid-stable insulin-like growth factor binding protein from the pig (Sus Scrofa). Comparative Biochemistry and Physiology (In Press).

Walton, P.E. and T.D. Etherton, 1986. Stimulation of lipogenesis by insulin in swine adipose tissue: Antagonism by porcine growth hormone. J. Anim. Sci. 62:1584-1595.

Walton, P.E. and T.D. Etherton, 1987. The culture of adipose tissue explants in serum-free medium. J. Anim. Sci. 65(Suppl. 2) : 25-30.

Walton, P.E. and T.D. Etherton, 1988. Effects of porcine growth hormone and insulin-like growth factor I (IGF-1) on immunoreactive IGF binding protein concentration in pigs. J. Endocrinol. (In Press).

Walton, P.E., T.D. Etherton and C.S. Chung, 1987. Exogenous pituitary and recombinant growth hormones induce insulin and insulin-like growth factor I resistance in pig adipose tissue. Dom. Anim. Endocrinol. 4: 183-189.

124

Walton, P.E., T.D. Etherton and C.M. Evock, 1986. Antagonism of insulin action in cultured pig adipose tissue by Pituitary and recombinant porcine growth hormone: Potentiation by hydrocortisone. Endocrinology 118 :2577-2581.

Walton, P.E., R. Gopinath, B.D. Burleigh and T.D. Etherton, 1988b. Infusion of recombinant human IGF-1 into pigs : Determination of circulating half-lives and chromatographic profiles. Harm. Res. (In Press).

Walton, P.E., R.Gopinath, and T.D. Etherton, 1988c. Porcine insulin-like growth factor (IGF) binding protein blocks IGF-1 action on porcine adipose tissue. Proc. Soc. Expel. Biol. Med. (In Press).

INFLUENCE OF PORCINE SOMATOTROPIN ON ENERGY METABOLISM IN PIGS

M.W.A. Verstegen, W. van der Hel, E.J. van Weerden
Agricultural University Wageningen and Institute of Animal Nutrition and Physiology, ILOB, Wageningen, The Netherlands

Summary

There is evidence that application of porcine somatotropin (pST) to growing pigs increases the metabolic rate. The magnitude of this increase seems to be most clear at similar intake of metabolizable energy in both pST and control animals. At present there is inadequate information on the cause of the increased metabolic rate in treated pigs. The magnitude of the increase from two studies seems to be comparable to an increase of about 10% in maintenance. Whether this is related to increased muscle mass is not clear. Also reduced efficiency of protein and fat gain may be associated with this. It was calculated that at similar maintenance the deposition of fat and protein does not occur at a lower rate of partial efficiency. The possibility of increased metabolic rate due to reduced fatness and thus insulation and therefore increased thermal demand can not be excluded. It needs to be evaluated further what the relation of this heat production is with protein and fat synthesis and what the nutritional consequences are.

Keywords: porcine somatotropin, metabolic rate, maintenance, partial efficiency.

Introduction

Administration of exogenous porcine somatotropine (pST) has been the subject of various studies: Machlin (1972), Chung et al. (1985), Rebhun et al. (1985), Verstegen et al. (1989).

It was found in these studies that protein accretion is markedly increased and that fat gain is drastically impaired by pST. It is important to discuss how metabolism is altered as a result of administration of pST.

Effect on production

Campbell et al. (1988) found with administration of endogenous porcine somatotropin that growth rate in pigs of 25 to 55 kg increased with 16 to 22% and protein deposition with 34 to 50%. These results showed that effects on growth performance and energy and protein metabolism were largely independent of and additive to that of the energy intake. In experiments at our university of Huisman et al. (1988) and Van der Hel et al. (1988) it was found that rate of gain in animals (Pietrain, Duroc and crossbreds between Dutch Landrace and Dutch Yorkshire) from 80 kg onwards with recombinant pST was increased with about 100 g/day at constant feeding level (2.6 times maintenance).

Table 1. Rate of gain (kg/d) and feed conversion of animals of three genotypes at constant feeding level during 6 weeks (5-10 weeks after initial administration).

		Rate of gain	Feed/gain
Pietrain	C	$.87^b$	2.94^b
	T	$.99^a$	2.79^c
Duroc	C	$.72^d$	3.40^a
	T	$.80^c$	3.19^a
DYxDL	C	$.92^b$	2.90^b
	T	1.04^a	2.70^d

In Table 1 data on performance are given. Data clearly show an increased rate of gain and a concomitant decreased feed to gain ratio in animals given the same feeding level. In the experiments of Huisman et al. (1988) and Van der Hel et al. (1988) protein and fat gain were measured with control and with pST treatment. In Table 2 data on these aspects are given for animals of about 80 kg.

Table 2. Effect of pST on rate of gain in protein and fat (g/d).

Genotype	Treatment	protein (g/d)	Fat (g/d)
Pietrain	Control	142	263
	pST	191	249
Duroc	Control	119	275
	pST	166	215
DYxDL	Control	168	280
	pST	210	218

On an average protein gain was increased with about 40 g/d and fat gain was decreased with 47, 18 and 64 g/d in Duroc, Pietrain and DyxDL respectively in these experiments (Table 2).

In addition Reeds (1987) stated that β-adrenergic agents also have a marked repartitioning effect associated with increased energy expenditure.

Table 3. Manipulation of growth by alterations in growth hormone status (Reeds, 1976).

1. Immunization against somatostatin: The removal of a constraint on growth hormone release. Responses in protein deposition associated with enhanced skeletal growth.
2. Administration of growth hormone: A forced increase in systemic growth hormone levels. Pigs: Tendency towards lower food intake with ad libitum feeding. Marginal to zero effect on skeletal growth. Marked repartitioning effect.
3. Introduction of growth hormone or growth hormone releasing factor gene: Persistent secretion of growth hormone. Marked increase in skeletal growth in mice. Presumably marked increase in appetite. No published information on body composition.

According to Table 3 a characteristic effect of alterations in growth hormone is a coordinated growth with all components of the body increased in size. In addition Campbell et al. (1988) concluded that an increased energy expenditure occured with the use of endogenous somatotropin.

It is not clear why increased energy expenditure is associated with the application of extra somatotropine or with the application of β-adrenergic anabolic agents.

According to Machlin's work (1972) with pigs, pST directs nutrients to the muscle during growth. To understand the metabolic effect of somatotropine on metabolism it is important to note that any intervention that alters the rate of a major route of nutrient (or energy) storage will also alter the rate of storage pathways (Reeds, 1987). Therefore it is important to distinguish between the mechanisms which are responsible for a reduction in e.g. fat deposition that might arise from a specific stimulus of protein deposition and those that appear to stem primarily from an increase in energy expenditure. It is not clear how the increase in serum glucose and insuline levels after

somatotropin applications in pigs (Etherton et al., 1986; Boyd, 1987) is associated with increased energy expenditure. Campbell et al. (1988) showed in pigs that changes in lipid and protein metabolism elicited by pST were largely independent of energy intake.

Metabolic heat production

Energy expenditure in animals can be calculated as follows: We first assume that animals are kept at thermoneutral conditions. Heat (or thermal losses) is produced as a result of the many metabolic processes occurring within the animal, the extent to which it occurs is not only characteristic of the animal per se but it is also dependent upon nutritional, productive, environmental and other related factors. Thus no simple system can be used to describe the contribution made by the various factors to metabolic heat production.

In practice, and in order to facilitate the application of energy evaluation systems, it has been customary to divide thermal losses into those associated with maintenance, on the one hand, and those resulting from the deposition of tissue or products formed within the body, on the other. The former, the maintenance heat loss, represents an animal in a state of energy equilibrium, that is neither losing nor gaining energy, so that the intake of dietary energy exactly balances the animal's heat output. The heat arising from the accretion of tissues or products within the body represents the amount of work done in their deposition and varies with the nutritional state of the animal, so that the higher the level of feed intake, the higher the rate of tissue accretion and the greater the heat output associated with these processes, i.e. the heat increment of feeding (which is synonymous with "specific dynamic action" and "dietary induced thermogenesis"). Both the maintenance heat loss and heat produced as a result of tissue deposition are influenced by a number of factors. As the rate of the animal's heat loss increases at any given level of feed intake, there will be a reduction in the rate at which energy is retained and hence a change in the energetic efficiency of growth. For practical purposes it is important to know to what extent heat production varies in relation to those factors which influence it, since this determines the extent and efficiency of energy utilisation.

It is appropriate to express the energy retained by an animal as a function of its bodyweight and the quality and quantity of the ration provided. Food can then be described in its capacity to sustain maintenance (ME_m) and to promote energy gain (RE). This is illustrated in Figure 1, where
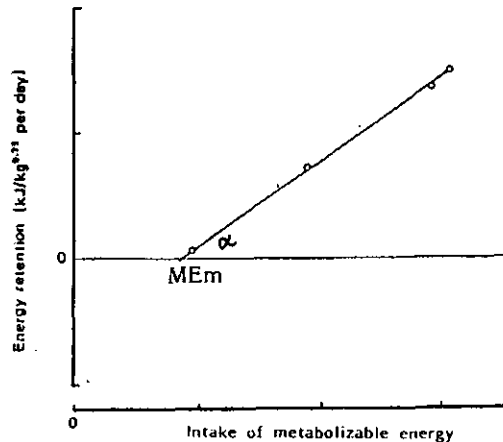

Figure 1. The Relation between energy retention ($kJ/kg^{0.75}$ per day) and metabolizable energy ($kJ/kg^{0.75}$ per day) in the pig at thermoneutral condition. $T_g\alpha$ is partial efficiency above maintenance. ME_m is metabolizable energy needed for maintenance.

129

metabolizable energy (ME) intake, i.e. the gross energy of the feed minus the energy lost in faeces, urine and methane, is related to energy retained (RE).

We assume that partial efficiency ($t_g\alpha$ in Figure 1) was not altered with increase in ME intake. The inefficiency $1-t_g\alpha$ is for heat increment.

Above the basal or fasting level of metabolism, each increment in ME is associated with an increment in heat production (H). However, the increment in ME exceeds the increment in H so that the animal has the capacity to retain energy (RE), although RE only becomes positive at intakes above the maintenance energy requirement, that is at ME_m - RE is zero. The efficiency with which energy is retained is equal to dRE/dME. As we are working with growing animals feed intake is normally above maintenance. We assumed linearity between energy retention and intake of metabolizable energy. Energy retention can be described as:

$$RE = k_g * ME - b \qquad (1)$$

in which: RE = retained energy
ME = metabolizable energy
k_g = dRE/dME
b/k_g = maintenance requirement.

This procedure was applied by Campbell et al. (1988). They regressed RE on ME intake. They used digestible energy instead of metabolizable energy. This is justified because there is a nearly fixed ratio of digestible to metabolizable energy above maintenance. Since there is a very high correlation between metabolizable energy and digestible energy (DE) this formula (1) also holds for DE. The value $(1-k_g)$ represents the increase in energy expenditure with feed intake above maintenance (ME_p).

The efficiency is representative for total energy gain from ME and does not account for differences in its composition, reflected in the rates of protein and fat deposition. Separate estimates of the energetic efficiency of protein deposition (k_p) and fat deposition (kf) can be calculated with the respective heat increments being $ME_{protein}$ $(1-k_p)$ and ME_{fat} $(1-k_f)$. Thus total thermal loss associated with he metabolism of dietary energy is the sum of the energy costs of maintenance (ME_m) and the heat increment associated with the deposition of tissue, calculated as ME_p $(1-kg)$ or partitioned into that associated with protein deposition, ME $_{protein*(1-kp)}$ and fat deposition, ME $_{fat*(1-kf)}$.

Relation of partial efficiency and maintenance to metabolic rate

In the literature there are many estimates of the partial efficiencies of fat and protein accretion k_p and k_f. Theoretically the efficiency of utilisation of ME for protein synthesis may be about 0.85 (Van Es and Boekholt, 1987). In studies with young pigs mostly values of .35 to .60 are derived (ARC, 1981). It should be mentioned here that higher protein turnover may be responsible for the higher heat production per unit of protein gain compared to the theoretical values. In fat gain theoretical values for k_f and measured values are nearly similar. This similarity can be explained by the low turnover in fat (see Van Es, 1978). In the ARC study of (1981) values of k_p and k_f were assumed at 0.54 and 0.77, respectively. These results mean that k_g in formula (1) depends on the ratio in which protein and fat are deposited. The lower value with k_p is generally associated with protein turnover. The protein gain accretion is then the net result of protein synthesis and proteolysis. If this ratio is altered with application of pST, k_p will be altered.

Table 4. Heat production and energy balances in control (C) and pST (T) animals.

		Heat production (H) kJ/kg$^{0.75}$	Retained energy (RE) kJ/kg$^{0.75}$
Pietrain	C	632	448
	T	653	427
Duroc	C	611	469
	T	669	418
Crossbred	C	623	469
	T	682	427

In the experiments of Van der Hel et al. (1988) heat production has been measured and also protein and fat gain were determined. From the data of Table 4 it is clear that heat production in pST animals was higher than in C animals and retained energy is reduced at the same feed intake (Figure 2). This increase can not be explained totally by the increase in protein accretion.
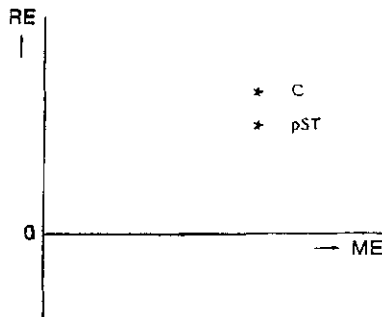
Figure 2. Effect of pST on RE.

In Figure 2 effect of pST on RE is given. The reduced RE can be related to ME intake in various ways:

— Increased maintenance requirement.

— Decreased efficiency of energy utilization for protein accretion.

— Decreased efficiency of energy utilization for fat accretion.

Maintenance requirement

This way is depicted in Figure 3 where it has been assumed that the effect of pST is on maintenance and not on partial efficiency. Maintenance increase can be caused by various factors. It may be related to increased protein content in the body, activity and increased thermal demand.
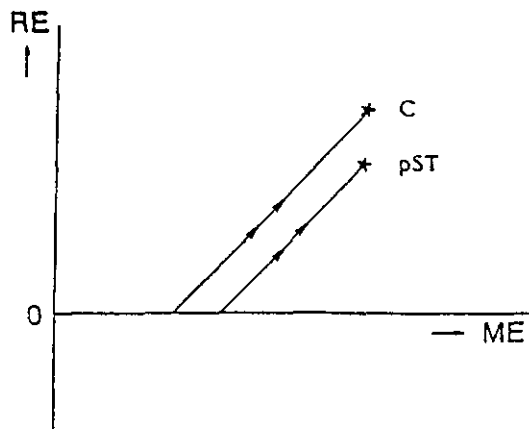
efficiency is similar

Figure 3. Effect of pST on maintenance requirement (ME).

Maintenance requirement (ME_m) was calculated as: ME_{intake} - Energy in fat retained/k_f - Energy in protein retained/k_p. If no change in energy requirement per kJ retained in fat and protein is assumed, than maintenance requirement is as follows:

$$\text{Controls: } ME_m = 393 \text{ kJ ME/kg}^{0.75};$$
$$\text{pST treated: } ME_m = 491 \text{ kJ ME/kg}^{0.75}.$$

Campbell et al. (1988) assumed a higher maintenance requirement for pST treated animals as well. Kanis et al. (1989) found in their experiments that lean in animals at 100 kg was increased from 55.5% to 59.5% with pST.

With the following assumptions the calculations in Table 5 can be made:

— mean weight of 80 kg during application in the second half of the fattening period.

— carcass weight = 0.77 x weight = 61.6 kg (0.77 from Walstra, 1980).

— lean in body = 1/0.58 x lean in carcass (from Whittemore, 1983).

— protein in body = 1/4.39 lean (Metz et al., 1983).

— calculated maintenance requirement for protein in the body as ME_m (in MJ day) = 1.85 x protein$^{0.78}$ (Whittemore, 1983)

Tabel 5. Calculation of maintenance requirement for protein.

	Control	pST treated
Lean (kg)	33.14	36.65
Protein (kg)	13.13	14.52
Maintenance requirement for protein (MJ)	13.70	14.91
Maintenance requirement for protein (MJ/kg$^{0.75}$)	.51	.56

By presenting results in this way part of the increased metabolic rate would be explained. In addition if pigs treated with somatotropine are more active and/or more sensitive to cold as

suggested by Curtis (1987) such an increased maintenance requirement would be expected. If we first assume that our animals were in the zone of thermoneutrality than increased metabolic rate is not due to coldness. Reeds (1987) and Campbell et al. (1988) indicate an increased metabolic rate with pST as well.

In experiments of Kanis et al. (1988) it was found that with pST backfat was reduced with about 18%. This may alter heat loss from animals to the environment. Heat transfer from the animal to the environmental depends on insulation value of:

— Boundary layer of air around the animal.

— Hair coat.

— Tissue.

The first two are termed external insulation. Maximal tissue insulation at vaso constriction depends on the layer of fat around the body. It can be easily calculated what the effect of reduced (backfat) thickness on tissue insulation and thus total insulation will be. Hovell et al. (1977) measured insulation value in thin and in normal sows. They calculated that the tissue insulation of a normal pig is less than half of the total insulation. Therefore it is important to note that Curtis (1987) calculated that a 50% reduction in fat layer reduced the insulation value by more than 10%. This means that one of the avenues of heat transport from the animal's core to the environment is easier.

It depends on the contribution of the tissue insulation to total insulation how much the lower critical temperature is altered (increased) by this. Almost certainly the critical temperature is increased by some degrees by pST depending on the degree of reduction in the fat layer surrounding the body. On the other hand however, as metabolic rate is increased the critical temperature is lowered. It needs to be assessed what the consequences of the combination of the increased metabolic rate and decreased backfat thickness will be. In Figure 4 both situations have been depicted.
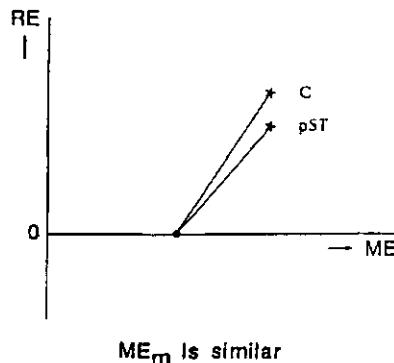
Figure 4. Possible effects of pST on thermal demand.

In Figure 4 the $t_g\alpha$ is for increased thermal demand below thermoneutrality and as insulation in pST animals is less than in controls, thermal demand is increased.

Differences in maintenance requirement have been reported for pigs with different genetic capacities for growth (Campbell and Taverner, 1985) and in pigs selected for different backfat thickness (Sundstøl et al., 1979). Also in mice selected for low body weight Van der Wal et al. (1976) reported a higher maintenance compared to control animals.

Protein gain

In Figure 5 it is shown how, with similar maintenance, differences in efficiency of retained energy can occur. Furthermore, this efficiency can be calculated from energy in protein or from energy in fat gain.
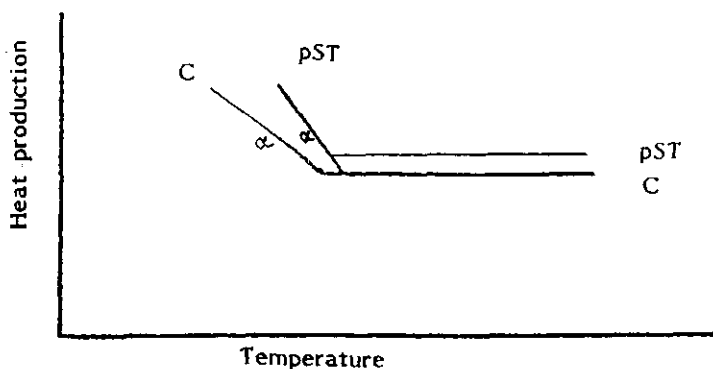

Figure 5. Effect of pST on efficiency of feed utilisation above maintenance.

Net protein synthesis is increased with the administration of pST. The efficiency of feed N utilization is greatly improved. However this does not mean that the partial energetic efficiency of protein accretion is also increased. It may be that the increase in protein accretion as a result of pST is associated with a more rapid protein turnover, resulting from simultaneously increased anabolic and catabolic processes. This would lead to an increased metabolic rate.

If we assume the same maintenance (420 kJ ME/kg $^{0.75}$) in all animals and the same partial efficiency for fat deposition ($k_f = 0.74$) in all animals, then the resulting partial efficiency of energy utilization for protein accretion (k_p) is as follows:

Controls: $k_p = .59$;
pST treated: $k_p = .48$.

Campbell et al. (1988) assumed that the higher metabolic rate with pST resulted from higher protein accretion. With the assumptions made above, our results showed that the partial energy efficiency of protein accretion in control animals (k_p) was similar to the ARC (1981) estimate. However k_p in pST animals was markedly reduced.

Fat gain

There may be a third reason for the increase in heat production. Increased lypolysis (Etherton et al., 1986) may increase fat "turnover" and as a result the partial efficiency of fat deposition from metabolizable energy is reduced. This implies that k_f in pST animals should be less than .74 compared to control animals. When we calculate k_f by assuming that maintenance is equal in all groups (420 KJ ME/kg$^{0.75}$) and partial energy efficiency for protein formation was also equal ($k_p = 0.54$) then the resulting energy required per kJ (k_f) was as follows:

Controls: $k_f = 0.77$;
pST treated: $k_f = 0.68$.

Campbell et al. (1988) mentioned that the inhibition of lipogenesis may cause the decrease in fat accretion. They however also suggest that the reduced amount of energy available for lipogenesis

may contribute in a passive way to reduction in fat accretion. Their results of increased fat accretion with extra energy intake and pST showed that the reduced availability of energy above that for protein synthesis and/or maintenance may be responsible for the lower deposition. It is possible that energy requirement for maximum protein gain is increased with pST. Thus metabolic changes in pST animals need to be assessed with regard to requirements of protein and energy. It can be concluded that pST increases protein gain, reduces fat gain and increases metabolic rate. Until now it is not clear, whether the cause is altered maintenance or lower efficiency of energy gain.

References

ARC, 1980. The nutrient requirement of pigs. Agricultural Research Council Commonwealth Agricultural Bureaux, Slough, England, 341 pp.

Boyd, R.D., 1987. Somatotropin and productive efficiency in swine. Animal Health & Nutrition, Febr. 1987, p. 23.

Campbell, R.G., N.C. Steele, T.J. Caperna, J.P.M.C. McMurty, M.B. Solomon and A.D. Mitchell, 1988. Interrelationship between energy intake and endogenous porcine growth hormone administration (pGH) on the performance, body composition and protein and energy metabolism of growing pigs weighing 25 to 55 kg live weight. J. Anim. Sci. 66: 1643-1655.

Campbell, R.G. and M.R. Taverner, 1985. The effects of strain and sex on protein and energy metabolism in growing pigs. In: P.W. Moe, H.F. Tyrell and P.J. Reynolds, (Eds. EAAP-publ. no. 31. Proc. En. Met. Virginia, p. 78-81. Roman and Littlefield, USA.

Chung, G.S., T.D. Etherton and J.P. Wiggins, 1985. Stimulation of swine growth by porcine growth hormone. J.Anim.Sci. 60: 118-130.

Curtis, S.E., 1983. Environmental management in animal agriculture. Iowa University Press. 409 pp.

Curtis, S.E., 1987. Management and environmental considerations for successful use of Repartitioning Agents, p. 64-68. In: Pork Industry Conf. Urbana, 10-11 Dec.

Etherton, T.D., J.P. Wiggins, C.S. Chung, C.M. Evock, J.F. Rebhun and P.E. Walton, 1986. Stimulation of pig growth performance by porcine growth hormone and growth hormone releasing factor. J.Anim.Sci. 63: 1389.

Van der Hel, W., M.W.A. Verstegen, J. Huisman, E. Kanis, E.J. van Weerden and P. van der Wal, 1988. Effect of pST treatment on energy balance traits and metabolic rate in pigs. J.Anim.Sci. 66, (Suppl. 1):299 (Abstr.).

Huisman, J., E.J. van Weerden, W. van der Hel, M.W.A. Verstegen, E. Kanis and P. van der Wal, 1988. Effect of rpST treatment on rate of gain in protein and fat in two breeds of pigs and crossbreds. J.Anim.Sci. 66,(Suppl. 1): p. 259, (Abstr.).

Hovell, F.D. de, J.G. Gordon and R.M. MacPherson, 1977. Thin sows. 2 Observations on the energy and nitrogen exchanges of thin and normal sows in environmental temperatures of 20 and 5°C. J. Agric. Sci. 89: 923-933.

Kanis, E., G.J. Nieuwhof, K.H. de Greef, W. van der Hel, M.W.A. Verstegen, J. Huisman and P. van der Wal, 1989. Effect of recombinant porcine somatotropin on growth and carcass quality in growing pigs dependent on genotype and slaughter weight. J.Anim.Sci. (to be submitted).

Machlin, L.J., 1972. Effect of porcine growth hormone on growth and carcass composition of the pig. J.Anim.Sci. 35: 794.

Metz, S.H.M., F.W. Kamphuis, A.C.M. Mentink, E. Kanis, C.M.C. van de Peet-Schwering and M.W.A. Verstegen, 1986. Simulation of growth performance in growing/fattening pigs. 37th Annual Meeting of the EAAP, Budapest.

Reeds, P.J., 1987. Metabolic control and future opportunities for growth regulation. Anim.Prod. 46: 149-160.

Rebhun, J.F., T.D. Etherton, J.P. Wiggins, C.S. Chung, P.E. Walton and N.C. Steele, 1985. Stimulation of swine growth performance by porcine growth hormone (pGH): Determination of the maximally effective pGH dose. J.Anim.Sci. 61 (Suppl. 1): 291 (Abstr.).

Sundst øl, F., N. Standal and O. Vangen, 1979. Energy metabolism in lines of pigs selected for thickness of backfat and rate of gain. Acta Agriculture Scandinavica 29: 337-345.

Verstegen, M.W.A., W. van der Hel, A.M. Henken, J. Huisman, E. Kanis, P. van der Wal and E.J. van Weerden, 1989. Effect of exogenous porcine somatotropine administration on partitioning nitrogen and energy metabolism in three genotypes of pigs. J. Anim. Sci. (Submitted).

Van der Wal, H., M.W.A. Verstegen and W. van der Hel, 1976. Protein and fat deposition in selected lines of mice in relation to feed intake. EAAP publ. no. 19. Proc. En. Metab. Vichy: 125-129.

Van Es, A.J.H., 1978. Nutritional efficiency of protein and fat deposition. In: H. de Boer and J. Martin (Eds.). Patterns of growth and development in cattle. Martinus Nijhoff Publishers, Dordrecht, p. 361-382.

Van Es, A.J.H. and H.A. Boekholt, 1987. Energy metabolism of farm animals. In: Energy metabolism of farm animals. M.W.A. Verstegen and A.M. Henken, (Eds.). Martinus Nijhoff Publishers, Dordrecht, p. 3-19.

Walstra, P., 1980. Growth and carcass composition from birth to maturity in relation to feeding level and sex in Dutch Landrace pigs. Communications Agricultural University 80-4, Wageningen.

Whittemore, C.T., 1983. Development of recommended energy and protein allowances for growing pigs. Agricultural Systems 11: 159-186.

IMPLICATIONS OF BIOTECHNOLOGICAL TECHNIQUES FOR MANIPULATING ANIMAL GROWTH AND DEVELOPMENT ON TISSUE AND DIETARY NUTRIENT REQUIREMENTS OF PIGS

R.G. Campbell, R.J. Johnson and R.H. King
Animal Research Institute, Werribee, Victoria 3030, Australia

Summary

Exogenous administration of porcine growth hormone pGH, GH releasing factors and possibly IGF-1 enhance protein and mineral accretion rates resulting in more rapid skeletal development, improved growth performance and reduce carcass fat content. However the effect these technologies have on the growing pigs requirement for dietary nutrients remains unclear. For pigs 30 to 60 kg exogenous GH administration increases protein deposition 25-40%, but because of unknown improvements in amino acid utilisation has little effect on the levels of dietary protein and amino acids required to support near maximum growth performance. In contract pGH administration between 60 and 100 kg increases protein deposition 50 to 80 % (depend on animal sex) and there is a concomitant 30-45 % increase in the level of dietary protein (amino acids) required for near maximal growth performance. The stimulation of protein metabolism elicited by pGH is mediated via IGF-1 and results from increases in the rates of both protein synthesis and breakdown. However to fully evaluate the impact of pGH and related technologies on dietary nutrient requirements further information is required on the magnitude of increases in protein and mineral accretion rates able to be achieved by these technologies and on the associated changes in intermediary amino acid and mineral metabolism.

Keywords: somatotropin, swine, nutrient requirements, protein, minerals.

Introduction

Research conducted over the last five years has demonstrated the potential role of biotechnology in improving the efficiency and profitability of animal agriculture.

The marked improvements in growth performance and carcass merit which have been reported for pigs administered porcine growth hormone (pGH) have encouraged a number of companies to pursue the commercialisation of this and related technologies.

However, the extent that the animals' dietary nutrient requirements and other management procedures might need to be altered to ensure the success of these technologies remain unclear. There is, nevertheless, increasing information becoming available on the response of treated pigs to nutrient intake and on the changes in tissue accretion rates elicited by the various technologies in growing pigs. The present paper attempts to review the relevant data and to highlight where this is either inadequate or misleading.

Effects on protein metabolism and dietary protein / amino acid requirements

It has become clear from recent research findings that the endocrine system, and endogenous GH secretion in particular, is the major factor constraining protein accretion in growing pigs. This is illustrated in Tables 1 and 2 which show the changes in protein deposition and growth performance elicited by exogenous pGH administration in pigs growing from 25 to 55 and from 60 to approximately 100 kg live weight respectively.

Table 1. Effect of exogenous pGH administration (0.1 mg pituitary derived GH.kg^{-1}.d^{-1}) on protein deposition and performance of ad libitum fed castrated male pigs growing from 25 to 55 kg (Campbell et al., 1988a).

	pGH(mg.kg^{-1}.d^{-1})	
	0.0	0.10
Protein deposition (g/d)	110	151
Fat deposition (g/d)	283	193
Daily gain (g/d)	905	1052
Feed intake (kg/d)	2.32	2.08
Feed:gain	2.57	1.96
Carcass fat (%)	28.0	20.0

Table 2. Effect of exogenous pGH administration between 60 at approximately 100 kg on protein deposition and performance of boars, gilts and castrated male pigs (Campbell et al., 1989).

SEX	BOAR		GILT		CASTRATE	
pGH (mg.kg^{-1}.d^{-1})	0.0	0.1	0.0	0.1	0.0	0.1
Protein deposition (g/d)	196	238	148	234	139	224
Fad deposition (g/d)	316	202	410	185	462	221
Daily gain (g)	1185	1341	1010	1237	1057	1124
Feed Intake (kg/d)	3.21	1.96	3.37	2.73	3.67	2.84
Feed:gain	2.72	2.21	3.36	2.20	3.65	2.32
Carcass fat (%)	24.3	18.6	28.7	18.9	32.7	21.5

It is clear from these and other results that the marked increase in protein deposition elicited by pGH administration, which in turn appears to be medicated via the somatomedins (IGF-1), is the mechanism by which pGH therapy stimulates growth rate and feed conversion efficiency. Similar changes in protein accretion, growth performance and carcass composition would be expected to resume from any technology which increases circulating pGH and IGF-1 levels.

Under 'normal' circumstances the initiation and maintenance of increases in protein accretion of the magnitudes shown in Tables 1 and 2 would be expected to require concomitant increases in the levels of dietary protein and amino acids. Indeed, using the factorial approach Boyd et al. (1988) predicted an almost two-fold increase in the dietary lysine requirement of pigs administered pGH (0.1 mg.kg^{-1}.d^{-1}) between 55 and 100 kg liveweight. However, the factorial approach requires accurate information on the rate and amino acid composition of protein gain and relies on numerous assumptions regarding the efficiency with which dietary nutrients are metabolized and integrated into animal tissues. It takes no account of the extent that the increase in protein deposition elicited by pGH administration and any related technology results from relative changes in the rates of protein synthesis and breakdown or in the efficiency of amino acid transfer or intermediary amino acid metabolism. All these factors however, affect the amount of dietary protein required to support protein growth at the tissue level.

Until more of this information is available the factorial approach will remain limited as a means of estimating the impact of biotechnological techniques for manipulating growth and development or the animal's dietary nutrient requirements. In the meantime, it is the empirical or descriptive type experiments which provide the more informative data.

A number of such experiments have been conducted with pGH treated pigs. Unfortunately, the value of most of these studies is limited by various design problems and/or by the narrow range of protein/amino acid inputs over which the animal's responses were assessed.

It was concluded from the results of Studies conducted at Kansas State University (Goodband et al., 1988) that pGH administration (4.0 mg.pig^{-1}.d$^{-1)}$ doubled the pig's dietary lysine requirement between approximately 60 and 100 kg liveweight (from 0.6 to 1.2% total lysine). However, the authors did not assess the responses of control animals to dietary lysine concentration beyond the lowest level tested (0.6%) and based their conclusion on the NRC (1988) estimate of lysine requirement for pigs between 60 and 100 kg. Based on growth performance it could also be suggested that there was little improvement in the growth rate or feed:gain of pGH treated pigs to levels of dietary lysine above 1.0% (0.68g total lysine/MJ DE) which is not much higher than the ARC (1981) estimate of requirement for female or castrated male pigs of similar weight and somewhat below the estimate of requirement for boars of slightly lighter body weight (ARC, 1981). Based on the results of a similar experiment conducted at the University of Illinois, Easter (1987) suggested that pGH administration (3mg.kg^{-1}.d^{-1}) increased the dietary protein requirement of castrated male pigs growing between 45 and 100 kg from 14 to 23.6%. However, again the responses of control pigs to dietary protein were not assessed. The improvements in growth rate and feed:gain in response to increasing dietary protein were also small and appeared to peak between 17 and 20% dietary protein.

Similar difficulties apply with the data of Fowler et al. (1988) who compared the performance and carcass merits of pigs given four pGH dosages (0.0, 1.75, 3.50 and 7.0 mg.pig^{-1}.d^{-1}) each at two levels of dietary protein (165 and 190 g/kg) between 30 and 95 kg. The results clearly indicated that the magnitude of the improvements in growth rate, feed:gain and in carcass quality (less fat) elicited by pGH were increased on the higher protein diet. However, because only two levels of dietary protein were tested, and the lower level was almost certainly deficient for pigs from 30 to 60 kg, the results do not provide the quantitative information required to determine the levels of dietary protein required to achieve the most economic responses in terms of growth performance and carcass characteristics for pGH treated pigs.

The results of a more quantitative experiment in which the responses of control and pGH treated boars to six levels of dietary ideal protein (ARC, 1981) were assessed between 30 and 60 kg liveweight are presented in Table 3.

Table 3. Effects of exogenous pGH administration on the responses of fast growing boars to dietary ideal protein between 30 and 60 kg (Campbell et al., 1988b).

Dietary * protein (g/kg)	pGH (mg.kg^{-1}.d$^{-1)}$	Protein deposition (g/d)	Fat deposition (g/d)	Daily gain (g)	Feed:gain (g/g)	Carcass fat (%)
83	0.0	72	234	605	3.08	31.1
	0.09	71	186	583	3.18	27.6
114	0.0	108	208	712	2.61	24.7
	0.09	111	175	750	2.47	21.9
145	0.0	122	210	776	2.36	24.2
	0.09	152	162	908	2.03	18.0
176	0.0	144	200	871	2.16	20.8
	0.09	166	133	977	1.87	15.6
207	0.0	146	192	790	2.26	22.1
	0.09	173	123	1007	1.81	14.7
238	0.0	139	187	866	2.14	21.2
	0.09	174	98	1004	1.78	13.5

*All pigs given 1.85 kg feed/d.

The results clearly demonstrate that at the lowest level of dietary protein tested (83g/kg), protein intake was inadequate to enable pGH to exert its stimulatory effect (via IGF-1) on protein deposition. Fat deposition on the other hand, was reduced 20% on the same diet by pGH administration resulting in growth performance being depressed compared to that of control animals and an 11% reduction in carcass fat content.

Apart from demonstrating independent effects of pGH on protein and lipid metabolism, the results also show that the stimulatory effect of the hormone on protein deposition increased with increasing dietary protein to a maximal rate of approximately 173 g/d compared to approximately 140 g/d for control pigs. More interesting however, was the fact that the level of dietary ideal protein required to support this 24% higher rate of protein deposition was only 4% above the required by control pigs (182 vs. 175 g ideal protein/kg). Similar results have been found for pigs of the same weight given diets of constant lysine content but varying widely in total nitrogen content by Stelle and Caperna (personal communication).

The results presented in Table 3 could not be predicted using the factorial approach. They further indicate that pGH may exert its effect on protein deposition by inhibiting protein breakdown and/or by increasing amino acid transfer or the efficiency of intermediary protein metabolism.

Effect of pGH administration on protein synthesis and breakdown

To investigate the effects of exogenous pGH administration on protein turnover, an experiment was conducted at the ARI, Werribee in which N^{15}-glycine was administered to gilts fitted with indwelling bladder catheters and treated with pGH (0.1 mg.kg^{-1}·d^{-1}) for a period of 18 days commencing at 60 kg live weight. The pigs were given a single diet in restrictive amounts (24 MJ DE/d) and N-balance and N^{15} enrichment was measured from faeces and urine collected every 12h for 72h.

The results showed that pGH administration increased N-retention by 38% (7.5 g/d) and that this was associated with a 47% increase in N-synthesis and 48% increase in N-breakdown.

These data (R.G. Campbell, R.J. Johnson, F. Thomas and R.H. King, unpublished results) demonstrate that pGH stimulates overall protein metabolism. The results also indicate that the positive effect of pGH on protein deposition occurs not because the hormone has a proportionally greater effect on protein synthesis than protein breakdown or vice versa but because in pigs up to 90 kg, at least, protein synthesis exceeds protein breakdown. The results however, raise the question as to the effectiveness of pGH and related technologies in stimulating the performance of heavier pigs (150-200 kg) in which the rates of protein synthesis and breakdown approach one another.

These findings clearly rule out an inhibitory effect of pGH on protein breakdown as a possible explanation for the similarity in the dietary protein requirements evidenced for pGH and control pigs in Table 3. Nevertheless, the proportional improvement in protein deposition elicited by pGH administration to the young fast growing boars used in this experiment (24%) is relatively small compared to that table to be achieved in heavier castrates and gilts. Clearly the extent that the treated pigs dietary protein requirement will be altered by any of the GH related technologies will be a direct reflection of the increase in protein deposition elicited by the technology. The magnitude of the improvement in protein deposition is known to be influenced by the age or weight of the pig, sex, dosage and by the technology employed.

Effects of liveweight

Any change in the dietary protein/amino acid requirements elicited by pGH or any of the related technologies will be less pronounced in light compared to heavy pigs, since maximal protein deposition (tissue requirement) is constrained by energy intake and by the endocrine system

respectively in the two groups. This was demonstrated by the results of a recently completed experiment at the Animal Research Institute, Werribee in which pGH administration $(0.09 \text{ mg.kg}^{-1}.d^{-1})$ was found to increase the maximal growth performance and dietary ideal protein requirement of intact male pigs growing from 60 to 90 kg by 52 and 68% respectively compared to controls.

Effects of sex and dosage

Because boars are less responsive in terms of protein accretion to exogenous pGH administration (Campbell et al., 1988b) and presumably any other technology which acts through the GH axis, the dietary protein requirement of boars would be expected to be proportionally smaller than that of castrated males or gilts. Similarly because protein deposition responds in a linear fashion to increasing GH and GHRF dosage (Etherton et al., 1987; Dubreuil et al., 1988) up to the point that protein growth becomes constrained by intrinsic factors other than GH (Campbell et al., 1988d). The animal's requirement for dietary protein will probably be unaltered at low doses and increase at higher doses.

Effects of feed intake

The reduction in voluntary feed intake induced by pGH administration, and observed in pigs transgenic for pGH (Seemark, personal communication) and bGH (Pursel et al., 1988) further complicates the interrelationship between these technologies and the animal's dietary nutrient requirements.

It is generally assumed that reduction in voluntary feed intake immediately necessitates an increase in dietary protein to support even the same daily protein intake as control animals. However, this proposition is only valid if the animal is exhibiting maximum protein deposition or alternatively when the latter is not constrained by energy intake. For pigs to 50-60 kg this situation rarely exists since during these earlier stages of growth the pig's ceiling for protein growth generally exceeds its appetite. Under these circumstances there is a constant relationship between energy intake and the animal's tissue and dietary protein (amino acid) requirements. Furthermore, the latter are unaffected by feed intake. These facts are well established for 'normal' or untreated pigs (Campbell et al., 1985a). A constant or linear relationship between energy intake and protein deposition has also been demonstrated for pigs administered pGH between 25 and 55 kg liveweight (Campbell et al., 1988a).

For adlibitum fed pigs above 60 kg the animal's dietary protein and amino acid requirements can only be expressed on a daily intake basis since protein deposition plateaus between 75 and 85% of adlibitum energy intake (Campbell et al., 1985b; Whittemore, 1986). Clearly, under these circumstances, any factor which affects voluntary feed intake will necessitate a change in dietary protein (amino acid) concentration. However, given the extremely large increases in protein deposition elicited by pGH administration in heavy castrates and gilts, it is possible that for treated pigs the relationship between energy intake and protein deposition no longer plateaus but remains linear as in the younger pig.

Presently there is no quantitative information on the form of the relationship between energy intake and protein deposition for pGH treated pigs above 60 kg. Such information is crucial if the implications of pGH and related technologies on dietary and tissue protein requirements are to be fully evaluated.

Effects on lipid metabolism and energy requirement for maintenance

Given the marked increases in protein turnover and lean body mass associated with pGH administration it is not surprising that the maintenance energy requirement (MER) of treated pigs has been reported to be 12-16% higher than that of control animals (Verstegen, personal communication; Campbell et al., 1988a).

Similar differences in heat production or MER have been reported between lean and obese rats (Webster et al., 1978), boars and gilts (Campbell et al., 1985b) and between pigs with low and high capacities for protein growth (Campbell and Taverner, 1988).

Increase in MER appears to be an inevitable consequence of raising an animal's capacity for protein accretion and although it cannot sensibly be counteracted at the dietary level, it clearly has to be taken into account when attempting to predict the changes in growth performance and carcass composition likely to be elicited by pGH administration or any related technology.

From a more practical aspect, unless appropriate changes are made to the animal's thermal environment, the increased heat production associated with pGH administration and clearly evidenced by pigs transgenic for bGH, (Pursel, personal communication) may further depress the voluntary feed intake of such animals particularly during periods of hot weather. For the same reason the viability of these technologies may be seriously threatened in the more tropical regions of the world.

The implications of the increased heat production associated with these technologies needs to be investigated over a range of environmental conditions and appropriate strategies developed to overcome any serious problems which are identified.

Effects on dietary requirements for calcium, phosphorus and micro nutrients

There is evidence that pGH administration increases the rates of deposition of calcium and phosphors (Campbell et al., 1988 a,b; Verstegen, personal communication). The changes elicited in calcium and phosphorus metabolism by pGH also appear more pronounced in pigs between 30 and 60 kg compared to those of heavier weight and in gilts compared to boars and castrates (Campbell et al., 1988b). However, because of lack of information on the extent that the metabolizability of these nutrients is altered by pGH or related technologies, it is not possible to determine their impact on dietary requirements. Circumstantial evidence nevertheless, suggests that the dietary levels of calcium and phosphors recommended by the ARC (1981), which are considerably higher than those recommended by the NRC (1988), are adequate to ensure structural soundness even in animals administered even high doses of pGH.

It is even more difficult to predict the effect of the various technologies for manipulating growth and development on pigs requirements for vitamins and other minerals, particularly as in the majority of experimental situations these are supplied in excess of currently recommended levels.

Conclusions

There is evidence that because of their dramatic effects on protein deposition, pGH and related technologies do increase the pigs requirements for dietary protein and amino acids and possibly for calcium and phosphors. The magnitude of changes however, are influenced by numerous factors including dosage, sex and live weight. Consequently, the most appropriate diet formulation will differ depending on the technology employed and the extent it stimulates protein and mineral metabolism.

At present there is inadequate quantitative information on the responses of 'treated' pigs to nutrient intake to fully evaluate the impact of the various biotechnological techniques on either tissue on dietary nutrient requirements, although it would appear that the early predictions of the

impact of pGH administration, particularly on the pigs requirements for dietary protein and amino acids may in fact be overestimates.

The data which is available is fragmentary, too imprecise and to some extent contradictory. Similar deficiencies in experimental design and lack of information on the interrelationships between the animal's tissue and dietary requirements have led to apparently contradictory theories concerning the nutrition of "untreated" pigs in the past. Because of the rapid development of these new technologies and the importance of nutritional management in ensuring their success, it is imperative that these problems be realized and rectified as soon as possible.

References

Agricultural Research Council, 1981. The Nutrient Requirements of Pigs. Commonwealth agricultural Bureaux, Slough, England.

Boyd, D.R., D. Wray-Cahen and B. Kirk, 1988. Implications of somatotropin on nutrient requirements of growing swine. Proceedings of International Seminar on the Science of Porcine Somatotropin. p. 122- 143.

Campbell, R.G., N.C. Steele, T.J. Caperna, J.P. Mcmurty, M.B. Solomon and A.D. Mitchell, 1988a. Interrelationships between energy intake and exogenous porcine growth hormoneadministration on the performance, body composition and protein and energy metabolism of growing pigs weighing 25 to 55 kg live weight. J.Anim.Sci. 66:1643-1655.

Campbell, R.G., N.C. Steele, T.J. Caperna, J.P. Mcmurty, M.B. Solomon and Mitchell, A.D., 1989. The Interrelationships between sex and exogenous porcine growth hormone administration on the performance, body composition and protein and fat accretion of growing pigs. J.Anim. Sci. 67:177-186.

Campbell, R.G. and M.R. Taverner, 1988a. Genotype and sex effects on the relationship between energy intake and protein deposition in growing pigs. J. Anim. Sci. 66:676-686.

Campbell, R.G. and M.R. Taverner, 1988b. Genotype and sex effects on the responsiveness of growing pigs to exogenous porcine growth hormone administration. J. Anim. Sci. 66:(Supplement 1): 257.

Campbell, R.G., M.R. Taverner and D.M. Curie, 1985a. The influence of feeding level on the protein requirement of pigs between 20 and 45 kg live weight. Anim. Prod. 40:489-496.

Campbell, R.G., M.R. Taverner and D.M. Curic, 1985b. Effects of sex and energy intake between 48 and 90 kg live weight on protein deposition in growing pigs. Anim. Prod. 40:497-505.

Campbell, R G., M.R. Taverner, R.J. Johnson, C. Reid and W. Brown, 1988b. The effect of exogenous porcine growth hormone (pGH) administration on the response of fast growing young boars to dietary ideal protein. Proceedings of International Seminar on the Science of Porcine Somatotropin. p. 223-233.

Dubreuil, P., S. Pommier, P. Gaudreau, G. Pelletier, D. Petitcerc, C. Farmer, H. Laplerre, Y. Couture and T.F. Mowles, 1988. Effect of does and frequency of a potent analog of human growthhormone releasing factor on growth performance and carcass characteristics of growing pigs. J. Anim. Sci. 66:(Supplement 1):296.

Easter, R.A., 1987. Nutritional requirements and repartitioning agents. Proc. The partitioning revolution: Impact of somatotropin and beta adrenergic agents on future pork production. University of Illinois, Pork Industry Conference. p. 193-199.

Etherton, T.D., J.P. Wiggins, C.M. Evock, C.S. Chung, J.F. Rebhun, P.E. Walton and N.C. Steele, 1987. Stimulation of pig growth performance by porcine growth hormone Determination of the dose-response relationship. J. Anim. Sci. 64:433-444.

Fowler, V.R., M. Kay, H.M. Thikey, R.M. Livingstone, K. Pennie and I.C. Hart, 1988. The effect of recombinant porcine somatotropin on the growth of pigs given different concentrations of protein in the diet. Proceedings of International Seminar on the Science of Porcine Somatotropin. p. 273-284.

Goodband, R.D., J.L. Nelssen, R.H. Hines and B.R. Schricker, 1988. The effects of porcine somatotropin (pST) and dietary lysine level on growth performance and carcass characteristics of finishing swine. Proceedings of International Seminar on the Science of porcine Somatotropin p. 235-251.

N.R.C., 1988. Nutrient Requirements of Swine. National Research Council, Washington D.C., USA.

Pursel, V.G., R.G. Campbell, K.F. Miller, R.R. Behringer, R.D. Palmiter and R.L. Brinster, 1988. Growth potential of transgenic pigs expressing a bovine growth hormonegene. J. Anim. Sci. 66(Supplement 1):267.

Webster, A.J.F., G. Lobley, F.J. Reeds and J.A. Pullan, 1978. Protein mass, protein synthesis and heat loss in the Zucker rat. Proc. Nutr. Soc. 37:21A.

Whittemore, C.T., 1986. An approach to pig growth modelling. J. Anim. Sci. 62:615-621.

EFFECTS OF SOMATOTROPIN ON THE IMMUNE SYSTEM

Keith W. Kelley and Carl K. Edwards, III

Laboratory of Immunophysiology, Department of Animal Sciences, 162 ASL, 1207 West Gregory Drive, University of Illinois, Urbana, Illinois 61801 USA

Summary

Somatotropin has long been suggested to affect cells of the immune system. It is now known to increase size of the thymus gland, augment a number of activities of lymphoid cells, prime macrophages for the release of reactive oxygen intermediates and augment the differentiation of neutrophils and erythrocytes. Somatotropin is even synthesized by lymphoid cells. These recent findings suggest that, in addition to augmenting growth rate and milk production, somatotropin modulates functional activities of lymphocytes and macrophages.

Keywords: somatotropin, lymphocytes, macrophages, granulocytes.

Introduction

Somatotropin consists of 191 amino acids and is synthesized in the adenohypophysis. This molecule is of great interest to animal scientists because it improves growth rate and feed efficiency in pigs and augments milk production by dairy cows. Somatotropin has also generated much interest in human clinical medicine. The recombinant form of this molecule was approved for human use in October 1985, and is now being extensively used to treat a large number of children born with a somatotropin deficiency. Other potential clinical uses of somatotropin have generated much excitement, and concern, by medical scientists. Somatotropin may be useful for controlling obesity in middle-aged humans, reversing some aspects of the aging process, improving wound healing in burn patients and augmenting the physical abilities of athletes. Unfortunately, however, it is unclear how somatotropin affects human and animal health.

Cells of the immune system are absolutely essential for protection of the host against infectious diseases. A large body of literature has accumulated during the past twenty years which shows that somatotropin affects a number of functional activities of lymphocytes and macrophages. Pork producers in the United States loose more than $1 billion annually due to swine diseases, and respiratory diseases such as pneumonia cause the majority of these losses. It is therefore important to learn whether somatotropin positively or negatively affects the incidence, or severity of swine diseases. To answer this question, we have begun to investigate the role of somatotropin on macrophages from the lungs of domestic pigs.

Somatotropin and the immune response

Although somatotropin was discovered and has been classically defined by its ability to induce body growth, it seems likely that somatotropin affects other physiological responses as well. Similarly, certain immunologic events that were originally thought to be mediated by only one cytokine are now known to be affected by other lymphokines. For example, although IL-(interleukin) 2 was thought for a number of years to be the only molecule that was required for

the proliferation of T cells, it is now known that IL-4 also shares this biologic property. Similarly, interferon-γ (IFN-γ) was once defined as the only activator of macrophages, but now other molecules such as granulocyte-macrophage colony stimulating factor (GM-CSF) have also been shown to activate macrophages. These pleiotropic properties of cytokines clearly show that molecules that were intially discovered because of their activity in one bioassay may possess potent effects in completely different bioassays. Given the hormone-like nature of cytokines, it certainly seems possible that hormones produced by the pituitary gland can have biological properties in addition to the one that led to their initial discovery (e.g., effects on macrophages). This idea, in turn, has led to the concept that intricate and important communication systems exist between the immune and neuroendocrine systems (Kelley, 1988).

Somatotropin affects a variety of activities of cells of the immune system, and these effects have been recently summarized (Kelley, 1989; Table 1). A deficiency of somatotropin in rodents leads to

Table 1. Somatotropin regulated activities of cells of the immune system (see Kelley, 1989 for references).

Somatotropin Deficiencies and Immunoregulation:

— Thymic atrophy and wasting in mice and dogs
— Reduced antibody synthesis in mice
— Delayed skin graft rejection in mice
— Normal lymphoid cell subsets and thymic histology with reduction in peripheral T and B cells
— Pituitary hypoplasia and thymic atrophy in humans
— X-linked somatotropin deficiency and complete inability to synthesize antibodies
— Reduction in activity of natural killer cells in humans
— Defective allogeneic mixed lymphocyte reaction
— Reduction in plasma thymulin in humans and mice
— Normal immunoglobulin concentrations and lymphoid cell subsets in humans
— Decreased insulin-induced somatotropin response in patients with telangiectasis and bowel disease

Somatotropin and the Thymus Gland:

— Increases thymic size and DNA synthesis in young rodents
— Improves thymic size and morphology in aged animals
— Increases plasma thymulin in humans and dogs

Somatotropin and Lymphoid Cells:

— Lymphocytes have receptors for somatotropin
— Augments antibody synthesis and reduces skin graft survival in vivo
— Increases lectin-induced T cell proliferation and IL-2 synthesis in vivo
— Stimulates proliferation of human lymphoblastoid cells
— Augments basal lymphocyte proliferation in vitro
— Increases activity of cytotoxic T lymphocytes in vitro
— Augments activity of natural killer cells in vivo
— Synthesized by lymphoid cells

Somatotropin and Phagocytic Cells:

— Primes macrophages for superoxide anion release in vitro and in vivo
— Augments respiratory burst in neutrophils from somatotropin-deficient patients in vivo
— Increases basal respiratory burst of human neutrophils and inhibits activated burst in vitro

Somatotropin and Hemopoiesis:

— Augments neutrophil differentiation in vitro
— Augments erythropoiesis

thymic atrophy and wasting disease, which is coupled with delayed skin graft rejection and a reduction in antibody synthesis. In contrast, humans that are deficient in somatotropin do not show profound susceptibility to infectious diseases. This species difference may occur because of the strong similarity between human prolactin and somatotropin. It is likely that prolactin mimics many of the immunomodulatory properties of somatotropin in humans.

One of the earliest and most consistent observations was that somatotropin augments thymic size in young rodents, and recently somatotropin has been demonstrated to reverse thymic atrophy that occurs in old animals. This improvement in thymic morphology is accompanied by an increase in plasma concentrations of a thymic hormone known as thymulin.

Specific somatotropin receptors exist on heterogeneous populations of lymphocytes and macrophages, and these receptors probably mediate the effects of somatotropin on lymphoid and myeloid cells. Unfortunately, however, the distribution of somatotropin receptors on mononuclear cell subsets is not known; the receptors could be present on any of a number of cell types including T lymphocytes, B lymphocytes, monocytes, natural killer cells and null cells. Somatotropin stimulates cell proliferation in a variety of lymphoid cells and augments antibody synthesis and improves graft rejection in vivo. It also increases the activity of two different types of cytolytic cells: cytotoxic T lymphocytes and natural killer cells. The enhancing effects of somatotropin on granulopoiesis and erythropoiesis in humans appear to be mediated in a paracrine manner by stimulating the synthesis of somatomedin C by bone marrow-derived monocytes (Merchav et al., 1988a, b). Transcripts for somatomedin C have been found in activated macrophages (Rappolee et al., 1988), and these transcripts are translated into the high molecular weight (26 kDa) tissue form of somatomedin C (Rom et al., 1988). Finally, another recent report (Weigent et al., 1988) has shown that somatotropin may even be produced by lymphoid cells, which creates the possibility that it may be synthesized locally at inflammatory sites.

Functional Activities of Macrophages

Macrophages are critical to the induction and expression of a number of immune responses (Adams and Hamilton, 1984; Unanue and Allen, 1987). Macrophages can be triggered to produce reactive oxygen intermediates, such as hydroxyl radicals, singlet oxygen molecules and superoxide anion (O_2^-), which nonspecifically kill ingested bacteria. Activated macrophages also process and present bacterial antigens to T cells, show enhanced expression of class II genes of the major histocompatibility complex, kill tumor cells and secrete a number of monokines, such as IL-1 and tumor necrosis factor-α.

The first line of defense of mammals against bacterial and parasitic organisms that have entered the body consists of phagocytosis of the invading microbe by polymorphonuclear leukocytes and macrophages. These cells phagocytize foreign particles and compartmentalize them into phagosomes. Ideally, pathogenic microbes are then degraded by lysomal enzymes that enter the phagosome after fusion between lysosomes and phagosomes. However, many facultative intracellular organisms are not degraded once they are enclosed in the phagosome and, in fact, may multiply and divide, thus killing the macrophage.

Macrophage Activation for Bacterial Killing

Fortunately, the host has developed a means to activate macrophages such that they may destroy organisms that otherwise might kill the cell and possibly even the host. The concept of activated macrophages was first developed by Metchnikoff nearly 100 years ago. This model was more fully developed by George Mackaness in the late 1950s. Mackaness studied what has been called "nonspecific immunity" by examining the effect of infection with **Mycobacterium bovis BCG** on

the resistance of mice to the immunologically unrelated organism **Listeria monocytogenes.** Mackaness found that peritoneal macrophages from mice infected with the attenuated mycobacterial strain became larger and displayed increased biochemical and metabolic activities when compared to peritoneal macrophages from normal, uninfected mice. Furthermore, mice treated with **M. bovis BCG** had increased host resistance when challenged with a lethal dose of **L. monocytogenes.** These studies not only established that enhanced antibacterial resistance in vivo is related to an increase in the activity of macrophages, but also that one infectious organism can enhance the resistance of animals to completely unrelated pathogens.

Emil Unanue subsequently showed that the increase in macrophage activity is directly dependent upon the specific antigenic stimulation of responsive lymphocytes which produce protein substances called lymphokines that act on the macrophage. It is now known that these lymphocytes are T cells, that they can be activated by microbial antigens to secrete a protein known as IFN-γ, and that this protein stimulates macrophages to acquire an enhanced degree of microbicidal activity as well as other functional activites that were described above (Nathan, 1986). Macrophages exposed to IFN-γ are known as primed macrophages, and these cells can subsequently be triggered by agents such as bacterial endotoxin to become fully activated macrophages.

The Respiratory Burst of Phagocytic Cells

Phagocytic cells consume oxygen during the process of ingestion, an effect which is probably mediated by an increase in activity of a cell membrane NADPH oxidase. Oxygen consumption by macrophages is induced by substances that are active at the cell membrane, such as opsonized- or complement-activated particles, or phorbol myristate acetate, which activates the calcium- and phospholipid-dependent enzyme protein kinase C. Most of the oxygen is reduced to O_2^- and the enzyme superoxide dismutase converts two moles of O_2^- in the presence of reducing equivalents to molecular oxygen and hydrogen peroxide (H_2O_2). In the presence of catalase (and the cofactor iron), H_2O_2 generates hydroxyl radicals. Furthermore, singlet oxygen can form spontaneously from O_2^- Hydroxyl radicals and singlet oxygen are the primary agents responsible for killing of intracellular bacteria. Interferon-γ is one product of activated T cells that enhances the production of reactive oxygen intermediates by macrophages, and this enhancement is known as priming. Since O_2^- is the earliest product of the respiratory burst and because the bulk of it is released into surroundings of the cell, measurement of O_2^- in the medium in which macrophages are suspended is an accurate method for quantitation of the suspended is an accurate method for quantitation of the respiratory burst.

Priming of Macrophages by Somatotropin

Although IFN-γ has been identified as the primary T cell product that primes macrophages, other macrophage activating factors such as GM-CSF, IL-4 and tumor necrosis factors-α and -β also can augment the respiratory burst. Studies conducted by Peter Heistand et al. (1986) at Sandoz in Basel, Switzerland showed that mRNA transcripts for somatotropin may actually be detected in activated lymphoid cells, which suggested to us that somatotropin may function as a cytokine. Similarly, as mentioned above (Weigent et al., 1988), Douglas Weigent and Ed Blalock have recently published convincing data that this mRNA is translated in both rat and human leukocytes, resulting in the synthesis and secretion of somatotropin.

Several years ago, Astaldi et al. (1973) demonstrated that monocytes that were incubated overnight with somatotropin acquired morphological characteristics of activated macrophages. We also noticed in preliminary experiments that porcine liver suspensions incubated with somatotropin

contained macrophages (Kupffer cells) that were morphologically similar to activated macrophages. Because these morphological changes were easily detectable with a light microscope, we wondered whether somatotropin might also affect functional activities of macrophages. We chose to first investigate the effect of somatotropin on respiratory burst activity and secretion of reactive oxygen intermediates because of the direct role of these compounds in the killing of intracellular bacteria.

We first incubated porcine peripheral blood monocytes overnight with increasing concentrations of native and recombinant porcine somatotropin and measured the O_2^- released from macrophages in response to opsonized-zymosan (op-zym) by a reduction in ferricytochrome c (Edwards et al., 1988). We found that 100 ng/ml of either native or recombinant porcine somatotropin caused a twenty-fold increase in the production of O_2^-. This enhancing effect could be totally blocked with a specific antibody to somatotropin, which indicated that macrophage priming was not caused by contaminating endotoxin in the hormone preparations.

We wondered whether the increase in the production of O_2^- by macrophages stimulated with op-zym was caused by augmenting the release of IFN-γ by residual contaminating T cells in the cell suspension or whether somatotropin was acting directly on macrophages. As an initial test of this possibility, we prepared highly purified populations of porcine alveolar macrophages (> 98% alpha-naphthyl butyrate esterase positive) and treated them with both native and recombinant porcine somatotropin (Table 2). As expected, op-zym caused a significant increase in the production of O_2^- (from 28 to 199 nMol O_2^-/mg protein/hr). This increase was specific because O_2^- is the only known substrate for superoxide dismutase, which totally blocked the augmentation caused by op-zym. Incubation of alveolar macrophages for 24 hr with 500 ng/ml of either recombinant or native porcine somatotropin more than doubled the production of O_2^-, and this effect was completely blocked by a specific antibody to somatotropin. These data argued that somatotropin directly primes macrophages for augmented production of O_2^-, rather than augmenting the synthesis of IFN-γ by contaminating lymphoid cells.

Table 2. Priming of porcine alveolar macrophages in vitro by native porcine somatotropin (npST) and recombinant porcine somatotropin (rpST). Means with different superscripts are different (P < .05). Data taken from Edwards et al . (1988).

Treatment	nMol O_2^- /mg protein/hr	SEM
Unstimulated	28[a]	14
Stimulated with Op Zym	199[b]	48
Op Zym + Superoxide Dismutase	28[a]	9
Op Zym + npST (500 ng/ml)	430[c]	90
Op Zym + rpST (500 ng/ml)	431[c]	81
Op Zym + rpST + ST antibody	48[a]	20
Op Zym + ST antibody	141[a,b]	30

Since somatotropin augmented production of O_2^- by macrophages in vitro, we asked whether it would also cause similar effects in vivo. This question was answered by injecting hypophysectomized rats with somatotropin (Table 3). The classic macrophage activating factor, recombinant rat IFN-γ (500 units for 9 days), caused a 400% increase in the production of O_2^-, and this treatment served as our positive control. Injection of various amounts of either native porcine somatotropin, recombinant porcine somatotropin or native rat somatotropin also caused significant increases in the production of O_2^- by resident peritoneal macrophages that were stimulated with op-zym, and the higher doses of somatotropin induced similar amounts of O_2^- as recombinant rat IFN-γ. Heightened production of O_2^- by somatotropin occurred at doses of somatotropin that increased growth rate, which suggests that priming of macrophages by somatotropin occurs at physiologic levels.

Table 3. Native, pituitary-derived rat somatotropin (nrST), npST and rpST induced respiratory burst activity in resident rat peritoneal macrophages in vivo (Edwards et al., 1988). Means with different superscripts are different (P < .05).

Item	Dose/ Rat/Day	Growth (g/Day)	nMol O_2^-/ mg protein/hr
Hypox Rats	-	0.392[a]	-40[a]
+ Vehicle	200 ul	0.282[a]	-17[a]
+ Rat IFN-	500 Units	0.252[a]	417[b]
+ npST	6 ug	1.322[c]	0[a]
	12 ug	1.633[d]	268[b]
	24 ug	2.060[e,f]	438[b]
+ rpST	6 ug	0.815[b]	-62[a]
	12 ug	1.067[b,c]	280[b]
	24 ug	1.297[c]	344[b]
+ nrST	12 ug	1.850[d,e]	3[a]
	24 ug	2.320[f]	267[b]
	48 ug	2.870[g]	247[b]
	96 ug	3.440[h]	309[b]

These experiments demonstrated that both native and recombinant somatotropin can prime blood-derived monocytes, alveolar macrophages and resident peritoneal macrophages to produce enhanced levels of O_2^- in response to a particulate stimulus, op-zym. Since macrophages are critical to the initiation of many immune responses, a variety of immune events could be affected by somatotropin. We initially chose to study the role of somatotropin on the production of O_2^- by macrophages because of the known bactericidal role of reactive oxygen intermediates. These data therefore support the idea that a pituitary hormone, somatotropin, has important effects on functional activities of cells of the immune system, and that macrophages are one target for the action of somatotropin. This interpretation is entirely consistent with a recent preliminary report which showed that bovine somatotropin promoted a significant improvement in milk production after mastitis induced by Escherichia coli (Vandeputte-van Messom et al., 1988).

b-Adrenergic Agonists and the Immune System

A number of analogs of norepinephrine has been developed in an attempt to increase muscle and decrease fat mass in pigs. Although much of our research has concentrated on somatotropin, the literature clearly indicates that both and β-adrenergic agents can affect cells of the immune system (Sanders and Munson, 1985a). Since it has been clearly established that both primary and secondary lymphoid tissues receive noradrenergic innervation (Felten et al., 1987), it is likely that norepinephrine is an important immunomodulator in the local environment of lymphoid cells. Both porcine (Westly and Kelley, 1987) and bovine (Ogunbiyi et al., 1988) mononuclear cells have receptors for β-adrenergic compounds. Indeed, β_1- but not β_2- adrenergic agonists inhibit the production of reactive oxygen intermediates by bovine alveolar macrophages (Ogunbiyi et al., 1988). Similarly, both norepinephrine and epinephrine block the activation of macrophages to a tumoricidal and anti-viral state (Koff and Dunegan, 1985, 1986). It is unknown whether this inhibition can be overcome by either somatotropin or classic macrophage activators such as IFN-γ. Stimulation of β-adrenoceptors augments antibody synthesis in rodents (Sanders and Munson, 1984a,b; Fujiwara and Orita, 1987), whereas β-adrenergic stimulation enhances the production of complement components by monocytes (Lappin and Whaley, 1982) and has mixed effects on antibody synthesis (Sanders and Munson, 1985b). Epinephrine affects lymphoid cell distribution in vivo and proliferation in vitro (Crary et al., 1983) and the activity of natural killer cells in humans (Hellstrand et al., 1985). Since these and other studies have shown that stimulation of adrenergic

receptors modulates at least some activities of cells of the immune system, it is likely that administration of β-adrenergic agents to domestic livestock affects their immune system as well.

Conclusions

A review of the literature indicates that somatotropin can affect a number of activities of lymphoid cells and macrophages. Other repartitioning agents, such as β-adrenergic agonists, have also been shown to affect cells of the immune system. These data clearly establish that compounds which have been developed to modify animal growth affect the immune system. In general, almost all of the immunomodulatory effects of somatotropin have led to an enhancement in a given immunological property, whereas the use of beta-adrenergic agents has revealed both suppressive and enhancing characteristics. However, it is not yet known whether the kinds of cells that are affected or whether the magnitude of effects that are caused by growth-promoting compounds are sufficient to modify animal health in either a positive or negative manner. It is also not known whether the immunomodulatory effects of somatotropin that are so clearly demonstrated in hypophysectomized rodents occur in young animals with normal amounts of circulating somatotropin.

Acknowledgements

References

Adams, D.O. and T.A. Hamilton, 1984. The cell biology of macrophage activation. Ann. Rev. Immunol. 2:283-318.

Astaldi, A., Jr., B. Yalcin, G. Meardi, G.R. Burgio, R. Merolla and G. Astaldi, 1973. Effects of growth hormone on lymphocyte transformation in cell culture. Blut 26:74-81.

Crary, B., M. Borysenko, D.C. Sutherland, I. Kutz, J.Z. Borysenko and H. Benson, 1983. Decrease in mitogen responsiveness of mononuclear cells from peripheral blood after epinephrine administration in humans. J. Immunol. 130:694-697.

Edwards, C.K. III, S.M. Ghiasuddin, J.M. Schepper, L.M. Yunger and K.W. Kelley, 1988. A newly defined property of somatotropin: Priming of macrophages for production of superoxide anion. Science 239:769-771.

Felten, D.J., S.Y. Felten, D.L. Bellinger, S.L. Carlson, K.D. Ackerman, K.S. Madden, J.A. Olschowski and S. Livnat, 1987. Noradrenergic sympathetic neural interactions with the immune system: Structure and function. Immunol. Rev. 100:225-260.

Fujiwara, R. and K. Orita, 1987. The enhancement of the immune response by pain stimulation in mice. 1. The enhancement effect on PFC production via sympathetic nervous system in vivo and in vitro. J. Immunol. 138:3699-3703.

Hellstrand, K., S. Hermodsson and O. Strannegard, 1985. Evidence for a β-adrenoceptor-mediated regulation of human natural killer cells. J. Immunol. 134:4095-4099.

Hiestand, P.C., P. Mekler, R. Nordmann, A. Grieder and C. Permmongkol, 1986. Prolactin as a modulator of lymphocyte responsiveness provides a possible mechanism of action for cyclosporine. Proc. Natl. Acad. Sci. USA 83:2599-2603.

Kelley, K.W., 1988. Cross-talk between the immune and endocrine systems. J. Anim. Sci. 66:2095-2108.

Kelley, K.W., 1989. Growth hormone, lymphocytes and macrophages. Biochemical Pharmacology (In Press).

Koff, W.C. and M.A. Dunegan, 1985. Modulation of macrophage-mediated tumoricidal activity by neuropeptides and neurohormones. J. Immunol. 135: 350-354.

Koff, W.C. and M.A. Dunegan, 1986. Neuroendocrine hormones suppress macrophage-mediated lysis of herpes simplex virus-infected cells. J. Immunol. 136:705-709.

Lappin, D. and K. Whaley, 1982. Adrenergic receptors on monocytes modulate complement component synthesis. Clin. Exp. Immunol. 47: 606-612.

Merchav, S., I. Tatarsky and Z. Hochberg, 1988a. Enhancement of human granulopoiesis in vitro by biosynthetic insulin-like growth factor I/somatomedin C and human growth hormone. J. Clin. Invest. 81: 791-797.

Merchav, S., I. Tatarsky and Z. Hochberg, 1988b. Enhancement of erythropoiesis in vitro by human growth hormone is mediated by insulin-like growth factor I. Brit. J. Haematology 70:267-271.

Nathan, C.F., 1986. Interferon-γ and macrophage activation in cell-mediated immunity. In: R.M. Steinman and R.J. North (Ed.): Mechanisms of host resistance to infectious agents, tumors, and allografts. Rockefeller University Press, New York, p. 165-184.

Ogunbiyi, P.O., P.D. Conlon, W.D. Black and P. Eyre, 1988. Levamisole-induced attenuation of alveolar macrophage dysfunction in respiratory virus-infected calves. Int. J. Immunopharmac. 10:377-385.

Rappolee, D.A., D. Mark, M.J. Banda and Z. Werb, 1988. Wound macrophages express TGF-α and other growth factors in vivo: analysis by mRNA phenotyping. Science 241:708-712.

Rom, W.N., P. Basset, G.A. Fells, T. Nukiwa, B.C. Trapnell and R.G. Crystal, 1988. Alveolar macrophages release an insulin-like growth factor I-type molecule. J. Clin. Invest. 82:1685-1693.

Sanders, V.M. and A.E. Munson, 1984a. Beta adrenoceptor mediation of the enhancing effect of norepinephrine on the murine primary antibody response in vitro. J. Pharmacol. Exp. Therapeutics 230: 183-192.

Sanders, V.M. and A.E. Munson, 1984b. Kinetics of the enhancing effect produced by norepinephrine and terbutaline on the murine primary antibody response in vitro. J. Pharmacol. Exp. Therapeutics 231:527-531.

Sanders, V.M. and A.E. Munson, 1985a. Norepinephrine and the antibody response. Pharmacol. Rev. 37:229-248.

Sanders, V.M. and A.E. Munson, 1985b. Role of alpha adrenoceptor activation in modulating the murine primary antibody response in vitro. J. Pharmacol. Exp. Therapeutics 232:395-400.

Unanue, E.R. and P.M. Allen, 1987. The basis for the immunoregulatory role of macrophages and other accessory cells. Science 236:551-557.

Vandeputte-van Messom, G., C. Burvenich, E. Roets and L.A. Devriese, 1988. Effect of bovine somatotropin on milk yield and composition during Escherichia coli induced mastitis in lactating cows: Some preliminary results. Vlaams Diergeneeskundig Tijdschrift 57:53-61.

Weigent, D.A., J.B. Baxter, W.E. Wear, L.R. Smith, K.L. Bost and J.E. Blalock, 1988. Production of immunoreactive growth hormone by mononuclear leukocytes. FASEB Journal 2:2812-2818.

Westly, H.J. and K.W. Kelley, 1987. Down-regulation of glucocorticoid and γ-adrenergic receptors on lectin-stimulated splenocytes. Proc. Soc. Exp. Biol. Med. 185:211-218.

POTENTIAL SIDE-EFFECTS OF EXOGENOUS SOMATOTROPIN IN PIGS

Stanley E. Curtis

Animal Sciences Department, University of Illinois, Urbana, IL 61801 USA

Summary

Two aspects of the pig's nature that might be affected by exogenous somatotropin are thermoregulation (and thus the pig's thermal environmental requirements) and eating behavior (and thus the design of the pig's living quarters and feeding system). The net effect of exogenous somatotropin on a 75-kg pig would be a 6°C increase in its lower critical effective environmental temperature and a decrease of several degrees in its upper critical temperature. Thus, the pig would be more sensitive to its thermal environment at both low and high ends of the temperature range. The marked reduction in feed intake observed in pigs being administered exogenous somatotropin may be due to thermal stress, social problems, or inadequate access to the feed. These possibilities should be explored and means of alleviating any documented effects should be sought.

Keywords: pigs, somatotropin, thermal environment, social environment, feeder design, feed intake.

Introduction

There would seem to be potential advantages to using exogenously administered porcine somatotropin to fashion pig growth so as to make pork more acceptable to consumers and pork production and processing more efficient. In the production phase, however, although we do not yet know much about the effects and side-effects of this new technology, what is known already has provoked questions regarding how swine management regimens might need to be changed in order to implement it in the pork industry. Two important aspects of the pig's nature that might be affected by exogenous somatotropin are thermoregulation (and thus the pig's thermal environmental requirements) and eating behavior (and thus the design of the pig's living quarters and feeding system).

Thermoregulation

The thermal status of a pig's body depends essentially on two factors: thermal insulation (which determines heat loss rate) and heat production rate. Somatotropin probably affects both. Therefore, the thermal environmental and dietary energy requirements of the pig might be affected by exogenous somatotropin.

Thermal insulation

The three thermal insulators between a pig's body core (the origin of most metabolic heat) and the surroundings (the animal's heat sink) are, from inside out: tissue insulation, hair insulation, and boundary insulation (the very thin layer of still air that envelopes the body). Total insulation equals the sum of the three. Hair and boundary insulations probably are independent of exogenous somatotropin, but the tissue insulation is not.

155

The contribution of hair insulation in a growing-finishing pig residing in a typical production setting averages ± .2°C m² h/kcal, and that of boundary insulation, ± .1 unit. The two combined total ± .3 unit of insulation.

Tissue insulation is due mainly to subcutaneous fat, which (when its blood vessels are constricted in response to a cold environment) yields a maximal insulation value of .1°C m² h/kcal per cm of thickness. Therefore, tissue insulation depends on the thickness of the subcutaneous fat, which may be determined in turn partly by exogenous somatotropin. When the subcutaneous fat that covers the entire body effectively averages 1 cm thick, then maximal tissue insulation would be ± .1 unit, and maximal total insulation (the sum of tissue, hair, and boundary insulations), ± .4 unit. But if effective subcutaneous fat thickness were reduced from 1 cm to .5 cm, then maximal total insulation would drop from ± .4 unit to ± .35 unit.

A pig weighing 75 kg would have a body surface area of ± 1.25 m². Thus, it can be calculated, the slope of its environmental heat demand line would be 3.1 kcal/h°C if the pig had 1 cm of subcutaneous fat and 3.6 unit if it had .5 cm. In other words, for any given decrease in environmental temperature, heat loss rate from the pig with less subcutaneous fat would increase at a rate some 16% faster than that from the fatter pig. This would make the leaner pig more vulnerable to cold environments, but less vulnerable to hot ones, provided all other factors remained the same (see below). In particular, the somatotropin-treated pig's lower critical effective environmental temperature (the temperature below which the pig would need to raise its metabolic rate above the thermoneutral level in order to maintain a normal body temperature) might be as much as 12°C higher than that of an untreated pig. The treated pig's upper critical temperature also would be higher in the face of less insulation, but probably only a few degrees higher.

Alas, other critical factors may not remain the same when exogenous somatotropin is being administered. Heat production rate must be considered, too.

Heat production rate

The metabolic stimulation due to exogenous somatotropin increases the pig's heat production rate. Present evidence indicates that this increase is associated at least partly with increased maintenance energy expenditure in the growing pig. Recent estimates are that maintenance energy expenditure is 17% to 24% higher in somatotropin-treated pigs, and this would be reflected by a commensurate increase in heat production rate.

Regardless of how this extra metabolic heat may be partitioned, it would affect the pig's thermal environmental requirements. With respect to the extra metabolic heat, the somatotropin-treated pig would be less vulnerable to cold environments, but more vulnerable to hot ones, provided all other factors remained the same (see below). In particular, under such conditions, the lower critical temperature of the somatotropin-treated 75-kg pig might be reduced by ±6°C, and the upper critical temperature also would drop by several degrees. However, as has been mentioned, under exogenous somatotropin administration, other critical factors may not remain the same.

Thermal environmental requirements

How would the combined effects of exogenous porcine somatotropin on subcutaneous fat thickness (and thus on tissue and total insulation values during cold-induced peripheral vasoconstriction) and heat production rate affect a pig's thermal environmental requirements, assuming the scenario outlined above obtains? A pig's lower critical temperature is determined by the junction between the thermoneutral heat production rate and the environmental heat demand line. The combined effects of these two consequences of somatotropin would be, on the cool end of the effective environmental temperature range, a 12°C increase in lower critical temperature due to less thermal insulation, but this would be offset by a 6°C decrease due to the higher heat production rate. Hence, the net effect would be a 6°C increase in the lower critical temperature of a 75-kg pig due to somatotropin treatment. In other words, the treated pig would be considerably more vulnerable to cool or frankly cold environments.

As for the upper critical effective environmental temperature (the point above which the pig would need to start to pant or to increase evaporative heat loss rate by some behavioral means such as wallowing in mud), on balance it might be expected that this critical point would drop by a few degrees. That is, the effect of the somatotropin-induced increase in heat production rate would be expected to override the effect of decreased thermal insulation, resulting overall in the pig's being more vulnerable to high environmental temperatures, as well. Although it is not possible to be as precise quantitatively in estimating the effect of exogenous somatotropin on the pig at the warm end of the temperature range, it is likely that in practical production settings in most temperate regions the pig's heightened vulnerability to warm or frankly hot surroundings would be of more economic consequence than that to cool or cold environments. High temperature-induced reduction in appetite probably would be considerable in many cases.

Eating behavior

Growing pigs being administered exogenous somatotropin gain both lean mass and total mass both at a faster rate and at a higher gain/feed ratio. These effects are all the more remarkable because they are associated with a marked depression in feed intake. Would somatotropin-treated pigs gain mass even faster and even more efficiently if they ate more each day?

Numerous physiologic mechanisms control feed intake in pigs. Several dietary and environmental factors affect it, too. Before the limiting factors can be minimized - thereby letting the pigs eat more and grow faster - these phenomena and their interrelations must be elucidated, and once they are elucidated and documented, then ways and means of ameliorating such effects must be sought.

Environmental temperature

Perhaps exogenous somatotropin's lowering of the pig's upper critical effective environmental temperature has been responsible for some or all of the depression of feed intake that has been observed. The higher metabolic heat production rate of these pigs might alone have reduced the pigs' appetites. Conventional growing-finishing pigs voluntarily take in 60 to 100 g less feed daily for every $1^{\circ}C$ that environmental temperature stands above $21^{\circ}C$. It is conceivable that somatotropin-treated pigs experience even larger depressions per degree, beginning at even lower environmental temperatures.

Another possibility is that the somatotropin-treated pig in conventional thermal environments finds itself in a zone of effective environmental temperature in which it chooses consciously to reduce its physical activity so as to reduce the heat increment due to physical activity in attempting to establish thermal equilibrium with its surroundings. In such circumstances, the pig might need to be hungrier before it is motivated to get up and approach the feeder to start an eating bout. If this be the case, more accessible means of offering feed to somatotropin-treated pigs might encourage them to consume feed at a rate more nearly that of untreated pigs. Moreover, if somatotropin-treated pigs indeed are relatively lethargic, and if this lethargy leads to fewer eating bouts each day, then any stimulation of feed intake that is due to social facilitation in conventional pigs presumably would be decreased in somatotropin-treated pigs.

Social relations

Dominance-subordinance relations among pigs in a group are important determinants of voluntary feed intake by the respective individual pigs. It is quite possible that metabolic changes (including increased heat production rate) due to exogenous somatotropin alter either the pig's perception of its individual groupmates or the thresholds of social-interactive behaviors in such ways that social inhibition of eating is magnified. For example, revolts occur even within established dominance orders of pigs, and it is possible that somatotropin-treated pigs are less prone

157

to completely resolve these conflicts, thus leaving the level of social tension in the group - which in turn may influence the effect of one pig on the eating behavior of another - relatively high.

Accessibility of feed

Providing the feed in feeders that have been designed and located in a quantitatively and qualitatively appropriate manner is crucial to ensuring that every pig in a group has unlimited access to feed, and thus the opportunity to maximize feed intake. Social effects on pig performance - and especially on interindividual variation in performance - become more pronounced as general access to feed becomes more limited.

When the pigs' environment is designed so only some of the individuals can eat at once, most of the pigs are drinking, dunging, or resting while some are eating. Therefore, appropriately designed and located watering, dunging, and resting places must be provided. Otherwise, pigs not even eating at some given moment can interfere with groupmates desiring to approach the feeder and eat.

References

Baxter, S.H., 1984. Intensive pig production: environmental management and design. Granada Technical Books, New York.

Curtis, S.E., 1983. Environmental management in animal agriculture. Iowa State University Press, Ames, Iowa.

Curtis, S.E., 1985a. Physiological responses and adaptations of swine: hot environments. In: M.K. Yousef (Ed.) : Stress physiology in livestock (vol. II). CRC Press, Boca Raton, Florida. p. 59-65.

Curtis, S.E., 1985b. Physiological responses and adaptations of swine: cold environments. In: M.K. Yousef (Ed.): Stress physiology in livestock (vol. II). CRC Press, Boca Raton, Florida. p. 129-139.

Curtis, S.E., 1987. Animal well-being and animal care. In: E. 0. Price (Ed.): Farm animal behavior. W.B. Saunders, Philadelphia. p. 369-382.

Curtis, S.E., 1987. Environmental and behavioral influences on feed intake by pigs. Proc. 8th Western Nutrition Conference. University of Alberta, Edmonton, Alberta. p. 21-24.

Etherton, T.D., J.P. Wiggins, C.S. Chung, C.M. Evock, J.F. Rebhun & P.E. Walton, 1986. Stimulation of pig growth performance by porcine growth hormone and growth hormone releasing factor. J. Anim. Sci. 63:1389-1399.

McLaren, D.G., G.L. Grebner, P.J. Bechtel, F.K. McKeith, J.E. Novakofski & R.A. Easter, 1987. Effect of graded levels of natural porcine somatotropin (PST) on growth performance of 57 to 103 kg pigs. J. Anim. Sci. 65 (Suppl. 1):245. (Abstr.)

Steele, N.C., R.G. Campbell & T.J. Caperna, 1987. Update of porcine growth hormone research: practical and biological implications. Proc. 1987 Cornell Nutrition Conference for Feed Manufacturers. Cornell University, Ithaca, New York. p. 15-21.

Taylor, I.A., S.E. Curtis, M. R. Backstrom & J. L. Groppel, 1988. Design of feeders for swine: kinematics, behavior, and individuality. In: Proc. 6th International Congress on Animal Hygiene. Report 21 (vol. II), Department of Animal Hygiene, Swedish University of Agricultural Sciences, Skara, Sweden. p. 705-708.

Van der Hel, W., M.W.A. Verstegen, J. Huisman, E. Kanis, E.J. van Weerden & P. van der Wal, 1988. Effect of rPST treatment on energy balance traits and metabolic rate in pigs. J. Anim. Sci. 66(Suppl. 1):255. (Abstr.)

THE EFFECT OF NEW GROWTH-PROMOTING TECHNOLOGIES ON REPRODUCTION AND LACTATION IN SWINE

B.N. Day, Steve Terlouw and August Rieke
Department of Animal Science, University of Missouri-Columbia, Columbia, MO 65211 USA

Summary

New biotechnologies are emerging that have been shown to be effective methods for major modification of growth and carcass composition of growing-finishing swine. Recent progress in gene insertion has resulted in the production of transgenic animals used for breeding purposes and offspring have been produced. However, major reproductive problems have been observed in transgenic boars and gilts expressing human growth hormone, including anestrus and lack of libido. Limited data have been reported to suggest that the lactation curve in sows can be altered and milk production increased by porcine pituitary growth hormone (pGH) or recombinant porcine growth hormone (rpST) treatment.

Reproductive disorders including delayed puberty and cystic follicles have occurred in gilts treated daily with pGH near the time for the onset of sexual maturity and when given during the proestrus phase of the estrous cycle. However, there was no adverse effect on interval from boar exposure to estrus, age at puberty, proportion of gilts reaching puberty prior to 240 days of age or pregnancy rate in gilts injected daily with recombinant porcine somatotropin (rpST) during the growing-finishing phase of reproduction (50 kg to 110 kg bodyweight). Similarly, pregnancy rate and average number of embryos on day 25 of pregnancy were unaffected by the administration of rpST between day 4 and 18 of gestation. These results indicate that subsequent reproductive performance in gilts is unaffected by the administration of rpST during the growing-finishing phase of production.

Keywords: swine, reproduction, growth hormone.

Introduction

Recent progress in efforts to alter the endocrine control of growth and development in swine has led to an interest in the effect of these emerging technologies on other components of the production cycle. For example, will transgenic pigs expressing a foreign gene for growth hormone production exhibit sexual behavior and be capable of producing offspring to amplify the presence of the foreign gene in the population? Can a technique that will effectively alter nutrient partitioning priority be used to an advantage during pregnancy and lactation? Further, what are the implications of major changes in growth rate and body composition during the growing-finishing phase of development on age at sexual maturity and subsequent reproductive performance of breeding replacement animals?

It is only recently that the results of preliminary studies designed to examine these and related questions have started to become available. Further, most reproductive characteristics are highly variable economic traits and require relatively large numbers of animals of different genotypes produced under various environmental conditions in order to reach conclusive evidence of general effects. For example, several years of study will likely be required to determine any minor

159

differences in expected levels of reproductive and lactational performance in transgenic animals. Earlier conclusions may be expected, however, for technologies directed toward the direct administration of compounds to alter nutrient partitioning priority. In this paper, we will briefly review expected effects of major differences in growth rate and body composition during the growing-finishing phases of development on age at puberty in gilts. Results will be presented on the level of reproductive performance in gilts that had previously receive recombinant porcine somatotropin. Available data on the direct effects of increased growth hormone in transgenic animals and following hormonal injection on reproductive traits and lactation will also be reviewed.

Growth rate, body composition and puberty

Considerable controversy exists on the relative roles of age and weight as determinants of reproductive activity in pigs. Anderson and Melampy (1972) reviewed the literature on the effects of energy intake on age and weight at puberty in swine. Restricted energy intake was found to delay puberty an average of 16 days in nine experiments but hastened puberty an average of 11 days in five studies. Although it is reasonable to assume a minimal weight exists for the expression of puberty, the range in weight at which puberty will occur in gilts is wide. In a study reported by Knott et al. (1984), the interval to puberty was similar for groups of gilts boar exposed and relocated between 70 and 116 kg body weight.

Since it does appear that differences in live weight above a minimal level exert only minor influence on puberty attainment, it follows that rate of growth during the prepuberal period would be without a major cause of differences in age at puberty within contemporary groups of gilts. Several studies have reported a lack of association between rate of gain and age at puberty (Burger, 1952; Gossett and Sorensen, 1959; Goode et al., 1965).

Only limited study has been made of the relationship between body composition and sexual maturation in the gilt. In humans, the adipose to lean tissue ratio is considered to be an important contributing factor to the attainment of puberty. However, although major breed differences exist in age at puberty and body condition, the relative effects of genotype and body composition have yet to be defined. Within genotype groups, the ability of gilts to exhibit puberty prior to time of rapid fat deposition would suggest a relatively low minimal body fat content requirement for the attainment of puberty.

Growth hormone and reproduction in gilts

Indirect effects

The administration of pituitary porcine growth hormone (pGH) or recombinant porcine somatotropin (rpST) during the growing-finishing phase of development will enhance growth rate and feed efficiency as well as induce major changes in body composition including a marked decrease in fat deposition (Chung et al., 1985; Etherton et al., 1986; Etherton et al., 1987; McLaren et al., 1987; Campbell et al., 1988). Although differences in rate of gain and body composition do not appear to be major causative factors of variation in age at puberty within genotype group, the question arises as to whether or not these modifications in growing animals induced by somatotropin may affect subsequent reproductive performance of replacement gilts. An experiment has been conducted, therefore, to gain information on possible indirect effect of rpST treatment on puberty, ovulation rate and conception rate in gilts (Unpublished data).

Forty crossbred gilts, including 19 littermate pairs, were assigned to the study at an average body weight of 50 kg. An equal number of gilts were randomly assigned within weight groups and litter number to control and rpST treatment groups. Control gilts received daily intramuscular injections of 1 ml of vehicle and rpST gilts were injected daily with 1 ml of vehicle containing 6 mg of prST.

160

The gilts were fed **ad libitum** a corn-soybean ration containing 18% protein and 1.2% lysine in a confinement facility. Gilts were located in five adjacent pens with four control and four treated gilts assigned to each pen. Treatment was continued until the pen average body weight reached 110 kg. The gilts were weighed periodically during the trial and body composition was estimated by ultrasonic determination at the end of the trial. The gilts were then moved to a confinement gestation unit and daily heat checks made with a mature boar to determine age at puberty. Gilts were bred at second estrus with embryo recovery made at day 11 of pregnancy to determine ovulation rate, conception rate and embryonic survival rate. The average age of all gilts at the initiation of rpST treatment was 102 days with last injections given at an average age of 162 days for a total treatment period of 60 days.

Table 1 and 2 present the effect of rpST treatment on growth rate and ultrasonic measurements of body composition. Growth rate was increased significantly (P < .05) by daily injection of 6 mg of rpST. Injections were ended when the body weight pen average of four gilts reached approximately 110 kg. On that day all gilts were measured by ultrasound to determine subcutaneous backfat thickness and loin eye area. All mean values of fat thickness (shoulder, loin, ham) were significantly less (P < .05) for gilts injected with rpST as compared to control gilts. Also, as shown in Table 2, loin eye area was increased significantly (P < .05) by rpST administration. These growth and body composition data confirm a positive response to rpST during the growing-finishing period.

Table 1. Effect of rpST on body weight gain in gilts treated from 50 to 110 kg body weight. [a]

Treatment	rpST/gilt/ day, mg	No. of gilts	Initial weight, kg	Final weight, kg	Total gain, kg
Control	0	20	53.9±1.1[b]	107.2±1.8[c]	53.51±.0[e]
rpST	6	20	53.8±1.1[b]	113.5±1.8[d]	59.81±.0[f]

[a] Least squares means ±SEM.
[b,c,d,e,f] Means within the same column with different superscripts are significantly different (P < .05).

Table 2. Effect of rpST on ultrasound measurements of body composition of gilts. [a]

Treatment	No. of gilts	Body weight, kg	Means adjusted for body weight		
			Backfat thickness, cm	Loin eye area, cm^2	
Control	20	107.2[b]	2.5[b]	32.2[b]	
rpST	20	113.5[c]	1.6[c]	36.9[c]	

[a] Least square means.
[b,c] Means within column with different superscripts are significantly different (P < .05).

All gilts were relocated to a breeding unit, mixed with different pen mates and boar exposed at an average age of 169 days. The range of the interval from end of rpST injection to initiation of stimuli to induce puberty was 4 to 11 days with an average interval of 5.1 days. Individual gilts in pens with slightly lower growth rates and longer injection period to 110 kg body weight target, exhibited puberty within 10 days following the last injection of rpST.

Table 3 and 4 summarize reproductive characteristics of control gilts and gilts treated previously with rpST. All control gilts and 19 of 20 rpST gilts exhibited puberty prior to 8 months of age. One control gilt was behaviorally anestrus following the first estrus. Average age at puberty was 182 days for both control and treated gilts. The average intervals from boar exposure to estrus, lengths of the first estrous and average intervals between first and second estrous periods were not statistically different for control and rpST gilts. Thirty-eight of forty gilts assigned to the study were artificially inseminated at the second estrus. All gilts inseminated were pregnant at laparotomy on

day 11 (day 0 = onset of estrus). Ovulation rate as determined by number of corpora lutea present on day 11 of pregnancy was 14.3 and 14.9 for control and treated gilts, respectively. Embryonic survival rate calculated as the percentage of corpora lutea represented by normal embryos was not different between experimental groups (76.2% and 87.9%, respectively, for control and rpST treated gilts).

Table 3. Effect of rpST on age at puberty and estrus. [a,b]

Parameter	Control	rpST	P
Gilts, no.	20	20	
Gilts exhibiting estrus, no.	20	19	
Age at puberty, days	182.1±3.1	182.4±3.3	NS
Boar exposure to estrus, days	12.8±2.7	14.2±2.8	NS
Length of first estrous period, days	1.8±0.1	1.9±0.1	NS
Estrous cycle length, days	20.2±0.4	20.6±0.4	NS

[a] Least squares means ±SEM, days.
[b] Daily IM injection of 6 mg rpST from 50 to 110 kg body weight.

Table 4. Effect of rpST on ovulation rate and embryo survival. [a]

Treatment	bred	No. of gilts pregnant on d 11	Number of corpora lutea	Embryonic survival rate, %
Control	19	19	14.3±0.6	76.2
Treated	19	19	14.9±0.6	87.9

[a] Least squares means ±SEM

These data provide initial evidence that changes in growth rate and body composition in gilts receiving rpST during the growing-finishing phase of development are without an adverse effect on age at puberty or fertility level at first breeding. A similar conclusion was reached by Bryan et al. (1988). Prepuberal gilts weighing an average of 80 kg received 70 g of porcine pituitary growth hormone per kilogram of body weight for 21 days and were then checked for estrus daily with a mature boar to stimulate the onset of puberty. A higher percentage of pGH-treated gilts (7 of 12) exhibited estrus during the experimental period (50 days), and of gilts exhibiting estrus, there was no difference between treatments in ovulation rate or number of embryos. The average interval from last injection of rpST to puberty was 3 weeks.

Direct effects

Follicular growth. Reproductive disorders have been observed when porcine pituitary growth hormone (pGH) was given to prepuberal gilts during the period puberty was anticipated and when given during proestrus in sexually-mature gilts. Hagen et al. (1987) compared age at puberty in gilts (mean weight = 72 kg) administered either vehicle or pGH (70 μ/kg body weight/day) for 65 days. Gilts were checked for estrus during the last 35 days of the treatment period. Non-cyclic gilts were slaughtered on day 66 for ovarian examination. Of eight gilts per treatment group, seven control and one pGH treated gilts exhibited estrus. The authors concluded that exogenous pGH inhibited ovarian development of prepubertal gilts. However, in a subsequent study, gilts treated similarly with pGH for a 42 day period did not show delayed puberty in comparison with control animals (Bryan et al., 1988). Further studies will be needed to clarify this inconsistency in results.

In a study involving sexually-mature gilts, Kirkwood and Aherne (1985) observed a high degree of anestrus in gilts administered exogenous growth hormone (90 μg/kg body weight/gilt/day) from day 14 after puberty until the end of the second estrus. Ovarian morphology was determined in gilts

failing to show a second estrus by day 30 after puberty. In a related experiment (Kirkwood and Aherne, 1985), prepuberal gilts were injected with either vehicle or growth hormone from 150 to 159 days of age. At 154 days, all gilts received an injection of pregnant mare serum gonadotropin followed by an ovulatory dose of human chorionic gonadotropin. Ovarian examinations were made on day 163. All control gilts had normal ovarian morphology whereas only 36% of gilts injected with growth hormone were classified to have normal ovaries due to the presence of large cystic follicles in the remaining gilts.

The mechanism whereby exogenous growth hormone may interfere with ovarian function is not clear. In prepuberal gilts, ovarian activity appeared to be depressed as indicated by delayed puberty in some studies, whereas in sexually-mature gilts the presence of cystic follicles suggests hyperstimulation of follicular growth. In both instances, serum IGF-1 concentrations were higher in gilts receiving growth hormone than in control gilts (Hagen et al., 1987; Kirkwood and Aherne, 1985). High corticoid concentrations have been reported to be a cause of anestrus (Esbenshade and Day, 1980) and also cystic follicles (Liptrap, 1970) in pigs. Further studies will be needed to clarify the suggested detrimental effects of exogenous growth hormone during the period follicles are approaching mature size and at the time of ovulation. Little is presently known about rpST dose response relationships or mechanism of action at these stages of the reproductive cycle.

Early pregnancy. The effects of rpST on the uterine development and embryonic survival during early development is being examined in crossbred gilts bred at second estrus (Unpublished data). Preliminary results are available from 24 animals bred. Gilts were assigned at random at breeding to receive one of the following three treatments as daily milliliter injections per gilt from day 4 to 18 of pregnancy (day 0 = onset of estrus): (I) vehicle injection; (II) 3 mg rpST; (III) 6 mg of rpST. All gilts were checked for estrus until day 25 to 28 of pregnancy at which time a laparotomy was performed. All gilts were hysterectomized to obtain ovarian, embryonic and uterine measurements. Pregnancy rate, embryonic survival rate and number of normal embryos at 25 days after mating were similar for control and rpST gilts. Statistical analysis of measurements made of uterine and placental growth in control and rpST-treated gilts will be made following completion of the trial.

Detrimental effects have been observed in sows administered pGH during late gestation. Kveragas and Seerley (1986) reported that of 20 gilts and sows receiving 10 mg of pGH daily during late gestation, four died during the trial. Three of the four animals died during the hours immediately prior to or following parturition.

Transgenic animals

Growth hormone genes have been inserted successfully into pigs by micro-injection into pronuclei and the transgenes are transmitted to progeny (Pursel et al., 1986). Insufficient observations are available to provide general conclusions regarding the direct effect of elevated growth hormone concentrations in transgenic boars and gilts. Present data does indicate, however, that reproductive performance is depressed severely in transgenic boars and gilts with high concentrations of human growth hormone (hGH) due to expression of fusion genes consisting of the mouse metallothionein-I promoter ligated to the structural gene for human growth hormone (MThGH).

Boars expressing hGH failed to breed due to lack of libido, lethargy and leg ailments. Reproductive failure in gilts was characterized to be due to anestrus and ovarian examination confirmed the absence of ovulation (Rexroad and Pursel, 1988). Female transgenic mice that express the MThST of MTbST genes were also sterile (Hammer et al., 1984).

Growth hormone and lactation

Considerable variation exists in pig weaning weights among herds and litters within a herd. A significant cause of these differences in performance of nursing pigs is level of milk production of the sow. Several factors are known to influence milk production in sows including genotype, feed intake, parity and farrowing room temperature. The enhancement of milk production by methods that did not reduce subsequent reproductive performance of the sow may be expected to result in increased efficiencies in the swine production system.

The result of recent studies indicate that the administration of pGH or rpST to lactating sows alters both the level, and pattern, of milk production as well as milk composition (Boyd et al., 1983; Spence et al., 1984; Boyd et al., 1985; Harkins et al., 1985; Spence et al., 1985). Spence et al. (1984) determined the effect of pGH on lactation performance in sows. Daily injections of either a placebo or pGH (5.33 mg/sow/day) were given beginning on day 100 of gestation through a 21-day lactation. Control and pGH-treated sows had similar milk yields at two weeks but production was 15% greater by three weeks for sows administered pGH. Percent fat was increased in the colostrum and at day 13 for pGH sows. In a related study, Spence et al. (1985) reported that colostral fat concentration was increased 26%, milk produced elevated 16.9% on day 21 and feed intake decreased 25% in sows receiving 11 IU of pGH during the second and third week of lactation. The weaning weights of pigs from sows treated with pGH were similar to those weaned from control sows. Boyd et al. (1985) studied the effect of rpST on milk production, milk composition and pig weight at days 16, 22 and 28 of lactation. Subcutaneous injection of either placebo or rpST (8.22 mg/sow/day) were given daily beginning on day 12 through day 28 of lactation. Control sows and milk production continued to increase to levels 11% and 22% higher than controls on days 22 and 28, respectively. Total yield of solids, fat and lactose were, respectively, 24%, 29% and 30% higher in sows receiving rpST. Protein yield was not different. Pigs from sows receiving rpST were significantly heavier (0.34 kg) at weaning on day 28. Sows given rpST consumed 22% less feed and lost more weight and backfat during the lactation period than control sows. No adverse health effects were observed as a result of treatments.

Insufficient data exists to predict the effect of decreased feed intake, increased weight loss and decreased percentage body fat during lactation on subsequent reproductive performance. Of particular concern would be reduced feed intake in first litter sows. Further, innovative management systems are yet to be tested that are specifically designed to maximize the benefits of increased milk production, such as cross fostering to increase number of pigs suckling individual sows and early breeding of remaining sows in a farrowing group.

Further research will also be required to determine most suitable nutritional and management systems for sows administered pGH or rpST as well as preferred stage of lactation to wean the pigs of sows receiving exogenous growth hormone. Increased pig gains prior to day 21 to 24 may promote weaning at an earlier age whereas increases over controls in milk production are more pronounced after the third week of lactation. Changes in gestation management programs and early weaning may also provide a means of minimizing tissue loss during lactation to prevent depletion to a critical level that compromises post-weaning reproductive performance.

References

Anderson, L.L. and R.M. Melampy, 1972. Factors affecting ovulation rate in the pig. In: D.J.A. Cole (Ed.) Pig Production. Butterworth's, London, p 329.

Boyd, R.D., D.A. Spence, D.E. Bauman and W.R. Butler, 1983. Effect of exogenous growth hormone on fetal energy storage and lactation performance in swine. Proc. Cornell Nutr. Conf. p. 108-113.

Boyd, R.D., M. Harkins, D.E. Bauman and W.R. Butler, 1985. The effect and practical implications of recombinant porcine growth hormone on lactation performance of sows. Proc. Cornell Nutr. Conf. for Feed Manufacturers. p. 10-19.

Bryan, K.A., A.M. Clark and D.R. Hagen, 1988. Effect of treatment with and withdrawal of porcine growth hormone (pGH) on growth and reproductive performance of gilts. J.Anim. Sci. 66 (Suppl. 1):401.

Burger, J.F., 1952. Sex physiology of pigs. Onderstepoort J. vet. Res., Suppl. 2: 41-52.

Campbell, R.G., N.C. Steele, T.J. Caperna, J.P. McMurtry, M.B. Solomon and A.D.. Mitchell, 1988. Interrelationships between energy intake and endogenous porcine growth hormone administration on the performance, body composition and protein and energy metabolism of growing pigs weighing 25 to 55 kilograms live weight. J. Anim. Sci. 66:1643-1655.

Chung, C.S., T.D. Etherton and J.P. Wiggins, 1985, Stimulation of swine growth by porcine growth hormone. J. Anim. Sci. 60:118-130.

Esbenshade, K.L. and B.N. Day, 1980. The effects of triamcinolone acetonide on plasma glucocorticoid levels and occurrence of estrus in gilts. J. Anim. Sci. 51:153-157.

Etherton, T.D., C.M. Evock, C.S. Chung, P.E. Walton, M.N. Sillence, K.A. Magri and R.E. Ivy, 1986. Stimulation of pig growth performance by long-term treatment with pituitary porcine growth hormone (pGH) and a recombinant pGH. J. Anim. Sci. 63 (Suppl. 1):219.

Etherton, T.D., J.P. Wiggins, C.M. Evock, C.S. Chung, J.F. Rebhun, P.E. Walton and N.C. Steele, 1987. Stimulation of swine growth performance by procine growth hormone: determination of the dose-response relationship. J. Anim. Sci. 654: 433-443.

Goode, L., A.C. Warnick and H.D. Wallace, 1965. Effect of dietary energy levels upon reproduction and the relation of endometrial phosphatase activity to embryo survival in gilts. J. Anim. Sci. 24: 959-963.

Gossett, J.W. and A.M. Sorense, Jr., 1959. The effect of two levels of energy and seasons on reproductive phenomena in gilts. J. Anim. Sci. 18: 40-47.

Hagen, D.R., K.A. Bryan, J.M. Hammond, J. Mondschein and S. Canning, 1987. Effect of porcine pituitary growth hormone (pGH) in vivo on ovarian function of gilts in vivo and in vitro. J. Anim. Sci. 65 (Suppl 1): 370-371.

Hammer, R.E., R.D. Palmiter and R.L. Brinster, 1984. Partial correction of murine hereditary growth disorder by germ-line incorporation of a new gene. Nature 311: 65

Harkins, M., R.D. Boyd, D.E. Bauman and W.R. Butler, 1985. Effect of recombinant porcine growth hormone on milk production, and sow and litter performance. J. Anim. Sci. 61 (Suppl. 1): 316-317.

Kirkwood, R.N. and F.X. Aherne, 1985. Energy intake, body composition and reproductive performance of the gilt. J. Anim. Sci. 60:1518-1529.

Knott, R.E., D.C. England and W.H. Kennick, 1984. Estrus, ovulation, conception and embryo survival in confinement-managed gilts of three weight groups. J. Anim Sci. 58: 281-284.

Kverageas, C.L., R.W. Seerley, R.J. Martin and W.L. Vandergrift, 1986. Influence of exogenous growth hormone and gestational diet on sow blood and milk characteristics and on baby pig blood, body composition and performance. J. Anim. Sci. 63: 1877-1887.

Liptrap, R.M. 1970. Effect of corticotropin and corticosteroids on oestrus, ovulation and oestrogen excretion in the sow. J. Endocrinol. 47: 197.

McLaren, D.G., G.L. Grebner, P.J. Bechtel, F.K. McKeith, J.E. Novakofski and R.A. Easter, 1987. Effects of graded levels of natural porcine somatotropin (PST) on growth performance of 57 to 103 kg pigs. J. Anim. Sci. 65 (Suppl.1): 245.

Pursel, V.G., R.E. Hammer, D.J. Bolt, R.J. Wall, R.D. Palmiter and R.L. Brinster, 1986. Transgenic swine transmit foreign gene to progeny. J. Anim. Sci. 63 (Suppl. 1): 203.

Rexroad, C.E., Jr. and V.G. Pursel, 1988. Status of gene transfer in domestic animals. Proc. 11th Int. Cong. Anim. Reprod. and A.I., Dublin. p. 29-35.

Spence. C.A., R.D. Boyd, D.E. Bauman, W.R. Butler and C.D. Wray, 1984. Effect of exogenous growth hormone on fetal energy storage and lactation performance in sows. J. Anim. Sci. 59 (Suppl. 1): 246.

Spence. C.A., R.D. Boyd, D.E. Bauman, W.R. Butler and D. Wray-Cahen, 1985. Growth hormone in late gestation and lactation for swine: survival and milk production. Cornell Swine Res. Report. p.26-31.

CONSUMER ASPECTS

Safety of edible products

Nutritional and sensory characteristics

Consumer perception

BIOTECHNOLOGY AND THE CONTROL OF GROWTH AND PRODUCT QUALITY IN SWINE -- SAFETY OF EDIBLE PRODUCTS

M.A. Norcross, R.A. Carnevale, E.A. Brown, and A.R. Post

United States Department of Agriculture, Food Safety and Inspection Service, Washington, D.C. 20250

Summary

While many of the developed countries of the world enjoy a protein-rich food supply, much of the world has a need for technologies which improve the quantity and quality of food proteins. Drugs used to enhance growth and improve feed efficiency along with improved genetic and nutritional factors have made available greater amounts of protein from food- producing animals to more people than ever before. Anabolic agents, in spite of the sometimes unfavorable publicity they have attracted, have been especially advantageous in ensuring the feed efficiency of livestock.

Protein synthesis and its regulation have been the object of intensive research, both at the biochemical and molecular genetic levels. The correlation of specific gene products such as somatotropins with increased growth rates, enhanced feed efficiency and fat/protein repartitioning has stimulated interest in the possibility of manipulating protein synthesis in farm animals. Somatotropin and the related compounds, somatostatins, somatomedins and growth hormone releasing factors are the first products of recombinant DNA technology that may be economically feasible for use in increasing production efficiency for domestic and world agriculture.

If such products are to be used in the United States, approval for use must be obtained from the United States Food and Drug Administration (FDA). The safety and efficacy of these products must be demonstrated through well-controlled and properly designed scientific studies.

Numerous experimental regimens involving somatotropin, somatomedin and other factors including releasing factors have been submitted to the FDA for approval as investigational new animal drugs. Regulation of these new agents through pre-marketing approval and post-approval monitoring must be sufficiently protective of the public health, must ensure that products are rational for their proposed use and must ensure that they are effective in the intended animal species.

Keywords: biotechnology, food safety, animal drugs, public health.

Introduction

The use of agricultural chemicals in the second half of the twentieth century has been crucial in meeting the nutritional needs of an expanding world population. Pharmaceutical and other chemicals have been used destroy pests, enrich feed, control disease and promote to the growth of livestock and poultry. Today's farmer and veterinary practitioner can choose from a wide variety of drugs, medicated feed premixes and vaccines for maintaining animal health. Drugs used to enhance growth promotion and improve feed efficiency are making available greater amounts of protein from food-producing animals to more people than ever. Anabolic agents, in spite of the sometimes unfavorable publicity they have attracted, have been especially advantageous in ensuring an improvement in the feed efficiency of livestock.

Protein and fat synthesis and their physiological regulation have been the object of a significant amount of recent intensive research, both at the biochemical and molecular genetic levels. The correlation of specific gene products such as somatotropins (growth hormones) with increased growth rates, enhanced feed efficiency, adipose to muscle tissue repartitioning, and increased milk production in mature dairy cattle stimulated interest in the possibility of manipulating protein synthesis in livestock. These discoveries have been spaced over a period of three decades with data slowly accumulating as improved methods of biochemical purification of the test substances were developed. With the development and implementation of recombinant technologies, substantial amounts of natural anabolic agents will be available for large scale increases of production efficiency in the meat and poultry industry. Somatotropins, somatomedins and releasing factors are the first products of biotechnology with a potential for major impacts upon production efficiency for domestic and world agriculture. The use of exogenous somatotropins to supplement the natural level in livestock is a logical extension of the natural selection process practiced for decades by the farmer. Somatotropins are polypeptides of approximately 190 amino acids which are secreted by the anterior pituitary gland. They have anabolic activity and also have effects on fat and carbohydrate metabolism. Part of the growth promoting or anabolic effect is mediated by the secretion of other hormones, known as somatomedins, from the liver and other tissues. Because of its effects on tissue metabolism, there is great interest in the use of exogenous somatotropin to stimulate growth and lactation in farm animals (Norman and Litvack, 1987). The somatomedins have both insulin-like and cell proliferating-like activities. Consequently, somatomedins are also known as insulin-like growth factors. At present, two somatomedins have been identified, insulin-like growth factors -1 and -2 (IGF-1 and IGF-2). Somatomedins stimulate an increase in the number and size of a wide range of cell types. Specific receptors have been identified in many of these, e.g., in muscle and in fibrous tissue. Their stimulatory effect on bone growth is particularly important since that supports the greater disposition of soft tissue (Lamming and Peters, 1987).

Somatomedins are thought to be produced by the liver under the influence of somatotropin, however, other tissues such as the kidney (Murphy et al., 1987) also produce somatomedins. Other endogenous hormones, e.g., prolactin, insulin, corticosteroids and thyroid hormones also influence the production of somatomedins. High rates of growth in farm animals have been correlated with high levels of somatomedins and recent experiments have demonstrated an increase in the growth rate of laboratory animals following the administration of somatomedins (Lamming and Peters, 1987).

Although its existence has long been suspected, the hypothalmic growth-hormone-releasing factor (GRF) has only recently been isolated (Esch et al., 1983). GRF is a polypeptide consisting of 44 amino acids. Synthetic analogues of the factor have been prepared and have been shown to stimulate the release of somatotropins in animals (Moseley et al., 1984).

One of the reasons for the long delay in the discovery of GRF was subsequently found to be the concurrent existence in the brain of a somatotropin inhibiting factor. This compound, known as somatostatin, is also a peptide and consists of only 14 amino acids (Lamming and Peters, 1987). Somatostatin inhibits the release of somatotropins and insulin (Koerker et al., 1974).

There has been much recent interest in the practical exploitation of both GRF and somatostatin in controlling the growth of farm animals by the development of analogues of GRF and by immuno-neutralization of the effect of somatostatin (Lamming and Peters, 1987).

Regulatory concern

Certain regulatory concerns inevitably emerge from any new technological endeavor. With the development of the somatotropins and related compounds for food animal use, concerns relating to efficacy, animal safety and welfare and environmental safety have been expressed. Further, concerns regarding the patentability of transgenic animals have been mentioned and of paramount

concern are those factors relating to the human food safety aspects of new animal drugs, especially those produced by recombinant technology.

Target animal safety, safety to the environment and animal welfare concerns of the somatotropins and related compounds have been adequately addressed in the scientific literature.

Regarding the products of biotechnology and human food safety, the industrialized nations of the world have concluded that such products should be regulated under the same policies and procedures currently applicable to other animal drugs with the process of biotechnology regulated independently. The existing national regulatory processes are adequate to address the human food safety concerns of the somatotropins and related compounds (Anon, 1986).

Fortunately, the concerns for safety of the somatotropins are minimal, since these peptides are digested in the gastro-intestinal tract and are species specific (Apostolou, 1988).

The environmental effects of products produced by recombinant DNA technology are of considerable interest. It is possible that adverse effects could result from altering the genetic makeup of micro-organisms and allowing their inadvertent release into the environment. The concerns of responsible scientists and environmentalists are not to be dismissed since there are many examples of disastrous consequences resulting from organisms being introduced into new environments.

Safety of somatotropins and related compounds in food

Somatotropins hold the promise of producing meat with less fat and more protein, and more milk with greater feed efficiency. Therefore, there is interest in developing these compounds for widespread use in food-animal production. At this time, more than 60 experimental regimens have been submitted to the United States Food and Drug Administration for approval to conduct research with these compounds in target animals.

Although the primary species of interest at this Symposium is pigs, there are few non-proprietary data relating to products of biotechnology in these animals. Therefore, we must rely heavily on published information relating to bovine somatotropins (BST) in order to address in a public forum the human food safety aspects of porcine products. The data that have been reported in swine indicate that somatotropin has a pronounced effect on increasing muscle tissue while reducing fat synthesis. Dramatic alterations in the rate and efficiency of gain in swine have also been reported (Boyd, 1987).

Bovine somatotropin for dairy cows will likely be one of the first commercial applications for biotechnology in animal husbandry. Dairy cattle treated with BST often secrete low levels of somatotropin into the milk. However, cows injected with up to 50 mg/day BST did not show detectable levels in milk when assayed by a radio-immunoassay with a validated sensitivity of 2 ppb (Hart et al., 1985). In another study, milk from control and treated cows (40 mg/day BST) contained less than 2.5 ppb (Simkins, 1987). The Milk Marketing Board of the United Kingdom could not distinguish chemically between milk from BST treated cows and untreated cows even as to BST content (Phelps, 1987).

There are two primary reasons residues of BST in milk are unlikely to present a safety concern:

— BST is not orally active because gastric and intestinal proteases such as pepsin, trypsin and chymotrypsin digest the protein molecule into its constituent amino acids. Recombinantly derived BST was ineffective in rats after oral administration of amounts up to 4 mg/day either in producing growth or in the appearance of immunoreactive BST in the serum (Seaman et al., 1988).

— Somatotropins are species specific except between primates where lowered responses can be observed. Bovine somatotropin when administered parenterally to humans is inactive.

Furthermore, pasteurization and other manufacturing processes may inactivate somatotropin. Activity of somatotropin is lost by immersion in boiling water at pH 4.0, 7.5 and 8.9. Activity of recombinantly derived BST was lost after pasteurization of milk (Kronfeld, 1987).

Of course, these factors would be applicable to both BST and porcine somatotropin (PST) regarding potential residues of somatotropins in organ or muscle tissues. Thus, there is little likelihood of significant concerns resulting from residues of these proteins in meat from treated animals.

An issue of some concern is the relationship between insulin-like growth factors, particularly IGF-1, and somatotropin which has the potential to increase concentrations of IGF-1 in milk and meat from cows treated with BST. This question regarding IGF-1 must be resolved and is critical because of the potential for these shorter chain peptides to be absorbed through the gut, especially in neonates. Furthermore, these protein mediators are believed not to be species specific as with the somatotropins.

Satisfactory resolution of these issues will facilitate approval of these drugs in food animals, assuming all safety, efficacy and environmental standards are met.

Regulatory process in the United States

If somatotropins and related compounds are to be used in the United States, regulatory approval for on farm use must be obtained. The Food and Drug Administration (FDA) is responsible for the premarketing efficacy and safety evaluation and approval of new animal drugs and feed additives; for regulating their manufacture, sale and use; and for setting tolerances for residues permitted in food.

Under the U.S. Federal Food, Drug and Cosmetic Act (CFR, 1988 a), the term 'drugs' means substances recognized in the United States Pharmacopeia, Homeopathic Pharmacopeia of the United States, or the National Formulary; substances intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals, and substances other than food intended to affect the structure or function of the body of man or other animals. It also includes substances intended for use as a component of a drug. The Act defines a new animal drug (in part) as any drug intended for use in animals other than man, the composition of which is not generally recognized among experts qualified by scientific training and experience, as safe and effective for use under the conditions prescribed, recommended, or suggested in its labeling.

Before a new animal drug may receive formal FDA approval, it must be tested for effectiveness and safety by the sponsor of the drug product. If the product is intended for use in a food-producing animal, data must be obtained which demonstrate that the edible animal products do not contain unsafe residues. It is the responsibility of the drug sponsor to conduct the necessary tests.

When the sponsors are confident that sufficient data obtained under research protocols have established the safety and efficacy of the drug, they may apply for marketing approval. A New Animal Drug Application (NADA) must be submitted along with all data obtained, including adverse effects associated with the drug's use. The NADA must also include information on the drug's chemistry; composition and component ingredients; manufacturing methods, facilities and controls; proposed labeling; analytical methods for residue detection and analysis; and environmental impact.

The target animal safety and efficacy data for a drug product must relate to the dosage level and route of administration as proposed in the labeling. All data submitted must relate either directly or indirectly to the specific claims for the product.

Development of adequate methods for detecting drug residues in animal tissues from treated animals is frequently the most time-consuming and expensive item in developing a new animal drug for food-producing animals. Development of residue methodology is based on toxicological studies to establish safe residue levels or tolerances for humans consuming food products derived from treated animals. Methods may have to be developed for muscle, liver, kidney, fat, and milk which

are sensitive to levels that assure food safety. The proposed residue methodology must be validated prior to approval of the NADA and must show satisfactory performance in one USDA and two FDA laboratories. If the method proves to be practical, of sufficient sensitivity and is validated in the three laboratories, FDA will recommend its acceptance.

When a NADA is deemed approvable, a regulation is published in the **Federal Register** announcing its approval and it is incorporated into the Code of Federal Regulations.

Regulatory status

Based on the information previously presented, the Food and Drug Administration currently allows the marketing of edible products from animals which have been treated with BST or PST in investigational laboratory and field studies with no pre-slaughter withdrawal or milk discard restrictions. However, since U.S. food and drug law requires each new drug product to be supported by its own unique evidence of safety and because each proposed somatotropin product may be slightly different in amino acid sequence and physical formulation, certain safety data are required prior to approval of an individual application. Since recombinant BST molecules differ from the endogenous compound by only one to three amino acid groups (e.g., methionyl-BST), FDA does not consider these changes to be of toxicological concern. As new alterations to the molecule are developed, each will have to be tested to ensure that the alteration has not introduced toxic properties (Apostolou, 1988).

Generally, data which confirm the lack of oral activity of the particular somatotropin market product in laboratory animals at exaggerated doses will be expected as part of the application. In addition, it must be demonstrated that somatomedins are not significantly increased in milk or tissue subsequent to somatotropin treatment or if they are, that these hormone mediators do not possess oral activity. This could be accomplished by direct measurement of IGF levels between treated and control animals and/or short term oral overdose studies similar to those for somatotropin.

It is expected that somatotropins will be approved and regulated in the United States in a manner similar to the endogenous hormones (estradiol, progesterone and testosterone). A tolerance and preslaughter withdrawal period for these hormones are not necessary and no approved tissue residue method is required (CFR, 1988b).

With respect to the transfer of new genetic material into the genome of an animal (transgenic animals), the regulatory response should depend on the types and magnitude of the genetic changes induced. In general, it is not anticipated that transgenic animals will differ substantially in appearance, behavior or general health from current food animals (Gilles, 1988). Following assurances that food from these animals is safe for human consumption, they will be inspected like their more traditional counterparts.

Environmental impact

Originally the source of these compounds was the abbatoir. Careful extraction of the anterior pituitary gland from beef and pork carcasses yielded small amounts for biochemical research but not enough for use in animal production (Gilman et al., 1985). As a result of improvements in biotechnology, systems have been developed which are capable of producing enough hormone products for animal production use. The genetic material from animal cells has been isolated and transferred to bacterial cells and the cells are reproduced using standard fermentation techniques. The bacteria produce the hormone which is coded for by the transferred genetic material. The resulting substance is then isolated, purified and made available for commercial use.

The difference between routine bacterial fermentation processes, carried out safely for many years with antibiotic production, and recombinant DNA technology is the potential for release into the environment of organisms that possess new genetic information.

The FDA has determined that the investigational activities for BST will not significantly affect the human environment and has issued a Finding of No Significant Impact for each BST investigational application currently under consideration. The FDA will re-examine the environmental impact of the commercial-scale production and marketing of BST and PST and related compounds before approving their commercial use.

The particular variety (K-12) of **Escherichia coli** used for the production of BST seems to be only an opportunistic pathogen, like the parent (unmodified) organism. Based on this, the Commissioner of FDA has proposed to the National Institutes of Health Recombinant-DNA Advisory Committee that the containments for micro-organisms such as **E. coli** K-12 "be no greater than those appropriate for the unmodified parental organisms". The Advisory Committee has accepted the proposed change (Apostolou, 1988).

The production cost of synthetic hormonal proteins is important for commercial applications. Production costs for somatotropin have been estimated to be reasonable for their use in dairy animals to increase milk production (Fallert et al., 1987). Other issues of social and economic importance, particularly for many U.S. producers, such as the effect on the small farmer and changes in long term land usage, may also need to be addressed as part of an environmental impact assessment.

Monitoring by FSIS

Since 1967, the Food Safety and Inspection Service (FSIS), of the U.S. Department of Agriculture (USDA), has conducted a National Residue Program (NRP) to help prevent the marketing of animals containing illegal residues of drugs and other chemicals. FSIS is responsible for enforcing the Federal Meat Inspection Act (CFR, 1988c) and the Poultry Products Inspection Act (CFR, 1988d). Under these laws, the Agency ensures that meat and poultry products in interstate commerce and for import are wholesome, not adulterated, and properly labeled and packaged. The meat and poultry inspection laws provide for the retention or condemnation of carcasses suspected of containing or found to contain illegal drug and chemical residues. In 1987, USDA inspected 121 million head of livestock, nearly 5 billion birds, and 127 billion pounds of processed meat and poultry products. As part of this responsibility, samples of meat and poultry are collected at slaughtering establishments for further testing. Each year, over 2 million laboratory analyses and inplant tests are performed on over 450,000 samples to support the FSIS residue and microbiological monitoring and surveillance programs.

FSIS carries out its residue control program in cooperation with other Federal agencies. For the most part, these efforts are coordinated among FSIS, FDA, and the U.S. Environmental Protection Agency (EPA). Both FDA and EPA establish tolerances for compounds to which livestock and poultry are exposed. They also determine the approved methods of use of compounds on specific crops or animals to ensure that tolerances will not be exceeded. EPA establishes tolerances for pesticides, while FDA sets tolerances for animal drugs and other non-pesticide contamination in food.

If FSIS finds significant levels of residues in an animal, these findings are then reported to FDA which may subsequently decide to initiate a follow-up investigation to determine the source of the residue. If FSIS finds violative residues in an animal or group of animals, the meat or poultry may be condemned.

Criteria for compound evaluation and selection

It is not feasible to monitor for residues of all chemicals in meat and poultry. Further, this is not necessary to adequately protect public health. It is, however, important to assess the likelihood that animals exposed to chemicals may contain residues at levels of concern, and to conduct monitoring, where test methods are available, for those chemicals that are most likely to present the greatest potential risk. A hierarchic compound assessment scheme is used for this purpose.

Each compound is evaluated on a number of factors to judge the potential for animal exposure and significance for human health. These factors include:

- Amount of actual or probable use.
- Conditions of use as related to residues at slaughter.
- Potential for misuse to result in harmful residues.
- Metabolic patterns of the chemical in animals, plants, and the environment, including the bioavailability and persistence of residues.
- Toxicity of the residue.

Compounds are selected for monitoring after ranking and included in a plan for the calendar year based on several factors, including:

- Compound ranking assigned.
- Whether a practical test method is available and is suitable for regulatory use.
- Whether the compound is measurable in a multi-residue method where many compounds, even though all may not be assigned a high ranking, can be tested for a relatively low cost.
- Monitoring or other experience that shows whether adulterating residues are present in meat and poultry.

FSIS works from a list of about 400 compounds that includes certain environmental contaminants in addition to animal drugs and pesticides.

The process of compound evaluation and ranking is a dynamic one. Additional compounds have to be considered in the system as agricultural use practices change, and additional research on a compound's toxicity and its potential for leaving harmful residues may affect previous rankings.

FSIS uses a Compound Evaluation System (CES) which is designed to provide the Agency with a systematic approach to the categorization of compounds and to the analysis of their likelihood of occurrence in meat and poultry and their potential impact on public health (Anon, 1988).

Briefly, the CES addresses the risk of residues occurring in meat and poultry as a function of two major elements. They are hazard (adverse effects of a given compound) and exposure (residue level and amount of product consumed containing residues of concern). The system is a two-value, hierarchic compound ranking scheme that classifies a given pesticide, animal drug, or contaminant in any one of 16 categories. Compounds of greatest concern carry a designation of A-1 (high health hazard potential; high likelihood of residue occurrence); those compounds of least concern are designated D-4 (negligible health hazard potential; negligible likelihood of residue occurrence).

FSIS has tentatively assessed bovine and porcine somatotropins as D-4 using the CES system and available data from the scientific literature.

Research animals slaughtered in federal establishments

FSIS has the regulatory authority to perform ante-mortem and post-mortem inspection on livestock used in any research investigation involving an experimental biological product, drug, or chemical slaughtered at an official establishment.

Figure 1 describes the growing interest in the commercial use of these anabolic agents as evidenced by the dramatic increase in numbers of experimental animals. FSIS has inspected over the last few years more than 5,000 investigational animals that have been treated with somatotropins or related compounds. The only lesions noted have been injection lesions and abscesses. At this time, these compounds cannot be given in feed and must be injected, however, the future ideal delivery system for animal production will eliminate daily injections. These systems include depot injections of oil suspensions and the use of an osmotic pump. Both methods supply sustained release of BST for two or more weeks. The most extended release is from osmotic pumps, which must be excised at slaughter.
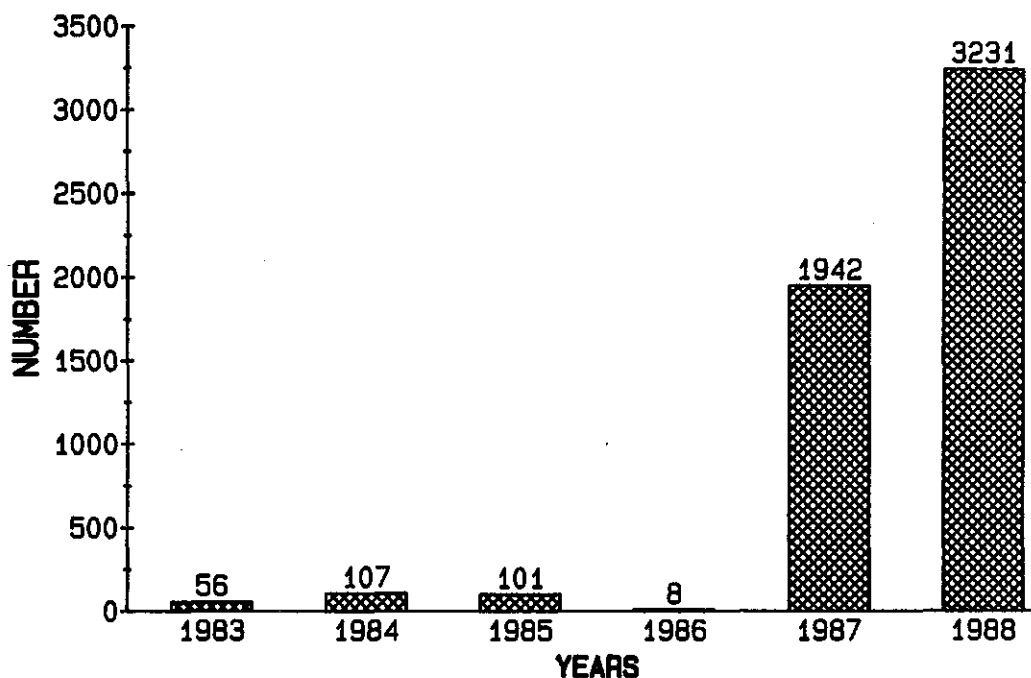
Figure 1. Number of research animals slaughtered in federally inspected establishments after administration of growth regulating agents.

Conclusion

The approach to food safety described is scientifically defensible for the regulation of somatotropins and related compounds. It embraces the proper level of concern for public health while at the same time recognizes the practical advantage of using these compounds in the rearing of livestock. It is at Symposia such as these that an international scientific consensus can be reached on the proper degree of regulation to apply to new technologies and products. This, of course, is of extreme importance in terms of future trade between nations.

The ideal situation occurs for consumers and farmers when the safety and efficacy of an animal drug have been demonstrated through scientific studies that form the basis for regulatory controls. Governments can then license such products and implement effective monitoring programs to ensure compliance with conditions of use. In order for this situation to be realized, public health decisions must be founded on scientific facts. When this is not the case, problems inevitably arise.

176

In the effort to harmonize international regulatory controls, there will be a continuing need for the exchange of scientific information and acceptance of shared data among trading nations. There must be a working relationship between industry, academia, and government, based on impeccable scientific principles that are comprehensible to the layman. That, will be the ultimate assurance of better international and regulatory cooperation.

References

Anon, 1986. Coordinated framework for regulation of biotechnology. Federal Register 51:23302.

Anon, 1988. Compound evaluation system. United States Department of Agriculture, Food Safety and Inspection Service. Federal Register 53:751.

Apostolou, A., 1988. Somatotropin safety - a short regulatory overview. Journal of the American Veterinary Medical Association 192:1698-1700.

Becker, G.S., and S. Taylor, 1986. Bovine GH: agricultural and regulatory issues. 86-1020 ENR/SPR. Congressional Research Service, The Library of Congress Washington, DC.

Boyd, R.C., 1987. Somatotropin and productive efficiency in swine. Animal Health and Nutrition, February, 23-26.

CFR, 1988a. Federal food drug and cosmetic act. U.S. Code of Federal Regulations, Title 21, Parts 510, 511, 514:76.

CFR, 1988b. U.S. Code of Federal Regulations, Title 21, Section 522.840:249.

CFR, 1988c. Federal meat inspection act. U.S. Code of Federal Regulations, Title 9, Part 301:89.

CFR, 1988d. Poultry Products Inspection Act. U.S. Code of Federal Regulations, Title 9, Part 381:389.

Esch, F., P. Bohlen, N. Ling, P. Brazeau, and R. Guillemin, 1983. Isolation and characterization of the bovine hypothalamic growth hormone releasing factor. Biochemical Biophysical Research Communications 117(3):772-779.

Fallert, R., T. McGuckin, C. Betts, and G. Bruner, 1987. BST and the dairy industry. Bulletin No. 535. Economic Research Service, U.S. Department of Agriculture, Washington, DC.

Gilles, K.A., 1988. Biotechnology: regulatory considerations. International Symposium on Biotechnology and Food Quality, College Park, Maryland.

Gilman, A.G., L.S. Goodman, T.W. Rall and F. Murad, 1985. The pharmacological basis of therapeutics, 7th Ed., Macmillan, New York.

Hart, I.C., J.A. Bines, S. James, and S.V. Morant, 1985. The effect of injecting or infusing a low dose of bovine growth hormone on the milk yield, milk composition, and the quantity of the hormone in the milk serum of cows. Animal Production 40:243-250.

Koerker, D.J., W. Ruch, E. Chickedel, J. Palmer, C. Goodner, J. Ensinck, and C.C. Gale, 1974. Somatostatin: hypothalamic inhibitor of the endocrine pancreas. Science 184:482.

Kronfield, D.S., 1987. The challenge of BST. Large Animal Veterinarian, November-December, 14-17.

Lamming, G.E. and A.R. Peters, 1987. Future developments in the manipulation of growth in farm animals. Veterinary Record 20:495-499.

Moseley, W.M., L.F. Krabill, A.R. Friedman and R.F. Olsen, 1984. Growth hormone response of steers injected with synthetic human pancreatic growth hormone-releasing factors. Journal of Animal Science 58:430-435.

Murphy, C.J., G.I. Bell and H.G. Friesen, 1987. Tissue distribution of IGF-I and IGF-II messenger RNA in the rat. Endocrinology 120:1279-1282.

Norman, A.W. and G. Litvack, 1987. Hormones. Academic Press, London.

Phelps, A., 1987. U.K. milk industry to permit bovine somatotropin use. Feedstuffs 59:4.

Seaman, W.J., J.L. Nappier, R.F. Olsen, M.D. Charlton, P.J. Skinner, R.J. Weaver, and G.A. Hoffman, 1988. The lack of a growth-promoting effect of orally administered bovine somatotropin in the rat body-weight-gain assay. Fundamental Applications of Toxicology 10:287-294.

Simkins, K.L., 1987. Symposium on nutrient partitioning. E.J. Robb (ed.) American Cyanamid Co., Wayne, New Jersey.

Welsh, T.H., 1985, Endocrine control of growth: current and emerging concepts. Animal Nutrition and Health, June-July, 14-19.

POTENTIAL OCCURENCE OF RESIDUES AFTER TREATMENT OF PIGS WITH RECOMBINANT SOMATOTROPIN

D. Schams[1], E.Kanis[2] and P. van der Wal[2]

[1]*Institut für Physiologie, Technische Universität München 8050 Freising-Weihenstephan, FRG and Animal Science Departments,*
[2]*Wageningen Agricultural University, Netherlands*

Summary

Recombinant porcine somatotropin (rpST) has in recent years shown to be highly effective improving growth characteristics such as average daily gain, feed efficiency and leaness of the animals treated. A first attempt is made to evaluate blood and tissue levels of pST, blood levels of IGF-1 prior and during slaughter of rpST treated pigs.

In trial 1 (94 pigs) 5 factors were regarded.Three breeds (Pietrain, Duroc and F1 from Great Yorkshire x Dutch Landrace); four litters per breed; two sexes (barrows and gilts); two treatments (rpST and placebo); two weights at slaughter (100 kg and 140 kg). Treatment (twice weekly, 14 mg rpST dissolved in buffer i.m./injection) started with 60 kg live weight. Blood from the jugular vein was collected 4.5 days after the last injection at slaughter. Trial 2; 36 barrows from 3 breeds; (Pietrain, Duroc and F1) were treated from 60 kg up to 120 kg live weight with rpST twice weekly i.m. with 14 mg/injection. Blood from the jugular vein was collected after the last injection within 1 h and 26-27 h later at slaughter. Additionally from 10 pigs (7 treated, 3 placebos) muscle tissue from the right shoulder was collected for pST residue analysis.

Porcine somatotropin and IGF-1 were evaluated by RIA. In trial 1, 4.5 days after the last rpST injection blood levels of pST of treated animals were similar to controls or significantly lower in Pietrain and Duroc breed. In trial 2 within 1 h after the last injection there was a tremendous increase on average from about 2 ng/ml up to 240 - 321 ng/ml 26-27 h later values of treated animals reached already control levels. Tissue concentrations were not significant different and were below levels of 5 ng/g wet tissue. Blood concentrations of IGF-1 were not significantly different between controls and treated animals in trial 1 and in trial 2 within one hour after the last injection. Levels increased significantly 26-27 h later. In conclusion no measurable residues of pST or IGF-1 were found after treatment with pST in blood or muscle tissue 4.5 days after the last injection of pST.

Keywords: somatotropin, insulin-like growth factors, residues, swine.

Introduction

Porcine somatotropin (pST) is a naturally - occurring protein produced by the pituitary gland. More recently material has been made available by recombinant gene technology. The particular molecule produced is identical to one of the naturally occurring somatotropins apart from an additional methionine at the N terminal end. Recombinant porcine somatotropin (rpST) has, in recent years shown to be highly effective in improving growth characteristics such as average daily gain, feed efficiency and leaness of the animals treated. Until now no data were published concerning safety and wholesomeness of products from pigs treated with rpST. A first attempt is

made to evaluate blood and tissue levels of pST and IGF-1 prior and during slaughter of rpST treated pigs.

Materials and Methods

Two trials of growth experiments were performed at Wageningen Agricultural University (for details see paper of V.Fowler and E.Kanis in this volume).

Trial 1: The experiment performed included five factors.

1. Three breeds: Pietrain, Duroc and F1 (Great Yorkshire and Dutch Landrace)
2. Four litters per breed
3. Two sexes: gilts and barrows
4. Two treatments: rpST or placebo
5. Two weights at slaughter: 100 and 140 kg live weight

pST application: rpST was dissolved in a buffer which also was used as placebo. The administration (14 mg intramuscularely twice a week) started with 60 kg live weight and was continued till four and a half days before slaughter. The animals were fed ad libitum.Blood was collected in heparinized tubes immediately after the killing by electrocution, centrifuged and plasma was stored until analyses at $-20^{\circ}C$ .96 samples (47 from rpST treated pigs and 47 placebo) were analyzed.

The animals with 100 kg or 140 kg slaughter weight received in total about 12 or 26 injections respectively.

Trial 2: Barrows of different breeds (Pietrain, Duroc and F1 (Great Yorkshire x Dutch Landrace, 12 per group) were treated with rpST (14 mg twice a week intramuscular) or placebo from 60 to 120 kg of body weight (about 18 injections for each individual in total). The first blood sample was taken by needle puncture of the jugular vein at the end of treatment period within 1 h after the last injection. The second sample was taken 26-27 h later right after the killing by electrocution.

Tissue samples

In trial 1 from six pigs (four treated, two controls) and trial 2 from four pigs (three treated, one control) tissue samples from the right hand shoulder were collected and kept frozen until assay. The last injection in that tissue was given 4.5 days before slaughter. In the six pigs from the first trial it was the last injection the animal had, the four pigs in the second trial had a consecutive injection in the left hand shoulder one day before slaughter.

Determination of pST in blood plasma

Porcine somatotropin was determined by radioimmunoassay employing rabbit antiserum raised against pig pituitary extracted growth hormone (USDA-pGH-B1). This antiserum was highly specific and showed no cross reactions with other anterior pituitary hormones. A pure pST preparation (USDA-pGH-I1) was used for iodination by the iodogen method (Salacinski et al., 1981). After separation of unlabeled from labeled pST by an anion exchange resin (AG2 - X8; BioRad Laboratories, Richmond, USA) further purification was achieved by column chromatography (Sephadex G-75). Standard or unknown sample (200 µl) plus 100 µl antiserum were incubated for 24 h at $4^{\circ}C$, than labeled hormone (100 µl; 15000 counts/min) was added and further incubated for two days. Separation of bound and free hormone was performed by the second antibody technique.

The pituitary preparation USDA-pGH-B1 (biological activity 5.4 IU/mg, tibia assay) served as reference preparation. The assay sensitivity was 0.25 ng/ml plasma. The intra-assay coefficient of variation estimated from control samples running at the beginning, middle and end of each assay was below 8 %.The inter-assay coefficient of variation estimated from four control samples of low, medium and high pST concentrations ranged from 7-14 %.

Evaluation of pST in tissue samples

Extraction procedure of tissue was carried out between 0 - 4°C. The extraction was modified as originally described for preparation of porcine growth hormone by Schleyer et al. (1974). Five gram muscle tissue was homogenized with an Ultra Turrax homogenizer (Janke and Kunkel, Germany) with five times tissue weight of precooled 2 % sodium chloride solution of pH 8.5, stirred for 1 h. After that time the homogenate was centrifuged at 17000 RPM. The pellet was homogenized again in 20 ml of 2% NaCl solution, stirred for another hour and centrifuged as described above. The supernatants were combined, an aliquot was assayed directly.

Determination of IGF-1 in blood plasma

IGF-1 was determined radioimmunologically after acid-ethanol extraction of plasma. Recombinant IGF-1 (Amersham, England) was used for iodination according to the lactoperoxidase method. As reference preparation synthetic IGF-1 (kindly supplied by C.H.Li, San Francisco, USA) was used for calibration of a plasma pool standard. The intra-assay variation was below 10 % and the inter-assay variation was 12-16 %.

Results and Discussion

The results of trial 1 for concentrations of pST and IGF-1 in blood 4.5 days after the last injection are summarized in Table 1. While there was no clear difference between barrows and gilts and of different final weights an overall mean for each breed was calculated. There is no difference between the control and treatment group for pST in F_1 (Great Yorkshire x Dutch Landrace). IGF-1 tended to be a little higher. Concentrations of pST are lower after treatment in Duroc and Pietrain. For IGF-1 there is no difference visible.

The results suggest that treatment for about 6 weeks (100 kg) or 13 weeks (140 kg) may lower endogenous secretion of pST immediately at the end of treatment. Nevertheless the injected rpST was cleaned from the circulation 4.5 days after the last injection and IGF-1 levels are not different from controls.

Table 1. Blood concentrations of pST and IGF-1 (ng/ml) at slaughter after treatment with rpST or placebo 4.5 days after the last injection (trial 1; mean ± S.D.).

| Breed | Control | | Treatment | |
	pST	IGF-1	pST	IGF-1
F1	1.8±0.7	n=14 299±130	1.5±0.8	n=16 369±149
Duroc	3.7±3.1	n=17 417±136	1.6±0.8	n=15 432±217
Pietrain	2.3±0.9	n=16 264±138	1.6±0.5	n=16 276±127

As shown in Table 2 (trial 2) treatment with rpST caused tremendous increase in blood concentrations within 1 h after the injection. 26-27 h later levels decreased in the treatment group to control values. The mean was higher only in the Duroc breed due to one animal (85 ng/ml) which also had the highest value after the injection. IGF-1 values tended to be a little higher 1 h after the injection if compared with controls and increased significantly 26 - 27 h after the injection. The data obtained indicate that intramuscular injected rpST is cleared from the circulation within 26 h. Stimulated IGF-1 concentrations decreased to control levels at least after 4.5 days. In contrast daily treatment of veal calfs for 9 weeks with recombinant bovine somatotropin delayed the clearance rate of bST significantly (Kirchgessner et al., 1987).

Table 2. Blood concentrations of pST and IGF-1 (ng/ml) after treatment with somatotropin or placebo within 1 h and 26 - 27 h after the last injection.

Breed	treatment	n	within 1 h		26 - 27 h after injection	
			pST	IGF-1	pST	IGF-1
F1	control	6	2.0±1.6	437±110	2.1±0.5	231±37
	rpST	5	240±113	749±346	3.1±3.2	793±89
Duroc	control	6	2.0±1.7	391±73	2.9±0.5	398±58
	rpST	6	321±84	531±172	14.9±32	1310±217
					1.7±0.3(n=5)	
Pietrain	control	6	2.0±0.6	193±81	2.7±0.9	183±45
	rpST	6	266±46	373±158	2.1±0.5	720±296

Muscle tissue concentrations for pST are below 5 ng/g wet tissue and so within the range of levels measured in the peripheral circulation.

Conclusions

The studies have indicated that after treatment with rpST twice weekly (14 mg/injection) there are no residues measurable 26 - 27 h after the last injection in peripheral circulation for pST and at least 4.5 days later for IGF-1. Concerning rpST there seems to be no risk for the consumer especially because pST is a protein and is not biologically active either orally nor parenterally in man.

Acknowledgements

References

Kirchgessner, M., F.X. Roth, D. Schams and H. Karg, 1987. Influence of exogenous growth hormone (GH) on performance and plasma GH concentrations of female veal calves.J. Anim.Physiol.Anim. Nutr. 58: 50-59.

Salacinski, P.R.P., C. McLean, J.E.C. Sykes, V.V. Clement-Jones and P.J. Lowry, 1981. Iodination of proteins, glycoproteins and peptides using a solid-phase oxidizing agent, 1,3,4,6-tetrachloro-3, 6-diphenyl glycoluril (Iodogen). Analyt. Biochem. 117: 136-146.

Schleyer, M., K.-H. Voigt and H. Etzrod, 1974. Preparation of porcine growth hormone. Hoppe Seyler s Z. Physiol. Chem. 355:1291-1298.

NUTRITIONAL AND SENSORY CHARACTERISTICS OF PORK FROM PIGS ADMINISTERED SOMATOTROPIN

K.J. Prusa

Department of Food and Nutrition, Iowa State University, Ames, Iowa 50011 U.S.A.

Summary

Although measurable differences in nutritional composition and sensory quality between somatotropin-treated and untreated pork have been reported, no major concerns are evident. Several reports have indicated that intramuscular fat content is lowered in response to porcine somatotropin (pST) administration. Intramuscular fat contents of less than 1% due to pST treatment have been reported. Protein and moisture contents of muscle tissue increased slightly in studies that reported a decrease in intramuscular fat content. No differences were noted in the fatty acid profiles or cholesterol contents of longissimus muscle from animals treated and then removed from pST zero days before slaughter. However, polyunsaturated fatty acid contents of raw pork and cholesterol contents of cooked pork were reported to increase slightly in 7-day withdrawal animals. Thiamin content of the tissue tended to decrease slightly, in response to pST treatment. Several studies have reported that pST administration has no detrimental effects on the sensory quality of the longissimus muscle. In contrast, minimal decreases in muscle tenderness, juiciness and flavor intensity in association with a high level of pST treatment have been reported.

Keywords: somatotropin, nutritional composition, sensory, quality.

Introduction

The use of biotechnology for the production of porcine somatotropin (pST) should have a dramatic impact on the future of the pork industry. Consumer demand for more uniform, lower-calorie pork should help secure a positive future for pST. However, it is imperative that all information, including meat product quality, be evaluated. Although pST administration opens a new avenue for the production of leaner pigs, the new technology may not reach full potential if consumer appraisal of the final meat product is negative. Research that focuses on nutritional composition and sensory quality of pork products from pST-treated pigs is essential for a full evaluation of somatotropin use.

Somatotropin injection into growing and finishing pigs has the potential to alter every known aspect concerning pork quality. When the metabolism of a muscle has the potential to change with pST injection, the composition and eating quality of the resultant meat product also has the potential to change. Therefore, this review will evaluate studies concerned with the nutritional composition and sensory quality of pork from pigs administered somatotropin.

Lipid characteristics

Intramuscular fat content

Dietary fat intake has received considerable attention in recent years. Numerous groups (American Heart Association, 1985; United States Department of Agriculture, 1985; National Research Council, 1988a) have recommended limited intake of dietary fat, including consumption of lean, well-trimmed meat cuts. It is without a doubt that the amount of trimmable fat on a pork carcass can be reduced significantly through the administration of pST (Etherton, 1988). However, the obvious question arises if the significant reduction of trimmable carcass fat translates into a reduction of intramuscular fat.

Several studies have indicated that intramuscular fat content is lowered or not affected in response to pST administration. Intramuscular fat contents of raw tissue (Beermann et al., 1988; Prusa, 1988b) and cooked tissue (Prusa, 1988b) of less than 1% have been found as a result of pST administration. The studies listed (Table 1) are a result of a variety of pST dose levels, injection periods and types of pST (natural or recombinant).

Table 1. Effects of pST on the intramuscular fat content of pork longissimus muscle.

Reference	Effect of pST
Beermann et al., 1988	Decreased
Ender, 1988 (Private Communication)	Decreased
Novakofski, 1987	Decreased
Prusa et al., 1988a	Decreased
Prusa, 1988b (Private Communication)	Decreased
Ellendorff, 1988 (Private Communication)	Decreased
Kanis et al., 1988	No effect
Prusa et al., 1988c	No effect
Chung et al., 1985	Increased

It is interesting to note that one study (Chung et al., 1985) found an increase in intramuscular fat content in response to pST treatment. Chung et al. (1985) indicated that an increased delivery of free fatty acids to the cell for metabolism may be responsible for the increase in lipid content. Animals removed from pST injections seven days before slaughter may have adequate time to metabolize the influx of free fatty acids and therefore have reduced intramuscular crude fat contents (Prusa et al., 1988a,d). But, if the animal is slaughtered with a zero-day withdrawal period (Chung et al., 1985; Prusa et al., 1988c), free fatty acids may be trapped in the cell and contribute to the intramuscular fat content. Therefore, the effects of pST on the intramuscular fat content may be related to the pST-withdrawal period.

Fatty acid profiles and cholesterol content

Generally, fatty acid profiles of the intramuscular fat extracted from raw and cooked longissimus muscle have been reported to not be affected greatly by pST treatment. No differences were noted in fatty acid profiles of intramuscular fat extracted from raw or cooked muscle from animals removed from pST treatment zero days before slaughter (Table 2). In a similar study, polyunsaturated fatty acid content of the intramuscular fat increased by 1.5% in response to 4 mg of pST per day (Prusa et al., 1988a).

Table 2. Effects of pST on the fatty acid profiles (%) of intramuscular fat from raw and broiled longissimus muscle.[1]

	Somatotropin level (mg/day)		
	0	4	8
Raw			
saturated	38.3[a]	37.1[a]	39.8[a]
monounsaturated	57.5[a]	57.9[a]	55.5[a]
Polyunsaturated	4.1[a]	5.0[a]	4.7[a]
Broiled (71°C)			
saturated	38.9[a]	40.6[a]	38.3[a]
monounsaturated	58.5[a]	57.0[a]	58.3[a]
polyunsaturated	2.5[a]	2.4[a]	3.3[a]

[1] From Prusa et al., 1988c.
[a] Means in a row are not significantly different (P < 0.05).

Fatty acid percentages reported by Prusa et al., (1988a,c) are well in the normal range reported for fresh pork (Skelley et al., 1975; Malmfors et al., 1978; Marchello et al., 1983).

The cholesterol content of raw and cooked longissimus muscle has been reported to not be affected by pST administration (Table 3). In a related study evaluating a 7-day withdrawal period, cholesterol contents of cooked muscles from animals treated with 8 mg pST daily were found to be slightly greater than cooked muscles from controls or animals that received 4 mg pST daily (Prusa et al., 1988a). The increase in cholesterol content (wet-weight basis) was relatively small with the muscles from the 8 mg treatment group containing approximately 5 mg more cholesterol than control muscles. The slight increase would be of little practical consequence for individuals concerned with cholesterol intake.

Table 3. Effects of pST on the cholesterol contents (mg/100g) of cooked longissimus muscle.[1]

	Somatotropin level (mg/day)		
	0	4	8
Cholesterol (wet-weight, raw)	52.1[a]	54.0[a]	54.4[a]
Cholesterol (wet-weight, cooked)	63.5[a]	65.2[a]	69.8[a]

[1] From Prusa et al., 1988a.
[a] Means in a row are not significantly different (P < 0.05).

Protein and moisture contents

Protein and moisture contents of the longissimus muscle have been found to increase slightly in studies reporting a decrease in longissimus intramuscular fat content due to pST administration (Prusa et al., 1988a; Beermann et al., 1988). In studies reporting no effect of pST on intramuscular fat contents, protein and moisture contents of pST-treated and untreated muscle samples were similar.

Thiamin and iron contents

The thiamin contents of longissimus muscles from pST-treated animals have been reported to be less than the longissimus muscles from control animals (Table 4).

Table 4. Thiamin contents (mg/100g) of raw and broiled longissimus muscle from animals treated with pST.[1]

	Somatotropin level (mg/day)		
	0	4	8
Raw			
Thiamin (wet-weight)	0.60[a]	0.39[b]	0.43[b]
Thiamin (moisture, fat-free)	2.49[a]	1.53[b]	1.67[b]
Broiled (71°C)			
Thiamin (wet-weight)	0.37[a]	0.28[b]	0.27[b]
Thiamin (moisture, fat-free)	1.19[a]	0.88[b]	0.83[b]

[1] From Prusa et al., 1988a.
[ab] Means not followed by a common letter are significantly different ($P < 0.05$)

Reduced thiamin contents of the tissue may be related to an altered animal metabolism. If greater amounts of fatty acids are present in the cell for metabolism (Chung et al., 1985), carbohydrate metabolism may be altered. Because thiamin is an essential component of carbohydrate metabolism (National Research Council, 1988b), the animal's need for thiamin may be decreased. Total iron contents of the longissimus muscle has been reported to not be affected by pST treatment (Prusa et al.,, 1988a,c).

Sensory quality

The use of intensity scales by trained sensory judges is the most beneficial for the measurement of the quality of pork from pST-treated animals. Studies that use a small number of judges with "liking" scales do not offer useful information pertaining to possible changes in tenderness, juiciness and flavor. Measurement of how much a specific attribute is "liked" will not relate to an increase or decrease in the intensity of that attribute.

Tenderness - human perception

Several studies have used sensory panels to evaluate the tenderness of the longissimus muscle from animals treated with pST (Table 5).

Table 5. Perception of tenderness of the longissimus muscle from pigs treated with pST.

Reference	Effect of pST
Prusa et al., 1988e	Decreased at 8 mg/day No effect at 4 mg/day
Beermann et al., 1988	Decreased at 60 ug/kg/day No effect at 30 or 90 ug/kg/day
Kanis et al., 1988	No effect
Novakofski, 1987	No effect
Evock et al., 1988	Degree of "liking" decreased
Althen, 1988 (Private Comm.)	Degree of "liking" decreased

Prusa et al. (1988e), using intensity scales, found a decrease in tenderness of the longissimus muscle from animals receiving 8 mg of pST daily; however, no differences were noted between control samples and muscles from animals receiving 4 mg pST daily. A slight decrease in tenderness between control muscles and muscles from animals receiving 60 ug pST/kg/day was noted by Beermann et al. (1988). In that study, no tenderness differences were noted between control samples and muscles from animals treated with 30 or 90 ug pST/kg/day. Kanis et al. (1988) and Novakofski et al. (1988) found no difference in tenderness of longissimus muscles due to pST

administration. Both Evock et al. (1988) and Althen (1988) indicated degree of "liking" scores for tenderness of the longissimus muscle decreased due to pST treatment. No reasons were reported why "liking" scores decreased.

Tenderness - Warner-Bratzler shear

The Warner-Bratzler shear is the most often used instrumental measure for the evaluation of meat texture (tenderness). Generally, no major differences have been reported for Warner-Bratzler shear values for muscles from pST-treated and untreated animals (Prusa et al., 1988e; Kanis et al., 1988; Beermann et al., 1988; Althen, 1988). In one study, Warner-Bratzler shear values of the longissimus muscle from animals receiving 9 mg pST daily increased 0.32 kg when compared with muscles from control animals (Novakofski, 1987); however, that increase was not considered significant.

Juiciness

Perceived juiciness of pork is an area of interest because of the potential of pST to lower the intramuscular fat content. However, few measurable differences in sensory juiciness due to pST treatment have been reported (Table 6).

Table 6. Effects of pST on the juiciness of pork muscles.

Reference	Effect of pST
Prusa et al., 1988e	Longissimus - no effect Semimembranosus - decreased at 8 mg/day
Beermann et al., 1988	Longissimus - decreased at 60 ug/kg/day No effect at 30 or 90 ug/kg/day
Novakofski, 1987	Longissimus - no effect
Evock et al., 1988	Longissimus - no effect "degree of liking"
Althen, 1988 (Private Communication)	Longissimus - no effect "degree of liking"

Roasted semimembranosus from animals treated with 8 mg pST/day were less juicy than samples from control animals (Prusa et al., 1988e). The lower juiciness scores could not be related to intramuscular fat content because fat contents of control and pST-treated roasts (in the cooked state) were similar. Following the same trend as for tenderness, (Beermann et al., 1988) reported decreased juiciness of samples from animals treated with 60 ug/kg/day; however, no differences were noted among samples from the control, 30 or 90 ug/kg/day treatments. Several studies detected no differences in juiciness or juiciness "degree of liking" due to pST administration.

Flavor, aroma and off-flavor

No major differences in flavor or aroma of pork have been reported in response to pST treatment (Novakofski, 1987; Beermann et al., 1988; Kanis et al., 1988). In contrast, Prusa et al., (1988e) indicated roasted semimembranosus muscles were judged lower in pork flavor than control roasts. Reasons why pork flavor was reduced is still under investigation (Prusa, 1988b). Generally, no off-flavors have been reported for pork from animals treated with pST.

Color

Few studies could be found that evaluated the color of muscles from pST-treated and untreated pork. Kanis et al. (1988) found longissimus muscles from pST-treated animals were lighter in color than muscles from control animals. In a different study, Prusa et al. (1988e) found no differences in

the color of broiled longissimus or roasted semimembranosus when pST-treated and control samples were compared.

Conclusion

Measurable differences in nutritional composition between pST-treated and untreated pork have been reported. The most notable effect is the potential to produce pork with intramuscular fat contents of less than 1%. A serving of cooked pork containing less than 1% fat would supply a minimal number of calories from the fat. With the potential of pST to lower dramatically intramuscular fat content, pork from pST-treated animals should rival other low fat meat sources.

Although slight alterations in sensory quality due to high levels of pST have been reported, no major detrimental effects were noted. The interaction between elevated dietary protein levels and pST treatment on the sensory quality of pork is in need of investigation. The next logical step after completing sensory analysis with trained judges is to conduct consumer acceptance tests utilizing large numbers of subjects. Preference consumer testing will afford insight into consumer appraisal of pork from pST-treated animals.

References

Althen, T.G., 1988. Private Communication. Mississippi State University, Mississippi State, MS. USA.

American Heart Association, 1985. An eating plan for healthy Americans. American Heart Association, Dallas, TX. USA .

Beermann, D.H., G. Armbruster, R.D. Boyd, K. Roneker and K.D. Fagin, 1988. Comparison of the effects of two recombinant forms of porcine somatotropin (pST) on pork composition and palatability. J. Anim. Sci. 66 (Suppl. 1):281.

Chung, C.S., T.D. Etherton and J.P. Wiggins, 1985. Stimulation of swine growth by porcine somatotropin. J. Anim. Sci. 60:118-130.

Ellendorff, F., 1988. Private Communication. Institut fur Tierzucht und Tierverhalten, FRG.

Ender, K., 1988. Private Communication. Research Centre Dummerstorf, University of Rostock, GDR.

Etherton, T.D., 1988. Anabolic effects of porcine somatotropin on pig growth. IN: Designing foods: Animal product options in the marketplace. National Academic Press, Washington, D.C. p.194-199.

Evock, C.M., T.D. Etherton, C.S. Chung and R.E. Ivy, 1988. Pituitary porcine growth hormone (pGH) and a recombinant pGH analog stimulate pig growth performance in a similar manner. J. Anim. Sci. 66:1928- 1941.

Kanis, E., W. van der Hel, W.J.A. Kouwenberg, J. Huisman, R.D. Politiek, M.W.A. Verstegen, P. van der Wal and E.J. van Weerden, 1988. Effects of recombinant porcine somatotropin (rpST) on meat quality of pigs. J. Anim. Sci. 66 (Suppl. 1) :280.

Malmfors, B., K. Lundstrom and I. Hansson, 1978. Fatty acid composition of porcine back fat and muscle lipids as affected by sex, weight and anatomical location. Swed. J. Agric. Res. 8:25-38.

Marchello, M.J., N.K. Cook, W.D. Slanger, V.K. Johnson, A.G. Fischer and W.E. Dinusson, 1983. Fatty acid composition of lean and fat tissue of swine fed various dietary levels of sunflower seed. J. Food Sci. 48:1331-1334.

National Research Council, 1988a. Designing foods: Animal product options in the marketplace. National Academy Press, Washington, D.C.

National Research Council, 1988b. Nutrient requirements of swine. 9th ed. National Academy Press, Washington, D.C.

Novakofski, J.E., 1987. Repartitioned pork: Sensory quality and consumer acceptance. Proc. of the University of Illinois, Pork Industry Conference. Champaign, IL. p 84-92.

Prusa, K.J., J.A. Love and L.F. Miller, 1988a. Composition of muscles from pigs treated with porcine somatotropin: 7-day withdrawal. J. Food Qual. . In review.

Prusa, K.J., 1988b. Private communication. Iowa State University, Ames, IA, USA.

Prusa, K.J., J.A. Love and L.F. Miller, 1988c. Composition of muscles from pigs treated with porcine somatotropin: O-day withdrawal. J. Food Qual. In review.

Prusa, K.J., J.A. Love and L.F. Miller, 1988d. Water-holding capacity, pH and cooking losses of muscles from pigs treated with porcine somatotropin. J. Food Qual. In review.

Prusa, K.J., J.A. Love and L.F. Miller, 1988e. Sensory and physical attributes of muscles from pigs treated with porcine somatotropin. J. Food Qual. In review.

Skelley, G.C., R.F. Borgman, D.L. Handlin, J.C. Acton, J.C. McConnell, F.B. Wardlaw and E.J. Evans, 1975. Influence of diet on quality, fatty acids and acceptability of pork. J. Anim. Sci. 41:1298-1304.

U. S. Department of Agriculture and U. S. Department of Health and Human Services, 1985. Dietary guidelines for Americans - 2nd ed. Hyattsville, MD, USA.

EFFECT OF RECOMBINANT PORCINE SOMATOTROPIN ON CARCASS AND MEAT QUALITY OF BELGIAN AND DUTCH PIGS

D. Demeyer[1,2], R. Verbeke[1], G. Van de Voorde[1], J. Fabry[3], E. Deroover[4] and R.H. Dalrymple[5]

[1] *University of Ghent, Ghent, Belgium;*

[2] *University of Brussels, Brussels, Belgium;*

[3] *Agricultural Research Centre, Gembloux, Belgium;*

[4] *Cyanamid Benelux NV, Mont-Saint-Guibert, Belgium;*

[5] *American Cyanamid company, Princeton, New Jersey, U.S.A.;*

Summary

Results, published in detail elsewhere, illustrating effects of recombinant porcine somatotropin (rPST) on carcass and meat quality of Belgian and Dutch pigs are summarized. Belgian finishing pigs (60 to ca. 100 kg) were treated with four levels of rPST (0, 1.5, 3 and 6 mg per day) by daily injection. They were fed a high protein, cereal based diet **ad libitum** (Expt. 1). Dutch pigs, fed a similar diet over a similar finishing period, were treated with 0 and 14 mg rPST, injected twice weekly (Expt. 2). In both experiments, data on carcass and organ yield, carcass quality and yield of commercial cuts, meat sensory quality, proximate composition and muscle protein composition (Expt. 2 only) were collected.

Carcass yields were slightly decreased, associated with increased yields of heart, liver and kidneys. Carcass quality was considerably improved, as indicated by decreases in various carcass fat measurements and improved carcass grades. Carcass meat joint yields were improved, with concomitant reductions in fat joints and trimmings.

No significant differences for rates of muscle pH decline were apparent, but there was some indication of higher temperatures shortly post mortem. Ultimate pH values were slightly but significantly increased. Various measurements of texture, colour and water holding capacity of the meat showed a slightly less red colour as the only statistically significant effect. Myofibrillar protein composition and sarcomere length of long.dorsi muscle was not affected, but crude protein content was slightly increased.

The studies demonstrated that various levels of rPST can increase meat yield and lower carcass fat, even in breeds selected for superior carcass composition, without further detrimental effects on meat sensory quality.

Keywords: somatotropin, swine, carcass quality, meat quality, organ weights.

Introduction

Injection of both pituitary derived porcine somatotropin (nPST) and its analogue produced by recombinant DNA technology (rPST) considerably improves performance and carcass composition of finishing pigs between 50 and 105 kg (references in Fabry et al., 1988). Some evidence suggests a somewhat lower activity of rPST (Ivy et al., 1985). Most reports deal however with pigs, feed and management practices in the U.S.A. Pigs in Europe are leaner than in the U.S.A., because of intense selection for meat production, whereas cereal grains rather than corn are used in feed formulation.

Fabry et al. (1988) and Kouwenberg (1988) conducted experiments to evaluate rPST efficacy in the finishing of lean pig breeds. Their specific attention went to the evaluation of effects on meat yield and meat quality. Indeed, it could be expected that effects on meat yield would be less outspoken with leaner animals, whereas such animals are known to be very susceptible to meat quality defects associated with rapid rates of post mortem pH fall (Eeckhout et al., 1966).

This paper summarizes results on carcass and meat quality, described in detail elsewhere,of the Belgian (Fabry et al., 1988) (Expt. 1) and Dutch (Kanis et al., 1988), (Kouwenberg, 1988) (Expt. 2) recent experiments.

Materials and methods

Details are described in Fabry et al. (1988) and Kouwenberg (1988). In both cases a total of 96 (Expt. 1) or 36 (Expt. 2) pigs was finished from ca. 60 to ca. 100 kg on diets containing 20% (Expt. 1) or 18.2% (Expt. 2) crude protein and 8.74 (Expt. 1) or 9.49 MJ net energy per kg Barley and wheat (Expt. 1) and tapioca (Expt. 2) were main energy sources. Treatments in Expt. 1 consisted of four (0 ; 1.5 ; 3 ; 6 mg/d) and in Expt. 2 of two (0 ; 14) dose levels of rPST injected behind the ears daily (Expt. 1) or twice weekly (Expt. 2) respectively. One breed (Belgian Landrace) was used in Expt. 1, whereas Expt. 2 involved three breeds (Pietrain, Duroc and a crossbred between Dutch Yorkshire and Dutch Landrace). Slaughtering and commercial jointing was carried out in both experiments following methods customary for the respective countries. Organ weights were recorded and carcasses evaluated through measurements of fat depths at various sites. Samples of Longissimus Dorsi muscle (36 animals only) were obtained in both experiments and used for determination of colour, texture and water holding capacity by various methods. Additional information on taste panel evaluation (Expt. 2) and myofibrillar protein composition (SDS-PAGE or sodium dodecyl sulphate polyacrylamide gel electrophoresis) (Expt. 1) of the muscle was obtained. Animals were grouped for treatments, and results analysed statistically by analysis of variance (Expt. 1) and using a linear model of additive effects (Expt. 2). In this paper, mean results per treatment only are reported, with indication of statistically significant effects.

Results and discussion

Carcass and organ yield

Table 1 shows that rPST slightly decreases carcass yield with slaughtering at 100 kg carcass weight (dressing %), although statistical significance is only reached in Expt. 2. A decrease, confirming earlier work (Evock et al., 1988), should obviously be observed however, because of associated significant increases in the relative proportions of mainly liver, kidneys and heart.

Differences in carcass yields between experiments are due to differences in breeds, pre-slaughter fasting periods and hot vs. cold carcass weights. In earlier work (cited in Kouwenberg, 1988) absolute, but not relative organ weight increases were reported. Such increase is however not surprising, in view of the increased overall metabolic activity reflected in protein turnover, kidney N retention and blood metabolite concentrations (Kouwenberg, 1988).

The latter author observed that expression of organ weights as proportion of fat free carcass weight did not abolish the enlarging effect of rPST and the same is true for the Belgian data: live weight % of liver, kidneys and heart are increased by 16 ; 33 and 18 % respectively at the highest rPST dose (Table 1), whereas calculated meat yield is increased by 9 % only (Table 2).

Table 1. Effect of Recombinant Porcine Somatotropin (rPST) on pig carcass and organ yields.[a]

rPST (mg/d)	Expt. 1 (22-24)[b]				Expt. 2 (24)	
	0	1.5	3	6	0	4
Carcass						
weight (kg)	78.5	79.1	78.3	79.5	76.5	75.7*
Dressing %[c]	83.0	83.3	82.6	82.2	78.7	77.8*
Organs (% of live weight)						
Intestine						
total	7.58	7.08*	7.23	7.65		
empty	5.55	5.28*	5.33*	5.68		
Stomach	.98	.78*	.84*	1.03*		
Bladder	.16	.18	.19	.14*		
Tongue	.40	.46*	.41	.49*		
Liver	1.65	1.68	1.83*	1.91*	1.68	1.74*
Kidneys	.36	.40	.46*	.48*	.34	.39*
Heart	.33	.35	.37*	.39*	.35	.36
Lungs	1.24	1.20	1.26	1.21*		
Spleen	.17	.18	.19	.20*	.18	.17
Pancreas	.19	.21*	.19	.19*		
Mesentery fat	.64	.58*	.63	.53*		

[a] mean values
[b] ( ) = no. of animals per cell
[c] measured on hot carcasses in Expt. 1
* significant difference from control, max. $p = .05$

Carcass quality

Table 2. Effect of Recombinant Porcine Somatotropin (rPST): measurements on hot carcasses (before cooling)[1].

rPST (mg/d)	Expt. 1 (22-24)				Expt. 2 (24)	
	0	1.5	3	6	0	4
Back fat depth[a] (mm Avge SKR)	24.4	22.7*	21.9*	17.6*	20.2	18.2
Length (cm)	79.9	78.3	79.9	80.3		
Meat %[b]	59.5	61.9*	61.5*	64.8*	51.2	53.7*
Classification[c]	7.0	8.1	7.5	8.4	2.1	2.0
pH						
.5 hrs gluteus[d]	5.9	5.7	5.8	5.8	6.0	6.0
long.D.[e]	5.9	5.9	5.9	5.8		
4 hrs gluteus	5.6	5.6	5.7	5.7		
long.D.[e]	5.5	5.5	5.5	5.6		
Temp.(°C)						
.5 hrs gluteus	40.1	40.6	40.3	40.8*		
long.D.[e]	40.7	41.1	40.8	41.3		
4 hrs gluteus	25.7	25.5	24.4	23.7		
long.D.[e]	24.2	24.7	24.5	23.7		

[1] Mean values only (cfr. Table 1)
[a] calculated as described by Casteels & Verbeke (1978) in expt. 1 and listed as "spekdikte" in expt. 2
[b] Meat % was calculated from average fat depth, cold halve carcass weight and carcass length in expt. 1 (Casteels & Verbeke, 1978) and from muscle and fat depth measurements in expt. 2 (Kouwenberg, 1988).
[c] expt. 1 : 10=EE,9=E,8=AA,7=A1,6=A2,5=A3,4=B1,3=B2,2=B3 and 1=IV (value increases with number) expt. 2 : 4=C,3=B,2=A and 1=AA (value decreases with number)
[d] measurement in "ham" for expt. 2, .75 hrs. post mortem
[e] number of observations 20,16,8 and 14 respectively at increasing rPST levels in expt. 1
* significant difference from control, max. $p = .05$

DEMEYER, VERBEKE, VAN DE VOORDE, FABRY,
DEROOVER AND DALRYMPLE

Carcass fat measurements taken at numerous locations on the hot (Table 2) as well as the cold (Table 3) carcass, represent the major reference sites used over the world for commercial as well as scientific evaluation of carcass quality.

The observed reductions in fat depth are clearly dose dependant in Expt. 1 (discussed in detail by Fabry et al., 1988) and of similar magnitude at all sites measured: 32 to 47 % reduction. Such reductions are reflected in meat yields calculated from established regressions involving fat depth:meat yield increases between 9 % (Expt. 1) and 5 % (Expt. 2) can be calculated (Table 2). They also explain the significant improvement in carcass grading in Expt. 1 as well as in Expt. 2 (Table 2).

Table 3. Effect of Recombinant Porcine Somatotropin (rPST): measurements on cooled carcasses and colour of cuts (after at least 24 hrs. of cooling)[1]

rPST (mg/d)	Expt. 1 (22-24)				Expt. 2 (24)	
	0	1.5	3	6	0	4
carcasses:						
fat depth (mm)[a]						
USA last rib	19	18.*	16.*	13.*		
last lumb.	17	13.*	12.*	8.*		
10th rib	21	19.*	19.*	14.*		
UK long.D. P_1	15	12.*	10.*	8.*		
P_2	13	10.*	10.*	7.*		
P_3	13	10.*	10.*	7.*		
EEC gluteus P_1	22	19.*	19.*	15.*		
P_2	16	13.*	12.*	8.*		
P_3	25	22.*	20.*	17.*		
pH						
ham 18 hrs					5.8	5.8
gluteus 24 hrs	5.7	5.7	5.8	5.8*		
long.D. 72 hrs	5.6	5.7	5.7	5.8*		
Meat cuts						
surface (cm^2)						
long.D.10th rib	37.5	43.5*	41.5*	43.0*		
12th rib[b]	43.6	48.7*	50.0*	50.5*		
colour[c]					2.2	2.5
long.D.[d]						
L	52.9	54.3	51.1	51.4	47.5	48.0*
a	7.5	7.5	7.4	7.9	5.9	5.1*
b	9.4	9.6	8.8	9.0	8.6	8.5

[1] Mean values only (cfr. Table 1)
[a] USA = National pork producers council,1985
   UK = Meat and Livestock Commission,1980
   EEC = described in De Boer et al. (1979)
[b] after freezing at -20C and thawing
[c] Subjective measurement using Japanese "Porcine colour scale" in expt. 2.
[d] Hunter colour values (L=lightness,a=redness,b=yellowness). 7th rib in expt. 1, 20 cm cranial from 1st lumbar in expt. 2
* significant difference from control, max. p = 0.05

Such increases confirm results obtained for long.dorsi surface area (Table 3) and from carcass jointing (Table 4) and illustrate effects of PST on adipose as well as on muscle tissue. Both such effects appear to be direct as a reduction in adipose tissue was observed in the absence of a reduced feed intake (lowest rPST level in Expt. 1, discussion in Fabry et al., 1988). Accretion of muscle tissue (meat) was not found to be as dose dependant as depression of fat tissue in contrast to other work (discussed by Fabry et al., 1988). This may be related to the inaccuracy of the prediction regressions used, depending on a few measurements only.

194

Slight differences in muscle pH values measured the first hour after slaughtering at the highest dose level in Expt. 1 do not reach statistical significance. A slight but significant increase in the associated temperature measurements however suggests a somewhat accelerated rate of post mortal glycolysis at the highest dose levels, at least in the gluteus muscle (Table 2). Such effects however are minor, compared to the rapid rates of pH fall often observed in pig breeds, selected for meat production where pH drops to 5.5 within the first hour after slaughtering (Eeckhout et al., 1966) (Bekaert et al., 1987). A tendency to acceleration of post mortal glycolysis is corroborated however by the finding that rPST produced a less red meat colour in Expt. 2 (Table 3). No effect was observed however in a slice more cranial from the first lumbar, nor in Expt. 1 but here negative effects of accelerated glycolysis on colour may be offset by the slightly but significantly higher final pH values in the muscle, known to be associated with darkening of meat colour (see e.g. Demeyer, 1974). Higher final pH values indicate more pre-slaughter depletion of muscle glycogen, in line with accelerated overall metabolism. It should be stressed however that the small differences discussed here are not liable to further increase frequency of meat quality defects associated with breeds selected for maximal meat production : P(ale),S(oft) and E(xudative) as well as D(ark),F(irm) and D(ry) meat (see e.g. Demeyer, 1974). This is illustrated e.g. by the absence of any effect of rPST on meat water holding capacity (Table 5).

Yield of commercial cuts

Table 4 summarizes the data collected during carcass jointing, separating one side of each carcass into trimmed lean and fat joints, following different but similar jointing methods in Belgium and Holland. Methodological differences are reflected in the % distribution of cuts over the carcasses, but it is clear that in both experiments a significant increase in yield of meat joints was obtained, associated with a lowered yield of fat joints. It is striking that in Expt. 2 an increased

Table 4. Effect of Recombinant Porcine Somatotropin (rPST) on % distribution of carcass joints(% of carcass weight)[1].

rPST (mg/d)	Expt. 1 (22-24)[a]				Expt. 2 (24)[b]	
	0	1.5	3	6	0	4
Lean joints						
shoulder	15.0	15.7*	15.4	16.0*	11.5	12.4*
ham	24.3	24.6	24.9*	25.5*	22.5	23.7*
loin[d]	25.0	26.3*	26.4*	27.4*	17.8	18.5
lean trimmings	1.6	1.7	1.7*	1.8*	2.9	2.9
total lean joints	65.9	68.3*	68.4*	70.9*		
Fat joints						
belly	16.2	15.5	15.6*	14.7*	13.5	13.1*
back fat[c]	5.9	4.8*	4.5*	3.4*	6.7	5.5*
flare fat[d]	1.3	1.1*	1.0*	0.8*	13.8	12.4*
total fat joints	23.4	21.4*	21.1*	18.9*		
Other joints						
Head	5.4	5.3	5.3	5.4	4.9	5.3*
shanks	1.9	1.8	2.0	2.0	2.6	2.7*
throat[e]	3.4	3.2	3.2	3.0	3.8	3.5*

[1] mean values only are shown (cfr. Table 1).
[a] jointing following the "Belgian national jointing method" (Verbeke and Casteels, 1985). Percentages were adjusted to a sum of 100%.
[b] jointing following the IVO standard method (Kouwenberg, 1988). Joint weights were converted to % of calculated weight of carcass halves.
[c] "rugspek" in expt. 2
[d] "vet, reuzel en krabbetje" in expt. 2
[e] "kinnebak" in expt. 2
* significant difference from control, max.p = .05

proportion of some cuts high in connective tissue was observed. This is in line with the contention that rPST treatment would result in a body conformation equal to that of a younger, non treated animal, showing more bone and organs as well as less adipose tissue (Kouwenberg, 1988). Use of rPST would thus allow to reach higher slaughter weights,without loss of conformation (Kouwenberg,1988).

Sensory meat quality

Table 5 summarizes results of objective measurements of meat quality. Tenderness was evaluated using various texture measurements. Water holding capacity is reflected in various measurements of drip loss, after thawing,cooking and grinding followed by centrifuging. This first report on the effect of rPST on water holding capacity of pork meat, indicates that no statistically significant effect could be observed.

Table 5. Effects of Recombinant Porcine Somatotropin (rPST): sensory characteristics and myofibrillar proteins determined after freezing and thawing of Longissimus Dorsi muscle[1].

rPST (mg/d)	Expt. 1 (22-24)				Expt. 2 (18)	
	0	1.5	3	6	0	4
Texture:						
Shear force (N)	49.5	46.3	52.2	49.1	33.2	34.8
Hardness (N)	74.1	80.2	80.0	78.5		
Cohesiveness[a]	.41	.40	.42	.42		
Drip Losses (%):						
during cooking	28.4	28.5	27.8	28.2	28.3	28.9
thawing	5.1	6.2	5.7	6.1	4.4	4.4
centrifuging	22.6	22.5	21.7	21.4		
Sarcomere length (um)	1.88	1.87	1.90	1.93		
Myofibrillar proteins (ug/mg)[b]						
Troponin-T	6.7	7.1	7.5	7.6		
30 kD	4.0	3.9	3.6	3.1		
Tropomyosin	14.7	14.0	13.8	12.2		
27 kD	5.7	6.5	6.9	7.4		
Titin	33.5	33.9	36.0	37.3		
Filamin	2.1	2.3	2.9	2.3		

[1] Mean values only (cfr. Table 1). All determinations were done on samples of long.D. between the 9th and 12th rib.
[a] ratio of work for a 2nd compression to that for a 1st one.
[b] separated by SDS-PAGE (Buts et al., 1986) and expressed as relative amounts of internal standard per mg of myofibrillar crude protein.

All rPST treatments in Expt. 1 however increase drip losses after thawing on the border of significance (S.E. of mean = .16). Such finding is in line with the suggestion of an accelerating effect of rPST on glycolysis, as discussed earlier. It should also be realized however that changes in water holding capacity can be brought about by changes in muscle fat content: higher fat contents resulting in lower drip losses. It is clear that differences in drip loss after thawing between Expts. 1 and 2 may be related to differences in muscle fat content for the breeds used (Table 6). It should finally be stressed that the processing properties of meat are probably best reflected in cooking losses and no effect of rPST on these losses was apparent.

The results of the various texture measurements indicate that rPST did not affect meat tenderness in line with other work as discussed by Fabry et al. (1988).

In general these results indicate that rPST treatments in amounts up to 6 mg/d did not significantly affect sensory meat quality measured objectively. A similar conclusion was reached by Kanis et al. (1988) and by Kouwenberg (1988), using subjective taste panel evaluation. These

authors stated furthermore that any slight effect observed (e.g. on colour) was negligible, compared with other sources of variation as genotype, sex and week of slaughter.

The absence of a significant effect on muscle structure and function is further indicated by measurements of sarcomere length (from laser diffraction) and myofibrillar protein composition (from SDS-PAGE). In both instances values were found reflecting normal (?) rates of contraction and protein fragmentation respectively (Buts et al., 1986). Other growth regulating substances such as beta agonists do affect e.g. myofibrillar protein fragmentation as evidenced from SDS-PAGE analysis (Fiems et al., 1988).

Proximate composition

Proximate composition data collected on longissimus dorsi showed that the major change brought about by rPST was a slight increase in the crude protein content of the muscle reaching statistical significance in Expt. 1 (Table 6) and confirming earlier work by Beermann et al. (1988).

Table 6. Effects of Recombinant Porcine Somatotropin (rPST): proximate composition of Longissimus Dorsi muscle[1].

rPST (mg/d)	Expt. 1 (22-24) 0	1.5	3	6	Expt. 2 (24) 0	4
% Dry Matter	25.9	26.3	26.1	25.9	26.3	26.2
% Crude Protein	24.1	24.7*	24.4*	24.3*	23.1	23.3
% Crude Fat	1.2	1.2	1.2	1.3	2.4	2.2
collagen (% in Dry matter)	1.99	1.97	1.94	2.02		

[1] Mean values only (cfr. Table 1)

The latter authors also reported however that longissimus fat content decreased dramatically in a dose dependant manner from 2.02 % in the controls down to .74 % in the dosed animals (ca. 4-9 mg/d). In contrast no significant change was observed in muscle fat content due to rPST treatment in either experiment. The inherently low muscle fat levels in the Belgian Landrace pigs may provide an explanation for the absence of an effect, but no such reasoning can be applied in the Dutch experiment.

From nutritional point of view it is important to note that no change was produced in meat collagen content, indicating no change in protein quality. One should realize however that collagen content is positively related to fat as well as to connective tissue content (Demeyer et al., 1984).

General Comments

The reported experiments on pork carcass and meat quality as affected by rPST treatment of animals clearly indicate that carcass quality is considerably improved, yielding more lean and less fat. Such shift is not associated with significant changes in sensory meat quality, even when animals selected for maximal meat production are used. The meat of such animals is however known to suffer more frequently from meat quality defects such as PSE and DFD conditions. Treatment with rPST does not significantly change that condition.

It could be worthwhile to try and improve meat yield from animals less prone to yield meat of aberrant quality. It may be so that rPST increases meat yield in such breeds without generating the associated defects in meat quality.

Such attempts may be even more indicated as direct introduction of chimeric growth hormone carrying genes has been achieved in pigs, resulting in reduction of back fat thickness (Wieghart et al., 1988).

Acknowledgements

We appreciate help with discussion and information from ir. B. Buts, Dr. L. Fiems, Dr. E. Kanis, W.J.A. Kouwenberg and Dr. P. van der Wal.

References

Beermann, D.H., G. Armbruster, R.D. Boyd, K. Roneker and K.D. Fagin, 1988. cited by Fabry et al. (1988).

Bekaert H., M. Casteels and F.X. Buysse, 1987. Effects of a beta agonist on performance, carcass and meat quality of growing-finishing pigs of the Belgian Landrace. Proc. E.E.C. Seminar "Beta-agonists and their effects on animal growth and carcass quality" Brussels,May 19th-20th.

De Boer, H., H. Nijeboer, G.S.M. Merkus and A.A.M. Jansen, 1979. cited in Fabry et al. (1988).

Buts, B., E. Claeys and D. Demeyer, 1986. Relation between concentration of troponin-T, 30,000 Dalton, and Titin on SDS-PAGE and tenderness of Bull longissimus dorsi. Proc. 32nd Europ. Meet. Meat Res. Work. Ghent, pp. 175 - 178.

Casteels, M. and R. Verbeke, 1978. Signification de la relation entre l'épaisseur du lard dorsal et la classification chez le porc de boucherie. Rev.Agric. 31: 113-122.

Demeyer, D.I., 1974. Biochemische aspecten van de Vleeskwaliteit. Verh.Fak.Landbouwwet. R.U.G. pp.1 - 23.

Demeyer, D.I., B. Buts, M. Casteels and R. Verbeke, 1984. Kwaliteitsaspecten van rundvlees. Landbouwtijdschr. 37 : 841-853.

Eeckhout W., M. Casteels and H. Bekaert, 1966. Studie van de intrinsieke kwaliteit van varkensvlees. Mededeling Rijksstation Veevoeding, Werkgroep Kwaliteitsverbetering Varkensvlees. pp. 1 - 29.

Evock, C.M., T.D. Etherton, C.S. Chung and R.E. Ivy, 1988. Pituitary porcine growth hormone (pGH) and a recombinant pGH analog stimulate pig growth performance in a similar manner. J.Anim.Sci. 66: 1298-1941.

Fabry, J.L., C.H. Bodart, M.F. Thielemans, R. Verbeke, G. Van de Voorde, B. Buts, D.I. Demeyer, S. Vanderhaeghe, C. Deroanne, P. Vanden Byvang, R. Oger, E. Deroover, R.W. Jones and R.H. Dalrymple, 1988. Evaluation of recombinant porcine somatotropine on growth performance,carcass characteristics,meat quality and myofibrillar proteins of Belgian Landrace pigs. In preparation.

Fiems, L.O., B. Buts, Ch.V. Boucqué, D.I. Demeyer and B.G. Cottyn, 1988. Effect of a beta agonist on meat quality and myofibrillar protein fragmentation in Bulls. In preparation.

Ivy, R.E., G.W. Wolfrom, C.D. Baldwin and D.E. Mouzin, 1985. cited in Kouwenberg (1988).

Kanis, E., W. van der Hel, W.J.A. Kouwenberg, J. Huisman, R.D. Politiek, M.W.A. Verstegen, P. van der Wal and E.J. van Weerden, 1988. Effects of recombinant porcine somatotropine on meat quality of pigs. Proc. Ann. Meet. Am. Soc. Anim. Sci., July 19 - 22.

Kouwenberg, W.J.A., 1988. De invloed van recombinant porcine somatotropine (rPST) op de vleeskwaliteit en karkasconformatie bij vleesvarkens. Afstudeeropdracht Vakgroep Veefokkerij, pp. 1 - 33, Wageningen Agricultural University.

Meat and Livestock Commission U.K., 1985. cited by Fabry et al. (1988).

National Pork Producers council U.S.A., 1985. cited by Fabry et al. (1988).

Verbeke, R. and M. Casteels, 1985. Een objectief classificatiesysteem voor varkenskarkassen getoetst op zijn commerciele waarde. Mededel. Rijksstation Veev. Gontrode, Belgium. no. 358, pp. 9-11.

Wieghart, M., J. Hoover, S.H. Chou, M.M. Macrane, F.M. Rottman, R.W. Hanson and T.E. Wagner, 1988. Genetic engineering of Livestock - Transgenic pigs containing chimeric bovine growth hormone (PEPCK/bGH) gene. J.Anim.Sci. Suppl. 1, p.266.

CONSUMER PERCEPTIONS OF FOOD TECHNOLOGY AND BIOTECHNOLOGY

Janet Graham
Consumers in the European Community Group

Summary

This is a UK consumer view. It is not specifically about PST as consumer awareness about this product and its application has yet to emerge. But at CECG our research into BST and other advances in modern food technology has enabled us to arrive at certain conclusions concerning consumer perceptions of some of these new techniques and their applications.

Consumers are increasingly concerned about modern methods of agriculture relying on the use of antibiotics, hormones, pesticides and genetically engineered proteins such as BST (Bovine Somatotropin) and PST (Porcine Somatotropin) is likely to come under similar scrutiny in due course. Some of the developments have contributed to bringing us attractive, consistent, plentiful supplies of an ever-wider range of food, but the advances have also alienated people who feel that their food is no longer "natural".

We need to establish criteria for judging new processes which include an assessment of consumer need. This would examine whether a particular advance would secure benefits for the consumer. Will a product be safer, cheaper, more varied, more widely available, more durable, more convenient, better packaged? Will it take a long time to be accepted or will it encounter consumer suspicion leading to consumer resistance? If, as seems likely, some new process or scientific break-through has some advantages and some drawbacks for consumers, pluses and minuses should be made clear for the public to decide.

Consumer rights in the affluent, developed countries include the very important right to choose the food we eat and to make that choice on the basis of full information: we do not wish to have our choice restricted by those who would ban new developments on principle. Equally, for our choice to be an informed one, those involved in food production and marketing from research to final sale must be more positive about providing information in a useful, useable form.

Keywords: biotechnology, human food, consumers perception, swine.

Introduction

Consumers in the European Community Group consists of 29 member organisations for whom we act as an umbrella body on matters relating to the EEC. All of these organisations are well-established and well-known within the United Kingdom. Our job therefore is to inform our members of developments within the Community, and in turn to inform decision-makers in London, Strasbourg and Brussels of consumer views on consumer protection, safety, agriculture, food, trade and competition. We also work closely with BEUC, the European Bureau of Consumer Unions based in Brussels, which is the umbrella organisation for consumers from all twelve EEC Member States.

As a consumer organisation, we are very much aware of the contribution of pharmaceutical industry to modern day life, particularly in eliminating disease. I hope we approach new technological advances in a positive manner. Similarly, we stress our support for a healthy pig

industry - healthy in all senses. Indeed, we have before now got together with UK pig producers to lobby our Agriculture Ministry for cuts in cereal prices, to benefit pig producers and consumers alike.

In view of the title of your conference, I will concentrate today mainly on biotechnology in relation to pigs, and in particular porcine somatotropin. Inevitably, I will be referring to our experience so far with bovine somatotropin. I know that there are important differences between BST and PST, but similar principles and questions apply. These are, for consumers:

— Safety.

— Consumer information and choice.

— Consumer demand.

And, we must recognise too that, with developments in biotechnology, there are other, wider factors which governments must consider.

Safety

First, let me make some general points about hormone growth promoters and the European Community Directive banning their use. CECG did not campaign for a ban on hormone growth promoters, although we were not in the least surprised that many continental consumer groups demanded one. Nor could we disagree with their reasons for wanting a ban. Hormone residue scandals in Belgium, Germany and Italy made it inevitable. Consumers were scarcely reassured when one of those held in jail in Belgium on a charge of illegal dealing in hormones sent out for vegetarian meals rather than eat the meat provided!

We would have preferred the suspension of growth promoters pending the report of the committee chaired by Prof. Eric Lamming, who has done so much to cast light on a difficult subject. The EEC scientific committee did of course eventually report that hormone growth promoters were safe, **under proper conditions of use**. However, the rush by EEC Farm Ministers to ban hormones was not the result of alarmist scares by consumers, or panic by the European Parliament. It stemmed directly from the failure of those responsible to put their own house in order by ensuring proper use.

Things do not seem to have improved. Indeed, only this summer we have seen a further scandal at calf units in West Germany, near the Dutch border, with 14,000 calves being seized by the state agriculture ministry. Some calves treated with banned hormones are thought to have been smuggled out of the area. The German state minister for agriculture and the environment has called for international police co-operation against what he described as "the hormone mafia". You will understand therefore why consumer organisations are not enthusiastic about hormone growth promoters in general.

PST falls into a different category of growth promotor and is, therefore, not covered by the EEC ban - a fact which has not escaped the notice of the consumer movement. From tests being carried out in the United States we gather pig producers are enthusiastic about the results. There is improved weight gain, giving a better food conversion rate and less carcass fat, leading to less fat meat. The fact that at the moment pigs have to receive a daily injection could, for emotive reasons, prejudice the public against the meat. No doubt this is why work in America is looking at long-lasting injections and slow release implants which would be altogether kinder to the pig, a sensitive animal capable of being easily stressed, and better for herd management.

But could this alter the position regarding residues? Would a detection test be needed? Would the health of the pig suffer in any way - or would it improve? I am told that some scientists in America see PST as a route to eliminating the need for prophylactic antibiotics (of which consumers are rightly or wrongly suspicious) and the way forward to healthier herds. These are all questions which will need to be addressed to dispel possible consumer apprehension of this type of product.

I understand too, from work going on elsewhere on genetic engineering and embryo transplants, that the possibility exists of actually breeding stock with enhanced levels of PST and this may well raise questions of an ethical nature. It is therefore important that, if you believe PST is capable of providing a potential benefit to consumers, you try to convince the public and the EEC that this is the case, rather than hope no-one will notice.

The relevance of biotechnology and its application to food production is increasingly being discovered by the consumer movement. Unfortunately few consumer organisations have the resources to enable them to carry out the necessary scientific research to enable them to discuss the technical aspects of biotechnology with the industry: consumers might be better reassured if they did. We can though call for the maximum possible independent assessment and scrutiny of PST before decisions are taken by governments, after an opinion has been sought from the EEC's Committee for Veterinary Medicinal Products. Indeed, it may be an appropriate subject for EEC legislation to prevent barriers to Community trade in meat.

We hope that, in arriving at a view, the Community and governments will want to consult consumers. The National Consumer Council published a Report this summer on "Food Policy and the Consumer". In it we suggest that consumer confidence in food safety would be strengthened if consumer representatives were more closely involved in decisions about food policy which are made on their behalf. The Report singled out two Commission bodies, the Consumers' Consultative Committee (CCC) and the Advisory Committee on Foodstuffs (ACF) for criticism, saying they had inadequate structures and resources, and describing them as wholly inadequate to represent the views of consumers on food policy matters. This needs Commission action.

As much information as possible should be made public, with the debate conducted in language non-scientists can understand. If this is neglected, the vacuum you leave will be filled by sensationalism, bad science and misleading information.

Information and choice

Second, information for consumers when they buy meat. Consumers must know what they're getting so that they can make an informed choice, and this means clear labelling. I must say that I disagree strongly when spokesmen for industries say that consumers don't want information, won't understand it and will find it confusing. This is patronising and, as experience with food labelling shows, simply untrue.

Out there, there are millions of people who because of their education, their jobs or their hobbies, understand micro-circuitry, the internal combustion engine, word-processing, astronomy, musical counter-point and double-entry book-keeping. They are not illiterate or innumerate. If in the past they have failed to grasp, for example, the difference between antibiotics used for human therapy and those used for animal growth promotion, the least likely explanation is that they are stupid. The most likely explanation is that no-one has taken the trouble to put it over to them.

In the case of bovine somatotropin, it has been suggested that labelling would obscure consumers' real choice, because, it is claimed, there is no difference between milk from cows produced with BST, and milk produced without. That appears to us irrelevant, and it would be just as irrelevant if the same was claimed about pork from pigs produced with PST and pork produced without PST.

Consumers are still entitled to the information. And they may want to buy meat from animals that have not been treated with PST for other reasons - such as their concerns about animal welfare, or doubts about the long-term effects of PST on human health. It also seems also to us that, without proper consumer information at the point of sale, the market would not be able to decide on PST. If producers are to gain or lose from public reaction, favourable or unfavourable, to PST, then it seems only reasonable that the benefits or losses should go to the appropriate producers.

It has not been helpful when industry spokesmen say in the farming press that there would be no public concern about animal drugs if only farmers would keep quiet about them. As history teaches

us, the more you try and cover something up, the more people, particularly journalists, want to know about it. Secrecy breeds suspicion.

Other factors

Before I go on to talk about consumer demand, we should note that decisions about biotechnology must not be taken only on safety grounds. It is increasingly the case that governments will wish to take economic, social, environmental and employment factors, and questions of need, into account in biotechnology, as well as safety. Is PST, in the words of a farmer describing BST, "More clever than useful?". Will it lead to less agricultural employment? Will the benefits claimed work through to the shopping basket? How will it affect trade in agricultural produce, inside and outside the Community? Governments are entitled to take a view on these matters, as well as on safety. We hope that the European Commission is already looking closely at all these issues.

Consumer demand

But once a product has been cleared as safe and useful by the appropriate authorities, its use becomes a matter for commercial judgement. Now, it is of course the perfectly legitimate role of manufacturers and their advertisers to make people think they need something, whether they actually do or not. If I may quote two examples, consumers did not know that they wanted very small portable personal cassette players until they were developed by Sony. They did not know that they definitely did not want a very small car until one was invented by Sir Clive Sinclair!

If the use of PST were made legal, and all tests of safety and need had been met, it would then be up to consumers to decide for themselves - provided they are given the information to enable them to make that choice. We think however that pig producers would still want to consider very carefully three points before using PST:

— The image of meat and public opinion.

— Current trends in demand for food.

— Growing consumer concerns about animal welfare issues.

The American writer Marshall MacLuhan wrote, about television, that the medium was the message. The appearance of reality, he observed, was more important than what reality actually was. Similarly, it may make no difference whether or not PST is a perfectly safe, useful product. It will have been in vain if the public at large thinks, even wrongly, that it is not. This may be unfair, but life is fundamentally unfair! And fairness and the ultimate state of scientific knowledge have little to do with marketing or public demand.

Perhaps I may quote from an issue of the UK magazine Farming News for 14 October 1988: "Britain's meat industry has a serious image problem and 47% now believe that meat is unhealthy".

"Vegetarian or anti-intensive farming campaigns will intensify. The longer the industry delays, the more acute the eventual cure" says Dominic Lyle, marketing consultant, working with the British Chicken Information Service.

"He told the Poultry South West Conference in Taunton, Somerset, that the sugar, salt and butter industries had suffered because public opinion was ignored for too long".

I don't want to suggest that Mr. Lyle shares my views about PST, but he does highlight a problem of public confidence in meat generally, and we cannot ignore it.

The European Commission's Eurobarometer Survey asked consumers in 1987 whether they agreed or disagreed that the foodstuffs we find nowadays are in many cases not as good as what one would buy in times past. 71.1% agreed completely or agreed to some extent. Only 20.2% disagreed

to some extent or disagreed completely. This is in spite of the fact that consumers now have a wider range of foods to choose from than ever before.

There is also a growing awareness among consumers throughout the EEC of the link between diet and health. 70% said farmers should produce more healthy food, even if this meant an increase in price: and that was in spite of the fact that a majority thought food prices were too high. 80% agreed that we must cut down on our use of fertilizers, weed-killers and pesticides, even if that also meant paying more for produce in order to keep agriculture profitable. These are findings which no-one involved in the food production industry can afford to take lightly.

So it is clear that many consumers today are more interested than before in what they eat and in the effects of their diet on the long-term health and well-being of themselves and their families. So the question for pig producers and meat retailers is not just the scientific one of is PST safe, although it must of course be asked, but what would PST do to public perception of pork and bacon? Would sales go up, remain the same or go down? Are the potential commercial benefits greater than the costs plus the potential risks? And who would get most of the commercial benefits, the manufacturer or the pig producer?

The current trend, in food buying, in manufactured food products, and in demand for farm produce, is clearly for more "natural" food. And there is a growing feeling by consumers that they want less intensive production, less use of chemical processes and, in short, that they don't want food and animals mucked about with more than is absolutely necessary.

In the UK, expectations about food are rising all the time. People want an ever wider range of foods, they know more about food, and they ask more questions about what they buy and the way it has been produced or manufactured. Some, though still only a minority, demand that their food is produced in a particular way. Eggs must be free range, meat must be 'real' (whatever that means): vegetables must be organic, fruit unsprayed, and so on. Times have changed, and while this sort of demand is for some a luxury born of plenty, it is here to stay and is likely to increase.

Even consumers who don't fall into the organic "Green" category are increasingly concerned about modern methods of agriculture which rely on the extensive use of antibiotics, probiotics, hormones, pesticides and new genetically engineered products such as BST and PST.

As I have said, we recognise that many scientific developments have helped to bring us attractive, consistent and plentiful supplies of an ever-wider range of foods. However, these very advances have also alarmed people who feel their food is no longer "natural". We think that consumers are more than entitled to express their views about such concerns, and must be able to adjust their buying policy accordingly if they wish.

Some myths

Whatever happens, I hope that we can have a sensible debate about PST, one conducted openly and fairly. In the case of bovine somatotropin, things have been said by some industry spokesmen which can only increase mistrust. We should look at some of these briefly, because many of them may, unhelpfully, be said about PST as well.

Then there is the Black Market argument. If you don't let us sell this legally, it runs, we'll do it anyway. That is a very unattractive sentiment. No industry is above the law, and this claim only proves the need for tougher enforcement measures. There is also the threat that, if such products do not go ahead, companies will be unable to continue vital and much-needed work on new drugs and foods. That is pure economic blackmail and no way to conduct an important policy discussion.

Nor do I think it is good sense when those who ask legitimate questions about safety and need are dismissed as Luddites. It is not even good history. The Luddites opposed a useful technological process which threatened their jobs. Those who question PST are not seeking to protect themselves: they are asking "is this a useful and safe technological process, and who will it benefit?"

Another bogus argument is that scientists have an obligation to go all out to maximise production, regardless of the consequences. We should note that Article 39 of the Treaty of Rome,

which concerns the Common Agricultural Policy, refers not to all-out increases in production but to the "rational" development of production. Lastly, it really is less than honest to describe some animal pharmaceutical products in terms of animal health. A farmer recently wrote to a UK farming journal and objected to what he called: "Subtle propaganda which seems to be aimed at twisting our minds into thinking that growth promoters, bovine somatotropin and similar substances are 'Animal Health Products'. They are not".

At the moment, we have to agree with this view. The newsletter of the European Federation of Animal Health (FEDESA) for February 1988 contains this quite remarkable statement:

"Animal health products, by definition, improve farmers' efficiency and hence their productivity".

In my dictionary, health products are defined as those which improve health, not farmers' incomes. The term "Animal health industry" has more to do with the health of the pharmaceutical industry than the health of animals. But since the issue of animal health has been raised, the industry must respond to fears that the use of such drugs, particularly the overuse of medicated feedstuffs, could become a substitute for good animal husbandry, rather than an adjunct to it.

Conclusion

These are all complicated issues which must be brought out into the open. This is why I much appreciate your willingness to have a consumer point of view at your conference.

In conclusion, I draw your attention to the famous contemporary of Shakespeare who observed that "We cannot command nature, except by obeying her". He seems particularly relevant in this debate. His name was Bacon.

ETHICAL ASPECTS OF THE USE OF BIOTECHNOLOGY FOR THE CONTROL OF GROWTH AND PRODUCT QUALITY IN SWINE

R. Dantzer

INRA-INSERM U.259, rue Camille Saint-Saens, 33077 Bordeaux Cedex

Summary

The development of new biotechnologies for improving growth and product quality in the pig industry is raising many concerns, some of which have strong ethical implications. Ethics of the use of biotechnologies in animal production need to be addressed at several levels. At the level of the animals themselves, there are two questions, one related to the perceived unnaturalness of biotechnological products and the other one related to the possible negative influence of the treatment on animal health. At the professional level, the increasing use of biotechnology could be seen as favoring subordination of animal scientists and veterinarians to economic interests at the expense of their more traditional concern for care of animals. At the level of the consumer, moral issues call not only for education but also for protection and freedom of choice. At the level of society, the potential impact of biotechnologies on the socio-economical structure of animal production needs to be addressed. Although biotechnologies have great potential for improving the efficiency of animal production, a thorough consideration of ethical issues raised by their introduction in agriculture is necessary for their understanding and acceptance by society.

Keywords: biotechnology, swine, somatotropin, transgenic pigs, ethic.

Introduction

Biotechnologies are likely to bring major advances in the swine industry. With a single product like recombinant porcine somatotropin, it is possible to obtain increases in growth rate and feed efficiency amounting to about 20%, with tremendous improvements in carcass composition and no adverse impact on pork palatability (e.g., Evock et al., 1988). Genetic engineering offers the possibility of modifying gene expression in specific tissues or organs for the expression of growth factors, their mediators or their receptors. Although nothing comparable to the dramatic increase in body size observed in transgenic mice that have developed from eggs microinjected with metallothionine-growth hormone fusion genes (Palmiter et al., 1982) has yet been obtained in farm animals, there is still much hope on this possibility. There is not one week without some press release about the potential applications of biotechnology to animal production, ranging from giant transgenic salmon and trout to enhanced milk production from cows that have been treated with bovine somatotropin.

Although the search for faster growth and better product quality in animal production is as old as agriculture itself, the pace at which such changes can take place has considerably accelerated due to the progress in biotechnology. Because of its impact on only a single aspect of animal constitution, biotechnology represents not only a quantitative but also a qualitative departure from the relatively slow process of modifying animals by traditional genetic methods and husbandry practices. The modification of specific genes expression allowed by transgenic techniques is very different in essence from the pleiotropic consequences of genetic selection on a single trait like

207

growth rate or feed efficiency. It is therefore appropriate to speak of a true revolution in both the biological perspectives created by the use of biotechnology and its potential for industry.

Periods of fast and profound technological changes always raise ethical concerns, especially when such changes are perceived as threatening our socio-cultural standards and our view of what surround us. Our opinion about what is good and what is bad for us and the society as a whole is profoundly dependent on our socio-cultural environment and, as such, has little to do with the latest scientific and technologic advances. The dialectic between right and wrong is the essence of ethic and in most occidental cultures, societies have set up ethical committees that are consulted to assess what type of progress is ethically acceptable or unacceptable on the basis of scientific evidence and social impact. These committees include philosophers, lawyers, religious personalities and very few, if any, representatives of the industry and biomedical sciences.

Whether the present prospects for the use of biotechnology in agriculture will impose the recourse to such ethical committees or whether acceptance by a professional administrative body will be sufficient for clearance and approval is not yet clear. In animal production, animal right activists have already demonstrated that they have a tremendous impact on the perception of the way animals are treated in intensive husbandry systems. Their use and abuse of emotional feelings of the public are much more efficient in this regard than the cold and objective information provided by animal scientists and industry representatives. In line with this perspective, it must be noted that it was proposed during the Fourth European Conference on the protection of farm animals which was held in Brussels on May 24 and 25 1988, that an international ethical committee be set up in order to report, within two years, on the welfare aspects of current and future systems of livestock management.

In view of this situation, it is the responsability of the promoters of a new technology to foresee the possible ethical problems raised by the use of this technology and to deal with them in the proper manner, in order to facilitate understanding and acceptance by the public. The aim of this paper is to identify and review the different aspects of the use of biotechnology to improve pork production that may be at the origin of ethical concerns.

The animal's viewpoint

A widely held concern about animals kept in intensive husbandry is that they have "unnatural" lives. Such ideas are held because animals are no longer able to wander freely in their natural environment and to express their natural instincts. There is little doubt of the fact that the life of farm animals has drastically changed with domestication and intensification. Whether this is sufficient per se to cause suffering is, however, very unlikely. Another concern about animals is that they have been changed by genetic selection in such a way that they have become "unnatural" and would be unable to survive in the wild. As pointed out by Marian Dawkins (1980), the comparison between wild and domestic animals is not straightforward. Experiments on feral animals, i.e. domesticated animals living in the wild, demonstrate that modern breeds of pigs and poultry have retained their basic behavioural repertoire and are able to deal with adversity of natural environments. In more general terms, it is not always easy to dissociate what is due to genetic factors from what is related to experience in a given population introduced into a specific environment. In addition, there are still important differences between breeds of domestic animals so that it is just not possible to generalize from one domestic strain to another. Genetic selection is a slow process, even when looked at from the viewpoint of natural evolution. However, genetic manipulation of animals has the capacity to introduce major changes in the genetic composition of animals within a very short interval. It is therefore felt by some people that there is a high risk of producing "unnatural" creatures or even monsters.

Ethical concerns are not limited to the "unnatural" aspect of animals modified by genetic engineering. Some animal rights activists claim that we cannot treat animals as simply assemblies of genes that are manipulated at will by humans and that genetic engineering would actually

208

threaten the inherent nature of animals. The present trend for patenting of animals in the US raises even more concerns: life seems to be reduced to the status of a manufactured commodity that is indistinguishable from other commercial products. These concerns are difficult to deal with. They are clearly related to socio-cultural aspects and to profound beliefs on the nature of animals and their position on the evolutionary scale. How far this image can be distorted by subordination of animals to human actions is a true ethical issue.

A positive aspect of changing genomic composition through genetic engineering is that, in theory, such techniques should allow us to target more precisely the intended changes in the organism and, therefore, they should reduce the risk of undesirable side effects related to the pleiotropism of some of the traits used for selection. In pig industry, the so-called "stress-susceptibility syndrome" is a typical example of the by-product of classical genetic selection on lean meat and growth rate, that could be prevented by genetic engineering techniques.

This is true, however, only if the result of genetic manipulations or the effects of treatments with recombinant products does not endanger animal health. Somatotropin stimulates growth, but has also important functions in modulation of immune functions and metabolism. On the positive side, somatotropin has potential beneficial effects on the health of treated animals since it restores suppressed immune functions in stressed mice (Gisler, 1974) and activates macrophages both in vitro and in vivo (Edwards et al., 1988). On the negative side, somatotropin affects differentiation of cartilage cells and this can lead to significant joint problems. As soon as 1972, Machlin reported that some pigs treated with purified porcine growth hormone developed arthritic-like symptoms. In a more recent study, Evock et al. (1988) reported that daily treatment of 27 kg pigs for 11 weeks with 35 or 70 µg/kg porcine natural or recombinant growth hormone induced osteochondrosis in about half the animals and that at the higher dose used (140 µg/kg), there were significant mobility problems. This is an issue which clearly requires further study.

The professional's viewpoint

The traditional purpose of veterinary medicine is to fight disease and improve health of animals. This view is apparent in the restriction of the use of sex steroids in EEC countries like France to the treatment of infertility problems. In human medicine, the use of recombinant human growth hormone is strictly restricted to the treatment of pituitary dwarfism and cannot be extended to other possible indications, such as prevention of short stature or doping of athletes. In accordance with this position, treatment with a natural or a synthetic product in the absence of a manifest disease might be perceived by some professionals not only as a deviation of their professional ethics but also as a total subordination of veterinary medicine to economics.

This somewhat extreme viewpoint is not easy to hold since veterinary medicine and animal science have always been profoundly influenced by economic considerations. Sickness in farm animals is treated only if the cost of the treatment does not exceed the commercial value of the animals under consideration. In addition, the traditional aim of animal science is to improve the efficiency of animal production. Welfare and ethical considerations represent constraints rather than primary motives for such a quest.

The consumer's viewpoint

In contrast to many feed additives and growth promoters, porcine somatotropin (PST) is unlikely to give rise to human safety issues. Most of the relevant work has been carried out on bovine somatotropin (BST). On the basis of evidence showing that there is no difference in the somatotropin content of milk coming from control and treated cows (Torkelson et al., 1987), that BST is not absorbed from the digestive tract of humans and that it is not bioactive even when

injected in humans because of the species-specificity structure of the hormone, many countries have authorized a zero withdrawal time for milk and meat from somatotropin-treated animals.

This viewpoint is not agreed upon by many consumer associations. They ask for banning of "unnatural" products obtained through the use of biotechnologies or, at least, a differential labeling to allow consumers' free choice.

The impact of biotechnology on social structures in agriculture

The use of biotechnology to improve animal growth in pig industry or milk production in dairy farms is seen by some farmers as increasing production surpluses on the short term and as accelerating in the future the trend to fewer and larger production units. This would intensify the industrial concentration process that is already taking place in agriculture and increase the pressure exerted on small scale producers. The risk is an acceleration of the rural desertification process, with all its negative consequences on the maintenance of landscape.

This argument appears to have been taken seriously by the CEC Veterinary Drug Committee since it requires from companies interested in commercializing products derived from biotechnology a socio-economic impact study in addition to the usual data file necessary for approval of a new drug. This is very new and has no known precedent.

In a prospective study commissioned by Monsanto, Mouchet, from the Department of Animal Science of the University of Rennes, concluded that the introduction of BST in dairy plant operations would slightly enhance the present trend to a decrease in the number of cows and closing of small-scale operations (3-4%).

Conclusion

In a book entitled "La valeur humaine de la science" (the human value of science), the famous French physicist Paul Langevin wrote more than 30 years ago: "Quelques bienfaisantes que soient certaines des applications de la science pour diminuer la peine et la souffrance des hommes, le rythme accéléré auquel elles se développent et leur introduction dans une société humaine insuffisamment préparée a les recevoir ou trop lente à s'y adapter, nous semblent aujourd'hui n'être pas sans danger" (even if technology is good for decreasing hard work and suffering of Man, the acceleration of its introduction in a society which is not prepared for it or which cannot adapt to it very quickly is risky). Baile and Krestel-Rickert (1988) recently discussed whether society will permit the potential of genetic engineering and biotechnology to advance the frontiers of biology and improve the efficiency of animal production. They concluded that production and consumer groups are likely to delay applications of these techniques because of lack of understanding and acceptance and that the only way to proceed for animal scientists involved in biotechnology is "to be extremely active in order to counteract the misuse of information by those unalterably opposed to biotechnology". This attitude cannot be operant, however, without a full understanding of the reasons why the public is reluctant to accept biotechnologies. I hope the present paper will serve this purpose.

References

Baile, C.A. & D.H. Krestel-Rickert, 1988. Will society permit the potential of genetic engineering to advance the frontiers of biology? J. Anim. Sci. 66: 2125-2130.

Dawkins, M.S., 1980. Animal suffering. Chapman and Hall, London.

Edwards, C. K., III, S.M. Ghiasuddin, J.M. Schepper, L.M. Yunger & K.W. Kelley, 1988. A newly defined property of somatotropin: priming of macrophages for production of superoxide anion. Science 238: 769-771.

Evock, C.M., T.D. Etherton, C.S. Chung & R.E. Ivy, 1988. Pituitary porcine growth hormone (pGH) and a recombinant pGH analog stimulate pig growth performance in a similar manner. J. Anim. Sci. 66: 1928-1941.

Gisler, R.H., 1974. Stress and the hormonal regulation of the immune response in mice. Psychother. Psychosom. 23: 197-208.

Machlin, L.J., 1972. Effect of porcine growth hormone on growth and carcass composition of the pig. J. Anim. Sci. 35: 794-798.

Mouchet, C., 1988. Consequences économiques de l'emploi de la BST dans la production laitière en France. Ecole Nationale Supérieure Agronomique de Rennes.

Palmiter, R.D., R.L. Brinster, R.E. Hammer, M.E. Trumbauer, M.G. Rosenfeld, N.C. Birnberg & R.M. Evans, 1982. Dramatic growth of mice that develop from eggs injected with metallothionein-growth hormone fusion genes. Nature 300: 611-613.

Torkelson, A.R., K.A. Dwyer, G.J. Rogan & R.L. Ryan, 1987. Radioimmuno-assay of somatotropin in milk from cows administered recombinant bovine somatotropin. Proc. 82nd Annual ADSA meeting, 70:146 (Abstr.).

ECONOMIC AND ENVIRONMENTAL IMPACT

Economic repercussions and effect on position of pork industry

Environmental pollution

ECONOMIC REPERCUSSIONS OF PORCINE SOMATOTROPIN ON THE PORK INDUSTRY

M. Hayenga, B. Buhr, K. Skold, S. Johnson, E. Grundmeier
Iowa State University, Ames, Iowa, United States

Summary

Porcine Somatotropin (pST) is likely to be the first product of a class of biotechnological growth promotants to achieve commercial application in the U.S. The adoption of pST will undoubtedly have economic impacts on nearly all participants in the pork industry, including producers, processors, retailers, and consumers. The objective of this report is to assess in advance the likely economic impacts pST will have on participants in the pork industry. To accomplish this objective, the technical changes associated with pST are incorporated into a dynamic econometric supply-demand model of the U.S. pork sector.

Keywords: porcine somatotropin, biotechnology, economic impacts.

Introduction

Pork production seems poised for potentially revolutionary changes as a consequence of the introduction of growth promotants. Until the recent development of recombinant DNA techniques, it was not possible, either economically or technically, to apply growth hormones to commercial pork production. However, with the use of recombinant DNA techniques, it is possible to produce porcine somatotropin (pST) on the large scale basis needed for commercial implementation, which may have broad impacts on both the technical and economic aspects of pork production, and the interrelationships of pork and competing meat products. The purpose of this report is to provide preliminary estimates of the effect pST will have on the typical U.S. pork producer, as well as macro effects on the pork industry.

In the following sections, we present a synopsis of previous economic studies and approaches in this area. Following a summary of the expected technical impacts of pST on pork production, they are incorporated into partial farm budgets which provide initial changes of cost and returns for the average pork producer. Finally, impacts on the U.S. pork industry are simulated through the use of a dynamic econometric model of the livestock industry. This analysis provides indications of the supply and demand adjustments after pST is adopted, how industry performance is likely to change, who is likely to benefit, and how much.

Previous studies

There are three previous studies of the economic impacts of growth promotants. The first two, one by Meltzer (1987) - the other by Lemieux and Richardson (1988), directly address the firm level economic impacts of pST on pork production. The third by Kalter (1985) provides a useful framework for analysis, but only looks at the impacts of bovine somatotropin on dairy production. We will briefly review the relevant findings of the first two studies.

Lemieux addresses the impact of pST on the pork industry alone through the use of linear programming techniques. She calculates the net benefits to producers varying in size of operation. The results suggest that over a five-year adoption period, the number of hogs produced will increase four to five percent, causing hog prices to decline 5.51 to 7.19 percent. Results indicate that operators of 50 sow grain - hog farms, experienced an increase in average annual net cash income of about $5,400 from the adoption of pST if they received a premium for the improved carcass they produced. For operators of 225 sow grain - hog farms the increase was at least $25,600. An interesting result emerges from use of pST on lactating sows. By using pST in lactating sows, a 30 percent increase in sow milk production results, which in turn improves litter size at weaning; this increases supply through this effect, and through increases in average daily gain and feed efficiency for market hogs. This study does not consider possible changes in consumer preferences due to changes in pork product quality.

Meltzer also uses a linear programming model, but considers the impacts of pST adoption on producers with differing production efficiency levels, beef production, crop rotations and government programs. This somewhat more comprehensive study shows that if pST improves feed efficiency 20 percent, the average pork producer would expect a $5.43 profit increase with the use of pST. Producers with average production efficiency achieve an increase in gross margin of approximately 12%, depending on the increase in feed efficiency with the use of pST. As a result of less corn fed to hogs, more corn was placed on the market, substantially increasing the government's price support program costs.

Although the methods and results provide some useful information, the linear programming models are optimization techniques which do not adequately account for the dynamic economic impacts which are likely with a technological change. These effects can be better accounted for by using the dynamic econometric models of the livestock sectors used in this study.

Physical impacts and production requirements

In this study, we focus on the likely effects of pST on growing and finishing swine. After injection of pST, there are three primary impacts on market hogs' growth process. First, there is an increase in average daily gain (ADG). This means there will be fewer days-on-feed given usual market weights. Second, it will require fewer pounds of feed to produce a pound of gain on the hog. Third, the carcass will be more lean and have much less fat deposited. Preliminary estimates of the magnitude of these impacts are summarized in Table 1.

Table 1. Technical impacts from feeding pST from 120 lbs to market.

	w/out pST	w/pST	Percentage Change
Average daily gain (lbs)	1.75	1.96	+12
Pounds of feed per pound of gain	3.75	2.81	-25
Carcass composition			
Backfat (inches)	1.10	0.72	-35
Lean	--	--	+15

Source: Various published sources and industry estimates

These estimates were obtained from published research and interviews with corporate and university scientists familiar with pST trials. Of course, with more testing, the true impacts will become more defined. However, they represent a general consensus of the likely physical impacts of pST in a typical feedlot environment.

The injections of pST have their greatest impacts during the 120 pound-to-market weight stage of the growth process. While the ultimate injection or implant frequency is not yet clear, it seems likely that it initially will be in the one to four week range between injections.

To obtain these physical impacts, a finishing ration with a higher protein content must be fed when pST is administered. The higher protein ration is required to sustain the increased protein deposition rate in the hog and make the essential nutrients available despite lower feed intake rates noted in hogs being administered pST. In Table 2, the likely finishing rations for the adopters and non-adopters of pST are compared. Hogs during the early growth period are typically fed the 14 percent crude protein ration. This holds true whether pST is subsequently injected or not. Thus, the hog growth process and production practices remain unchanged during the first stage of production.

Table 2. Suggested rations for feeding swine (120-240 pounds)

Ingredients	Ration without pST (14% crude protein)	Ration with pST (17% crude protein)
	(Pounds)	
Corn, Ground	1653.48	1486.35
Soybean meal	296.52	463.65
Premix	50.0	50.0

Source: Nutrient Requirements of Swine, National Research Council

Partial budgets

Equipped with the necessary technical information, it is now possible to transform this information into economic terms to aid in the analysis of the economic impacts on pork producers. To estimate the impacts of pST, we initially incorporate the technical changes into the cost structure of a typical Iowa pork producer. Through partial farm budgets, costs and returns are compared for pST adopters and nonadopters. The partial budgets do not reflect any dynamic supply and demand adjustments. The market impacts (in terms of price changes as a consequence of supply adjustment) are not factored into this analysis. The prices used in the partial budgets are average prices for the 1982 to 1987 period (Table 3).

Table 3. 1982 to 1987 Average Prices

Corn ($/bu)	2.08
Soybean ($/cwt)	8.43
Premix ($/50lbs)	11.25
Market hogs ($/cwt)	49.79
Feed pigs ($/lbs)	1.07

This process is completed by first creating a hog enterprise partial budget based on current production technology. Then the technical changes from using pST are incorporated into the budget to determine the static impacts of pST on a single hog producer.

Partial budget assumptions: conventional versus pST technology

The enterprise budgets directly compare conventional feeding practices to feeding with the use of pST (Table 4). As such, the assumptions used for constructing the two scenarios will be directly compared.

217

Table 4. Assumptions for partial budgeting: conventional feeding vs. feeding with pST

	Conventional Feeding	Feeding w/pST	Change
Days on feed			
40-120 lbs.	56 days	56 days	0
120-240 lbs.	68 days	60 days	- 8
Total	124 days	116 days	- 8
Feed efficiency (lbs. feed/lb. gain)			
40-120 lbs.	2.68	2.68	0
120-240 lbs.	3.75	2.81	+ 25 %
Average daily gain(lbs./day) (120-240 lbs.)	1.73	1.96	+ 12 %
Crude protein requirement (120-240 lbs.)	14 %	17 %	+ 3 %
Feed requirement (lbs.) (40-240 lbs.)			
Corn	549	427	- 122
Soybean meal	99	110	+ 11
Supplement	16.40	14.40	- 2
Total	664.40	551.40	+ 113
Feed costs (40-120 lbs.)			
Corn	$ 6.58	$ 6.58	0
Soybean meal	2.68	2.68	0
Supplement	1.21	1.21	0
Total	10.47	10.47	0
Feed costs (120-240 lbs.)			
Corn	$ 13.82	$ 9.31	$ - 4.51
Soybean meal	5.62	6.59	+.97
Supplement	2.53	1.90	-.63
Total	21.97	17.79	-4.18
Facilities, equipment, and machinery ($/hd)			
Facilities $100/3 litt/yr.	33.33	31.75	- 1.58
Feed storage and handling	10.00	10.00	0
Manure handling	3.00	3.00	0
Tractor	6.00	6.00	0.
Total investment	52.33	50.75	-1.58
Interest, taxes, insurance, depreciation a 13%	6.80	6.60	-.20

Feed costs, the largest cost item in finishing hogs, are dependent on feed requirements and feed prices. Note that changes occur only over the 120-pound-to-market stage of growth, since this is when pST is administered. The ration used is comprised of corn, soybean meal, and a vitamin-mineral supplement. The cost of each feed ingredient is based on each ingredient's respective price average from 1982 through the first quarter of 1987, multiplied by the quantity of the ingredient required.

The hog production unit size is assumed to be 200 market hogs, with a standard turnaround rate of three and the non feed cost per unit capacity of $100 per hog. As a result of the improved average daily gain due to the use of pST, the turnaround rate changes to 3.15.

Labor is valued at $6.00 per hour and .67 hours are required to finish a feeder pig. However, additional variable costs are incurred from the purchase cost of the somatotropin itself, and the labor required to administer it. While the actual frequency of injection is not known, it is tentatively assumed that four injections will be required in the final two month feeding period.

The purchase cost of pST was determined by comparing returns of adopters with nonadopters, and was priced at one-third the estimated "net" benefits, since that is the rule-of-thumb pricing method often used for new products in the animal health products industry. Given the historical prices used in the analysis, and the initial assumption of no carcass merit pricing, the total cost of pST per hog was $1.53, or $.38 per dose. The additional labor cost due to injections was assumed to be offset by the labor savings due to less days on feed.

Income is based on selling a 240-pound market hog on a live-weight basis, at the average of the past five years' prices.

Partial budget results

Table 5 provides the comparison of pST adoption with conventional feeding practices. This budget does not include any gains from carcass merit pricing, even though this should be an alternative for most producers given the improved carcass composition. The primary benefits of adopting pST in Table 5 are from the reduction in feed costs. The reduction in feed cost is due solely to increased feed efficiency induced by the pST. Labor cost savings due to less days-on-feed were assumed offset by increased labor cost for injections. Some additional cost savings are found in interest costs (fewer days to slaughter), marketing and miscellaneous costs (less interest cost), and in part to lower machinery and facilities costs (more rapid feedlot turnover). Total income per head increases $3.07 with pST adoption.

The adjustments necessary when carcass merit pricing is considered include the increased returns due to carcass merit pricing. According to Robert Kaufman's recent survey of packers' carcass merit pricing systems, a 35 percent reduction in backfat will result in an increase in value of approximately 2.3 percent of the market price. In addition, if the carcass has a higher muscle content, as would be expected with the use of somatotropins, then the market price paid would increase by another one percent. Taking the slightly higher cost of pST (since it is assumed to be based on the expected, improved returns to adopters) into account, producers selling on a carcass merit basis can further enhance their returns, above feed cost savings, by $1.13 per head when pST is adopted.

Table 5. Finishing feeder pigs enterprise budget

	Conventional	pST
Income		
Market hog (240lbs x $.4979/lb. x .96)	114.72	114.72
Variable costs		
Feeder pig (40 lb.)	42.93	42.93
Interest a 11%	124 days 1.60	116 days 1.50
Feed cost (40-120lbs)		
Corn	6.58	6.58
Soybean meal	2.68	2.68
Premix	1.21	1.21
Feed costs (120-240lbs)		
Corn	13.82	9.31
Soybean meal	5.62	6.59
Premix	2.53	1.90
Total feed costs	32.44	28.26
Veterinary and medical	2.00	2.00
Fuel, repairs, utilities	2.00	2.00
Marketing, misc.	2.00	2.00
Interest a 11% on feed, other costs	0.66	0.55
Labor a $6.00	4.02	4.02
Growth promotant cost	0.00	1.53
Total variable costs	87.66	84.79
Income over variable costs	27.06	29.93
Fixed costs		
Machinery, facilities	6.80	6.60
Total of all costs	94.46	91.39
Income over all costs	20.26	23.33

- Somatotropins are priced on a 3:1 return to cost ratio ($.38/dose).
- No increased labor for somatotropin usage as administration time is offset by fewer days on feed.
- No carcass merit pricing for possible carcass improvements with pST.

However, the limitation of the partial budget analysis is that the dynamic nature of the pork industry and its competitors is not accounted for. The partial budgets assumed constant prices, which only provide a first step in understanding the implications of pST on the pork sector if pST were to be widely adopted. The livestock model simulations that follow allow for the likely supply and demand shifts through time in the U.S. pork, beef and poultry sectors that would result from the introduction of pST.

Dynamic implications of pST

The impacts of pST on the pork sector over time were estimated using quarterly econometric livestock supply and demand models developed at the Center for Agricultural and Rural Development, Iowa State University. The detailed structure and specification of the pork model can be found in Skold, et al. (1988). The quarterly beef and chicken supply and demand were simulated in conjunction with the quarterly pork model to capture cross commodity effects. However, by assumption in the simulations, pST was only adopted by pork producers.

The quarterly pork model provides a complete representation of the aggregate structure of the pork industry. The model represents the various supply and demand components of the industry with sets of mathematical equations. These expressions are used to capture aggregate industry behavior, and thus can be used to explain and predict the pork sector's reaction to technological advances such as pST.

The quarterly pork model is linked to the other livestock models at the retail level, as depicted in Figure 1. Thus, consumers' reactions cause relative price changes which reverberate through the
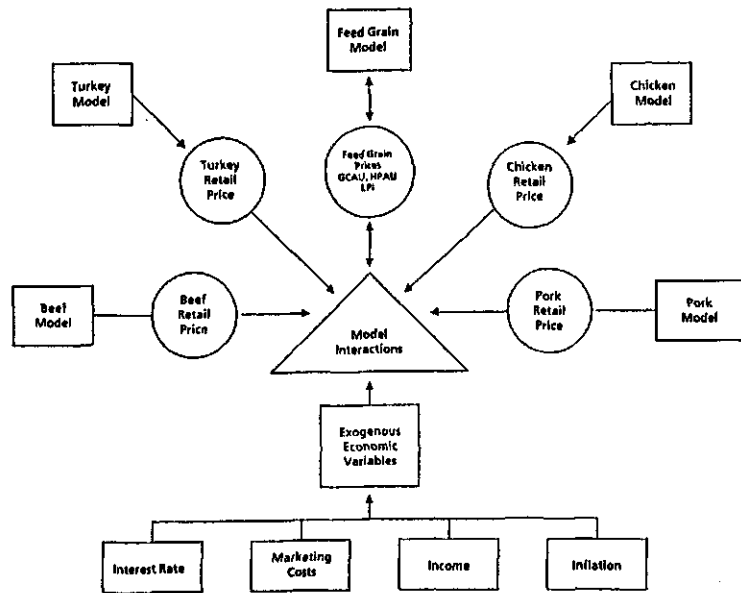
Figuur 1.Livestock sector model linkages

market, and in turn affect the profitability and subsequent production decisions of pork, beef, and chicken producers. Within the structure of the quarterly pork model, the size of the breeding herd determines the pig crop. Thus, the pig crop is simply a function of the current breeding herd. Barrow and gilt slaughter depends directly on the level of the past pig crop. Total farm pork production is determined by multiplying barrow and gilt slaughter and sow slaughter by their respective live weights. Farm production, which is in live weight, is transformed into commercial pork production in carcass weights through the use of a transformation ratio.

On the demand side, prices are determined at the retail level, since supply is assumed to be fixed in the short run. Consumers respond to changes in the supply of pork, prices of pork, prices of other meats, and income as shown in Figure 2. However, it is often true that consumers respond to relative changes in prices and income with some delay. Hence, the demand is structured to explicitly account for this persistence in demand. The price of slaughter hogs is linked to the retail pork price by a retail-farm margin. This margin accounts for both demand and supply shifts as well as processing costs.
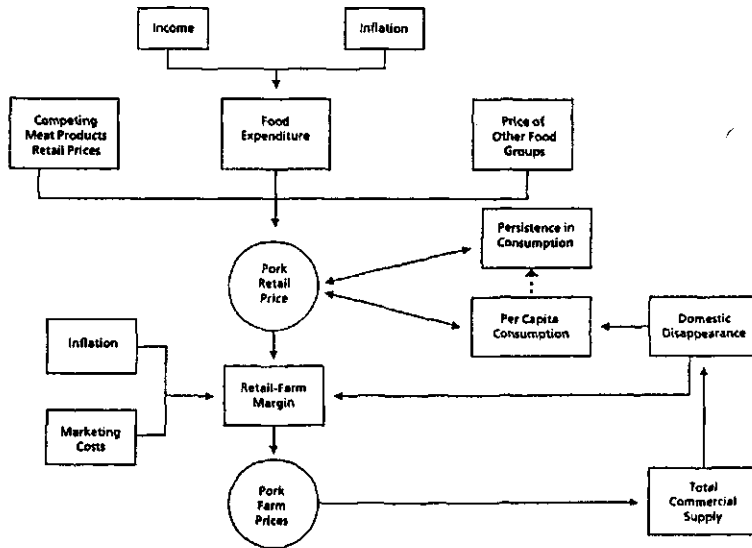
Figure 2. Price determination of the U.S. quarterly pork model

The total domestic disappearance is solved through the market clearing identity, which equates supply and demand. Included in the identity are on-farm production and other variables that are exogenous to the system, such as net exports and military use.

Porcine somatotropin simulation results

The estimated relationships in the model are based on typical market behavior during the 1967 to 1986 period. Thus, we're assuming that industry behavior would be very similar to what it has been in the past, except for the changes introduced due to the new technology.

To eliminate the variability caused by outside factors, all exogenous variables were set at their mean levels (1984 to 1986 average) for the entire simulation period. Thus, historical changes in feed costs and other exogenous variables do not clutter the associated impacts of pST. Also, all seasonal components within the model were removed to simplify the simulation process.

The model was simulated over a period of 15 years. Since the simulations at mean values do not correspond with any particular point in time, the year in which pST is first introduced is designated as year one. Subsequent years are numbered up to year 15. This is a sufficient time frame to allow pork, beef, and poultry producers to adjust to pST. The first producers adopting the technology will begin using pST on pigs born during the first quarter of the first year. Given the biology of the hog growth process, these pigs will not reach market weights until approximately the third quarter after pST adoption. Thus, the supply effects of pST will not be seen until those hogs are marketed during the third quarter of year one.

The pST adoption rates assumed in the simulations are: a) 12.5 percent of total hog production is assumed in each of the first four quarters; b) three percent of total production to adopt pST in each of the next eight quarters. Hence, 50 percent of total pork production is injected with pST at the end of the first year, and 74 percent by the end of the third year. Subsequently, the total percent of hogs injected with pST is held constant at 74 percent. This adoption rate was chosen based upon a New York dairy industry survey by Robert J. Kalter, et al. (1985), regarding bovine somatotropin adoption. The rate chosen for pST adoption is similar to his survey results. In addition, our survey of animal health industry members involved with development of pST indicates that the expected market penetration may be 70% in 2 to 3 years, based on similar animal health products. When more information is available, the likely producer acceptance of pST in their production processes will become more defined. The production cost adjustments due to pST were used to shift the price required for pork producers to maintain a particular size of breeding herd. The increased average daily gain, the 113 lbs. less feed required for hogs not receiving pST, and the higher protein and higher cost ration and the pST cost caused a net production cost decrease which was used to shift the supply curves for producers adopting pST.

In the simulation, feed prices of corn and soybean meal were incorporated into the model as endogenous variables. This allows the feed prices to adjust in response to changes in production levels and the changes in the feed demanded by pST adopters. This also changes the profitability of livestock production and subsequent production decisions by pork, beef, and poultry producers.

Simulation analyses

Four possible scenarios of pST adoption in the U.S. pork industry are analysed. The results are presented as graphs showing the movement of several key variables: total supply of pork, retail price of pork, farm price of pork, profits of adopters and non-adopters, and aggregate profits for the pork industry.

In addition to the key variables already mentioned, the change in hog waste production was estimated. According to animal scientists at Iowa State University, typical feed rations are 85% digestible. Thus, it is assumed that 15% of the feed is excreted as raw waste products. Thus, waste production is a function of the total feed consumed.

To obtain the baseline values it was necessary to simulate the model until it reached an equilibrium. After reaching an equilibrium, the model was simulated for fifteen more years. These fifteen years, with all exogenous variables fixed at their equilibrium values and no pST adoption, serve as the base against which all pST scenarios are compared. Four alternative scenarios are simulated and compared to the base. The assumptions of the four scenarios are shown in the following summary.

Alternative scenarios with pST adoption

Scenario I: Production Efficiency Scenario

— Includes production efficiency changes (feed efficiency, growth rate)

— Requires 17% crude protein ration

— Carcass composition improvements not reflected in prices received

Scenario II: Demand Scenario

— Scenario I plus 5 percent increase in consumer demand due to leaner pork products

Scenario III: Carcass Merit Scenario

— Scenario I plus adopters use carcass merit pricing to capture benefits of improved carcass composition

Scenario IV: Composite Scenario

— Composite of Scenarios I, II, and III.

An explanation of the results from each scenario is provided below. The actual results are shown in Figures 3-8.
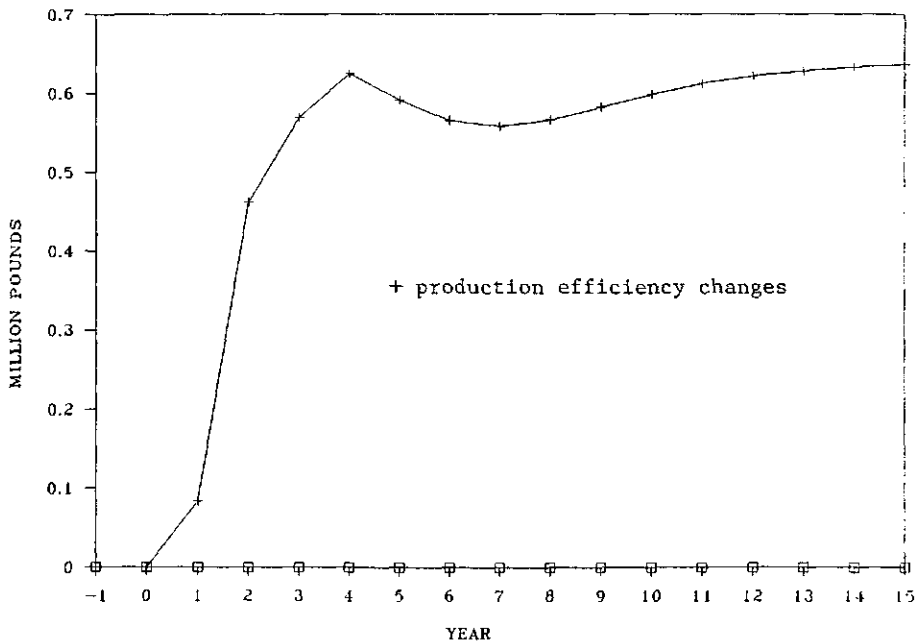
Figure 3. Change in pork supply
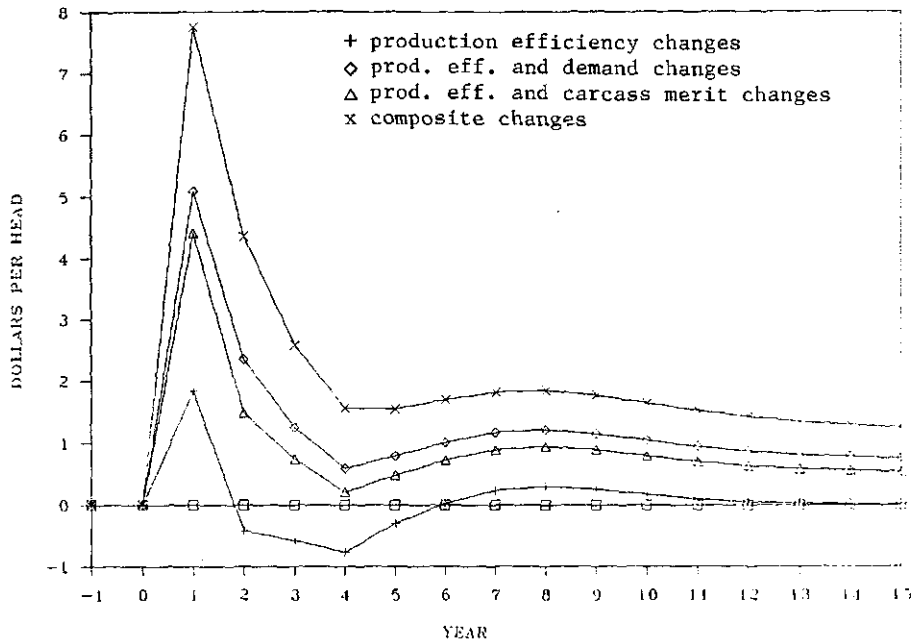
Figure 4. Change in adopter profits
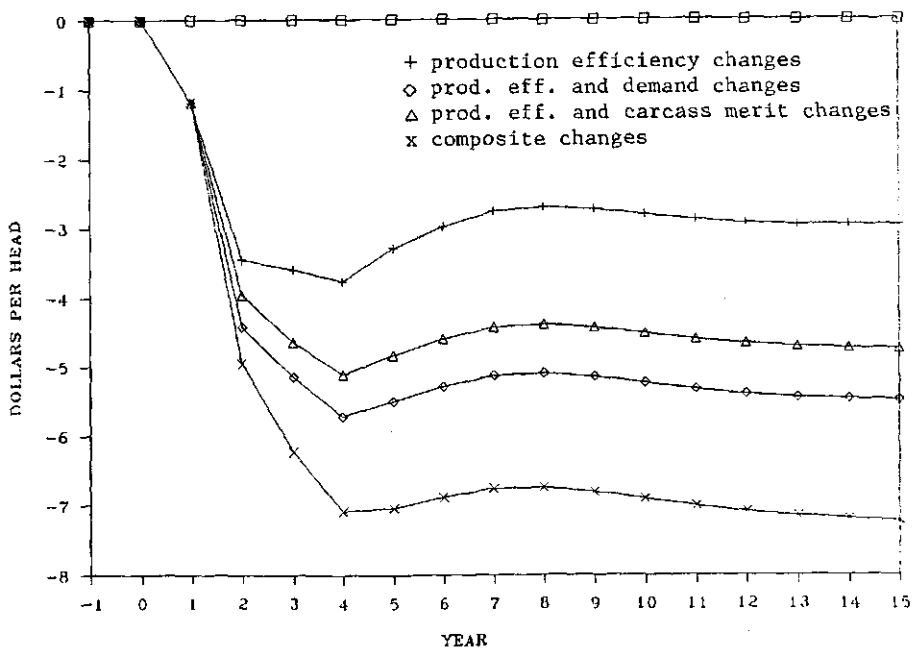
Figure 5. Change in non-adopter profits
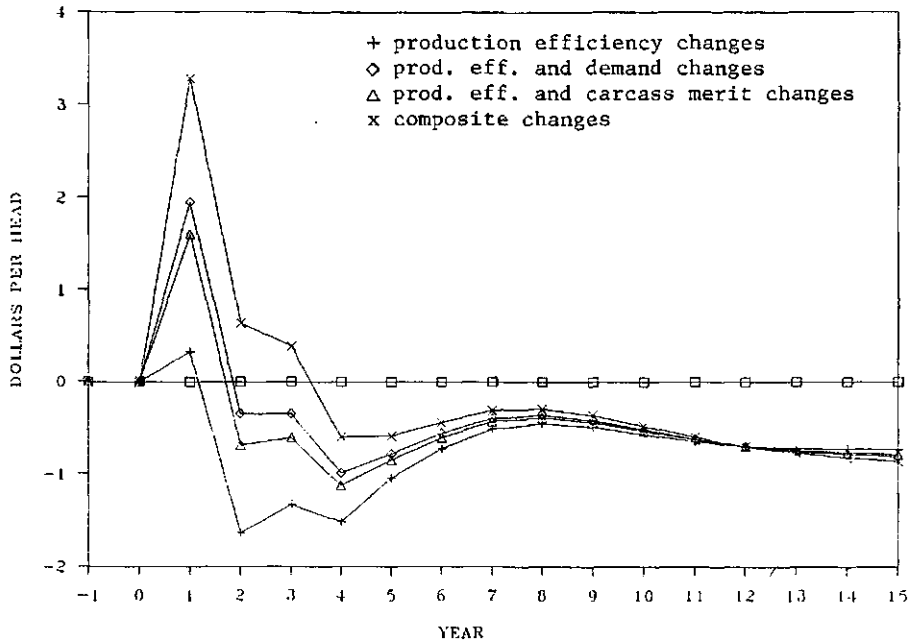
Figure 6. Change in aggregate industry profits
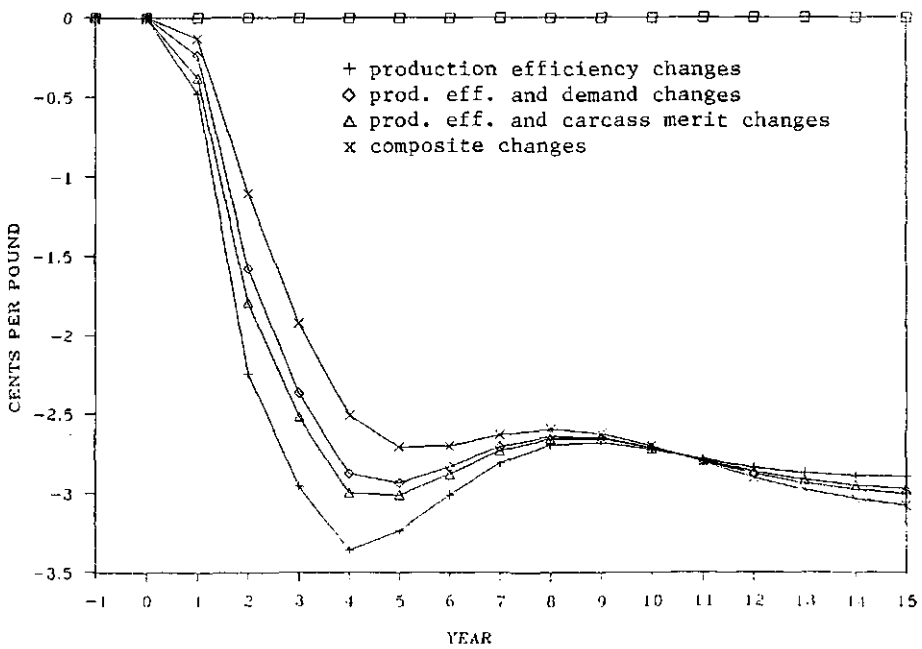
Figure 7. Change in farm price of pork
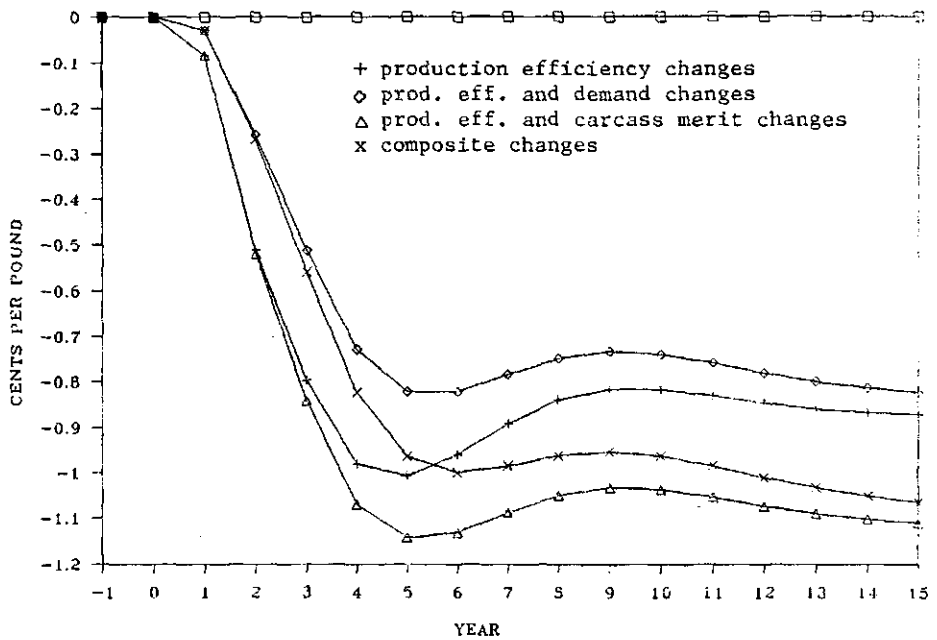
Figure 8. Change in retail price of pork

Scenario 1: Production efficiency improvements

The immediate impact of the introduction of pST is that producers adopting the new technology incur lower production costs. The lower production costs increase profitability, providing incentive to increase production by expanding the breeding herd. In the second half of the first year, total supply begins to increase as the first pST injected hogs begin to reach slaughter weights. The increase in supply shown in Figure 3 reduces both farm and retail prices. Pork producers improve their market share as supply increases and retail prices fall, causing per capita consumption of pork to rise. Profits of pST adopters increase greatly during the first year. Meanwhile, non-adopter profits decline rather rapidly. Note that during this period aggregate pork industry profits increase because the increase in profits for adopters exceeds the decline in profits for non-adopters. The profitability changes can be seen in Figures 4-6.

By the second year prices (Figures 7 and 8) fall very rapidly as production increases. Producers begin to sell of part of their breeding herd as profitability declines. Roth adopters and non-adopters realize a dramatic decline in profitability as a result of the lower farm price.The increasing trend in per capita pork consumption and improved market share continues. Beef and broiler production both decline in response to lower prices and profitability. Corn and soybean meal prices begin to fall as fewer hogs are needed to sustain the growth in total supply of pork. Lower production levels of beef and broilers also contribute to the decline as less feed is required in these industries.

By the fourth year, long-run impacts change from the trend of the first two years. The breeding herd continues to decline, but the total amount supplied shows its first drop during this year. Retail and farm prices level off by the fourth year and begin to increase in year five.Aggregate producer profits (adopters plus non-adopters) bounce back by year five, but never reach the original baseline levels in the aggregate, since the decrease for non-adopters exceeds the increase for adopters.This may be due to our assumption that adoption levels never exceed 74% which may be unrealistic in the long run. An 80% adoption rate would move aggregate industry profits back to previous levels in the long run. Feed prices continue their decline. By the seventh year all variables are closely approaching their equilibrium values.

226

Scenario 2: Demand expansion plus production efficiency improvements

The results from this scenario are similar to the first scenario. An assumed 5 percent increase in consumer demand due to leaner pork leads to higher breeding herd levels, market supply, and continuing expanded production one year longer than in the previous scenario. Both farm and retail prices are higher. In this scenario pST adopters realize increased profits during the first year, after which profits decline and follow the trend of the first scenario. Corn and soybean meal prices do not fall quite as rapidly as in the other scenarios.

Scenario 3: Carcass merit pricing plus production efficiency improvements

Short run effects are nearly identical to those in Scenario I. Supply increases and prices fall. Profits of pST adopters rise and profits of non-adopters fall. The pork industry continues to take market share from the beef and broiler industries because of leaner pork and lower prices.

By the second year, the breeding herd size and total supply are slightly above the first scenario. Farm prices received by adopters are higher as a result of carcass merit pricing, and retail prices are slightly below the levels of the previous scenario as a result of the supply increases. Feed prices do not decline quite as rapidly.

Scenario 4: Demand expansion, carcass merit pricing plus production efficiency improvements

This scenario incorporates the assumptions from the first three scenarios to give an aggregate result. The trends of this scenario are similar to previous scenarios although more pronounced. Profits for adopters reach their highest levels while profits for non-adopters reach their lowest levels. Supply increases rapidly in year one and continues upward until year three when it levels off. Both farm and retail prices decline. This occurs because the increase in supply as a result of carcass merit pricing is greater than demand increases.

There is less feed required for hogs treated with pST, and it takes fewer hogs to produce the same amount of pork. Thus, total feed consumption and waste output decline in all scenarios.

Summary and implications

This study provides a comprehensive analysis concerning the impact of pST on the pork sector. The study attempts to account for all of the dynamic economic impacts of the introduction of pST. However, it must be remembered that the results obtained from this study are limited by the assumptions used in the analysis, and by the limited availability of data on pST.

The overwhelming impact of pST is the reduction in cost combined with an increased lean yield per hog. The resulting greater profitability as producers adopt pST causes production to increase rapidly. More pork production forces down prices at both the farm and retail levels. Due to the lower production costs, producers adopting pST immediately reap higher profits, but the industry as a whole realizes lower returns as the expanded production pushes down farm prices. From a profitability perspective, there appears to be an incentive to pork producers to adopt the new technology due to the short term profit increases and the longer term competitive advantage of adopters compared to non-adopters in the pork industry. In addition, pork producers regain some of the ground lost to technological advances in poultry production over the last thirty years, and become a more viable competitor for the consumer's food dollar. Thus, higher production and lower price levels benefit processors and consumers, while late-adopters are on the "technological treadmill". Aggregate pork producer profits change very little in the long run, as you would expect in a competitive industry with free entry. Feed grain producers are hurt while soybean producers are not affected.

Several questions concerning the production impacts of pST as well as demand response by consumers still need to be answered. Until long-term production impacts and any possible side

227

effects are known with reasonable certainty, full scale adoption of pST will not occur. Consumer acceptance of meat from hogs injected with pST is still an important question that can have a profound impact on pST adoption. Some important issues not considered here include:

— The potential for meat packers to shift preferences to heavier slaughter hogs because of leaner carcasses, and the possible implications.

— The possible implications of differing international regulations on domestic use of pST and import restrictions in major pork producing and consuming countries.

— The effects of competing technological changes (e.g. other growth promotants, beta agonists, etc.) in the pork, beef and poultry industries.

Such changes could intensify or dramatically diminish some of the changes that we currently project as consequences of pST introduction. As more information becomes available we will be in a better position to more accurately assess the likely economic impacts of pST.

Acknowledgement

References

Kalter, Robert J. et al., 1985. Biotechnology and the Dairy Industry: Production Costs, Commercial Potential, and the Economic Impact of the Bovine Growth Hormone. A.E.Research 85-20, Cornell University, Ithaca, New York.

Kauffman, R.G., 1987. Producing Lean Pork: What's the Incentive? Department of Meat and Animal Science, University of Wisconsin-Madison.

Lemieux, C.M. & J.S. Richardson, 1988. Firm Level Impacts of pST. Adoption. Paper presented at AAEA annual meetings, Knoxville, TN.

Livestock Enterprise Budgets for Iowa-1988, 1987. Cooperative Extension Service Publication FM-1815, Iowa State University, Ames, Iowa.

Meltzer, Marion I., 1987. Repartitioning Agents in Livestock: Economic Impact of Porcine Growth Hormone. Master's Thesis, Cornell University, Ithaca, New York.

Nutrient Requirements of Swine, 1979. Publication ISBN 0-309-02870-1, Committee on Animal Nutrition, National Academy of Sciences, National Research Council, Washington, D.C.

Skold, K., E. Grundmeier and S.R. Johnson, 1988. CARD Livestock Model Documentation: Pork, Technical Report TR-88-02, The Center for Agricultural and Rural Development, Iowa State University, Ames, IA (manuscript in process).

GROWTH CONTROL OF PIGS IN THE EEC EFFECTS ON THE COMPETITIVE POSITIONS OF PORK, AND OF PLAYERS IN THE PORK CHAIN

A.H.R. Pease

SARC, Gex, France, (Formerly with GIRA s.a.)

Summary

New growth controlling techniques, of which PST administration is nearest to market, decrease the cost of production of lean pork. They are also likely to increase the value of bellies more than proportionally to the lean content.

The total advantage of PST to pork production is estimated as ECU 31 per pig.

Some of this benefit will accrue to the supplier of the growth promotion technique via the price, and the rest could be expected to accrue, at least in the first instance, to pig producers.

However, reasonable assumptions, based on published results on the effects of PST, and the commercial functioning of EEC Pork Chains, indicate that this is not so for two reasons:

— The new EUROPA grading system, although far more accurate than the previous system, will only pay an estimated 60% of the improved cut-out value of the carcasses;

— PST carcasses will be leaner, and the extra lean pork arriving on the market will lower market prices.

The producer prices for pigs are sensitive to volume, with estimates of elasticities from bi-monthly to annual series generally falling in the range -1 to -5. Estimates based on monthly series tend to be smaller.

Since the value of carcasses lies mainly in their lean pork content, it seems reasonable to assume that it is the weight of lean, rather than the weight of carcasses which largely determines prices. A conservative assumption was made, that the carcass price/lean pork slaughtered elasticity will be -1, with alternatives of -2 and -3.

These assumption lead to the following conclusions:

— For the first pigs slaughtered, 20% of the advantage will go to PST suppliers, 50% to pig producers (including EUROPA grading premia) and 30% to slaughterers/cutters.

— Within a few weeks or months the advantage will be divided 20% to PST suppliers and 80% to consumers.

Keywords: somatotropin, economic impact, Europe, swine.

Introduction

Administration of Porcine Somatotropin (PST) is the first of a new type of growth controlling techniques for pigs. Following behind are somatotropin related technologies based on immunisation, and gene transplant techniques. The magnitude of the technical effects, growth rate, feed efficiency and carcass composition have been demonstrated in numerous experiments.

The object of this paper is to evaluate the commercial value of the technical effects in money terms.

That is to say:

- The total value in ECU's per pig;
- How this value will be distributed in the first instance;
- How it will then flow up and down the Pork Chain;
- How it will effect competitive positions within sectors.

Social structures

If the techniques have a greater effect when the base performance is poor, then the social effects will be positive in the sense of favouring poor producers, many of whom are small and unspecialised. PST is taken as the main example, and differences from the other two techniques are discussed.

If, on the other hand, the techniques are difficult to use, but not particularly related to base performance, then they will favour specialised industrial type producers.

The market

Pork produced using these techniques will be cheaper and leaner. On the other hand it may carry an image of "artificial". In addition, loins and bellies may be sufficiently leaner to have some of the characteristics of new products, to which the market will adapt.

Essential information is lacking on which to draw conclusions on the above subjects, and they are, in any case, too complicated to be treated in a paper of this length. In what follows it has therefore been assumed that the positive and negative aspects cancel out. Most of the analysis applies to all of the new techniques, though PST has been taken as the main example.

Other assumptions made are as follows:

- The leanness will have a similar effect on prices as would the same amount of extra lean coming from more pigs;
- The slaughter price on slaughter volume elasticity will be between -1 and -3;
- The price of PST will represent 25% if the total advantage to pig producers.

Standard assumption are made as to the technical effects, and these, together with their financial implications are given in Table 1.

There are many examples to show that the results of improved animal production technology flow through to the consumer in a few months or years.

However, the intervening period can be very profitable for some operators.

The money flow following the introduction of PST in the EEC can be divided into five stages:

- The first pigs, insufficient in numbers to influence the market;
- The first half cycle (pig price cycle). The extra weight of lean pork coming on the market can be expected to depress prices. Benefit will thus be transferred from pig producers to consumers, with the PST supplier and slaughterers maintaining their share of the advantage;
- Competition between slaughterers. Initially slaughterers will benefit from PST, since the cut-out value of PST treated pigs will be greater than is estimated by the EUROPA grading system. As the slaughter industry becomes familiar with the effects of PST, competition will drive margins down to near their pre-PST level
- Later cycles. Depressed prices will cause some producers, particularly non-PST producers, to decrease or stop production in the classical pig cycle mechanism;

— *Competition between PST suppliers. Much later, maybe after 10 years, the PST market will* become saturated. By this time pig producers will no longer need technical support in order to use PST effectively, and competition between PST suppliers will drive down margins.

Table 1. Initial division of PST advantages

		Untreated	PST Treated	ECU	Difference %	
Feed conversion 70-100kg		4.0	3.0		- 25.0%	
Daily gain	g	750	863	113	+ 15.1%	
Feed cost	ECU	26	20	-6	- 23.1%	(1)
Other cost		20	18	-2	- 10.0%	
Cost to 70 kg		94	94			
Total production cost		140	132	-8	-5.7%	
Fat depth	mm	24	18	-6	- 25.0%	
Estimated lean		50.0%	54.6%	4.6%	+ 9.2%	(2)
Actual lean		50.0%	55.4%	5.4 %	+ 10.8%	
Price paid (EUROPA system)	ECU	150	163	13.35	+ 8.9%	(3)
Cut-out value		150	173	23.1	+ 15.4%	(4)
Production margin		10	31.4	21.4	+ 214.%	
of which: to PST supplier (25%)				5.3	17 %	
to pig producer				16.0	52 %	
Advantage to slaughterer				9.8	31 %	
Total advantage				31.1	100 %	

[1] = assumed 2% higher protein, slightly more expensive
[2] = allowing for bias due to using regression of individuals to predict population change
[3] = EUROPA payments slightly less than estimated lean, due to price classes
[4] = difference mainly due to the very high value of lean bellies
Source: GIRA based on various

The first pig

A 25% reduction in fat depths is not enough to produce an obviously different product. This means that the first pigs, if they are not announced, should be paid according to the EUROPA grading system, that is according to the weight of lean estimated by a regression equation.

This grading system will probably underestimate the lean content of PST pigs because:

— Grading is by categories, rather than on a continuous scale;

— The regression equations are calculated from individual pig differences. The slope is flatter than from a regression equation for population differences.

In addition, in Europe, lean weight underestimates the commercial value of lean pigs. The main reason for this is that lean bellies, which can be sold without transformation (other than smoking) are worth 2 - 5 times as much as fatter bellies which are broken down for manufacturing. The price difference is much greater than the difference in lean content.

GIRA estimates, that on average, about 60% of the extra commercial value of PST pigs will be paid for on the EUROPA grading system.

If the PST pigs are announced as such, then the payment differential will probably be less. The *first PST users will find themselves in a similar situation to those who tried to introduce once bred* gilt systems (which would have given a similar increase in productivity had they been allowed to develop). The producer will come onto the market with small quantities of an unknown product. He will lack negotiating power, and reasons will be found to downgrade his pigs compared to their grade value.

Figure 1 gives the PST benefit by sector, assuming that pigs are paid according to grade.

Source: GIRA
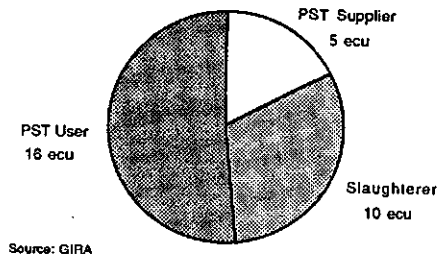
Figure 1. Distribution of benefit from first PST pigs

If the use of PST is not announced, then small producers will have a competitive advantage, since their small batches will be less likely to attract attention. If its use is known to the slaughterhouse, then large producers with negotiating power, and individuals with good negotiating ability will have a competitive advantage.

The effects of immunisation or gene manipulation would be similar to those of PST at this stage, though the price of the techniques might vary.

The first half cycle

During the first half of a price cycle after the introduction of a new technique (15 - 18 months) production cannot change, other than through pressure on the EEC to protect the market, or through varying the slaughter weight (if anything, over-supply tends to lead to heavier slaughter weights).

The loin represents 40% of the value of a carcass, and it cannot be stored without losing value. Possibilities for storing other cuts, for exports or for import substitution are limited, so that when there is over-supply, prices continue to fall until the market absorbs all of the loins and most of the rest of the pork.

Much of the adaptation is at the expense of other meats, when the price of pork relative to other meats falls, the relative consumption rises (Figure 2).

Source: GIRA based on various
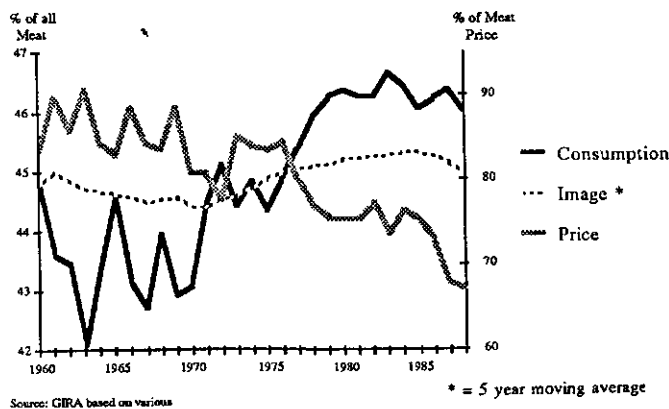
Figure 2. EEC pork relative price and relative consumption

232

This market effect appears in the form of elasticities of slaughter price on slaughter weight which generally fall in the range -1 to -5 when periods of one year are used. Elasticities tend to be smaller when the time trend is removed, and when shorter periods are used.

It is assumed that extra lean meat coming on the market in the form of leaner pigs, would have a similar, though perhaps smaller effect on prices to that of the same quantity of lean derived from increased slaughterings. Taking these factors together it is assumed that the slaughter price on weight of lean elasticity will be in the range -1 to -3, with -1 being the most likely figure.
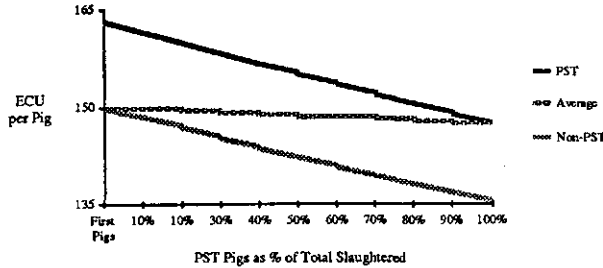
Figure 3. Slaughter prices by proportion of PST pigs slaughter price/volume elasticity = -1

The effect on prices of these assumptions are given in Figures 3 and 4 for elasticities of -1 and -2. When the elasticity is -1, the average price paid hardly changes: the improved grading being offset by the fall in market price.

The effect on the income of PST producers and of producers overall, taking account of the saving in production costs, and of the price of PST, is given in Figures 5 and 6. The initial effect on PST user margins is +16 ECU's per pig. With an elasticity of -1, this advantage disappears when all pigs on the market have been treated with PST. If the elasticity is below -1, then PST users, and the production industry as a whole, both lose margin, in spite of the increased productivity.
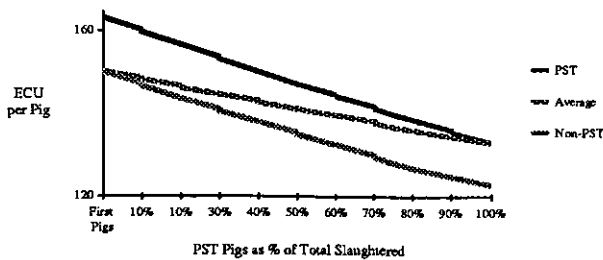
Figure 4. Slaughter prices by proportion of PST pigs slaughter price/volume elasticity = -2

233
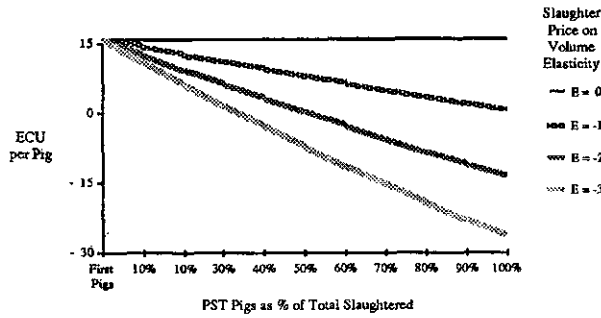
Figure 5. PST-Producer Income by elasticity - PST Users
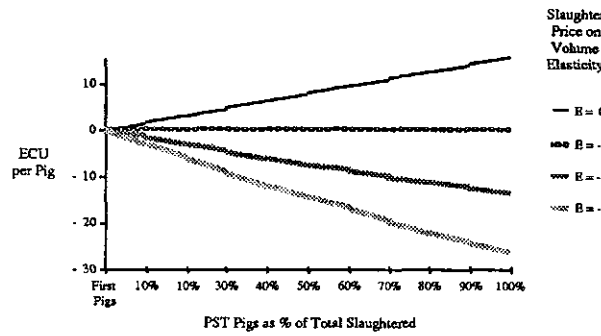
Figure 6. PST-Producer Income by elasticity - Average of all pigs

The benefit of PST by sector is illustrated in Figures 7 and 8 for elasticities of -1 and -2. Increasing the proportion of treated pigs leads to a transfer from producers to consumers. PST suppliers and slaughterers tend to maintain their share of the advantage over this period.
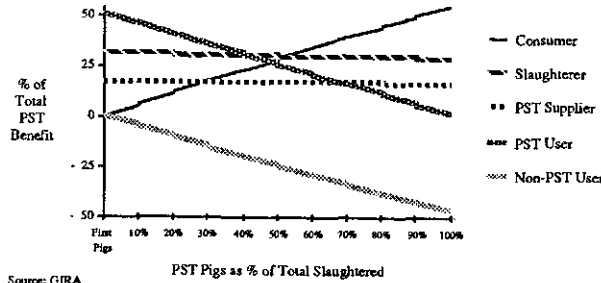
Figure 7. Who benefits? Short term elasticity -1
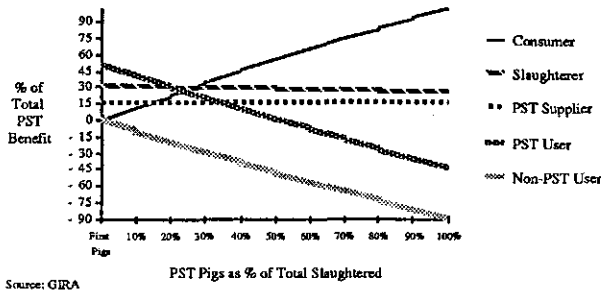
Figure 8. Who benefits? Short term elasticity -2

The main difference in effect between the three techniques (PST, Immunisation, and Gene manipulation), would be due to the speed of introduction. PST supplies, and probably those of a vaccine will be limited in the early months, so that the left hand parts of the above Figures are the most relevant.

The introduction of gene manipulation is likely to be slow. Starting from 100 manipulated sows, it would take ten years to build up to 2.5 mio slaughter pigs (Pease, 1974). The process would be speeded up a little if embryo transplants were used at the grandparent stage.

Since this intermediate period is limited to 18 months, "first pig" conditions are likely to hold as regards gene manipulation.

This intermediate period is likely to favour organisations which are vertically integrated down to slaughter. Such organisations would gain all of the benefit of the growth improvement. It would create a greater incentive to obtain priority for pork vs other meats.

Later cycles

The EEC pig price cycle only has about 40% of the amplitude of that of the USA, but it is nevertheless a major factor in Pork Chains. It can be thought of in terms of oscillation about a trend. Depending on the phase of the price cycle at the moment of introduction of PST, the result could be:

- A flattened peak;

- An unusually long trough;

- An unusually deep trough.

The PST effect may or may not be sufficient to compensate for the effect on market price, according to the price elasticity and the proportion of users. Non-users lose under all circumstances, and some of them will decide to reduce, or stop production.

Long term stability (though still with a cycle) will be reached either when:

- All producers use PST. In this case the pressure on their margins will be much the same as before the introduction. At this stage all of their benefit will have been passed on to consumers, or;

- The proportion of non-users stabilises. In this case the variability in the cost of production of lean pork will be increased, particularly if some users obtain better effects than others. Since the long term price is basically determined by the "pain level" of the poorest producers, this would imply a slight increase in average producer margins.

If the introduction of the new technique is slow, then the main effect will be on the long terms trend, rather than on increasing the cycle.

The competitive situation of good producers will be further improved. To the extent that specialised producers are better, this will tend to accelerate the long term concentration process.

Competition between slaughterers

The sale price of the meat from a PST pig in the standard assumptions is about ECU 173 + 18%, or 200 ECU. The short term extra margin is estimated as ECU 9.8, or 5% of turnover. A satisfactory net profit for a pork slaughter operation is about 1% of turnover, so initial profits from PST will be very large.

The competitive situation between slaughterers is analogous to that between pig producers, in that:

— There are sufficient numbers to ensure competition;

— There is actual or potential over-capacity.

There is little evidence as to how quickly competition will erode the extra margin, but it is reasonable to assume that much of it will have passed to consumers within the first half cycle.

There do not appear to be significant variations on this scenario, either for other techniques, or between countries.

Competition between suppliers

This section covers both competition between suppliers of PST and competition between competing techniques (PST, Immunisation and Gene Manipulation).

To treat all 280 mio OECD pigs would require 25 - 50t of PST per year. At present the capital requirement is of the order of $ 10 - 15 mio per tonne of capacity. Even allowing for improved production biotechnology, it is likely to be a number of years before the market is saturated, and prices drop.

If one of the other techniques comes to market, then it will presumably act as a partial substitute for PST, and increase price competition.

Conclusion

The most likely results of the introduction of PST are therefore that:

— for the first pigs slaughtered, 20% of the advantage will go to PST suppliers, 50% to pig producers (including EUROPA grading premia), and 30% to slaughterers/cutters;

— within a few weeks or months the advantage will be shared, with 20% going to PST suppliers and 80% to consumers.

Reference

Pease A.H.R. , 1974. Investment Strategies in Complex Breeding Programmes . Genetic Operations, Research Workshop, Trinity College Dublin.

EFFECT OF PST ON ENVIRONMENTAL N POLLUTION

E.J. van Weerden and M.W.A. Verstegen.
TNO Institute of Animal Nutrition and Physiology, ILOB department, Wageningen, The Netherlands. Department of Animal Nutrition, Agricultural University, Wageningen, The Netherlands.

Summary

Castrated male crossbred (Dutch Landrace x Dutch Yorkshire) pigs were injected with four mg per day recombinant porcine somatotropin (rpST) from 58 kg live weight onwards during ten weeks. An untreated placebo group served as a control. Animals were fed at a restricted level of 260 kcal metabolisable energy per kg body weight $^{.75}$ daily.

Parameters measured were N-balance in six test periods during the last six weeks of the treatment period, weight gain and feed conversion. N-balance was significantly increased with 31%; 7.7% more of the dietary N was retained in the body of the rpST treated animals. Weight gain was 10% faster and feed conversion was 7% more favourable in the rpST pigs. P and Ca balance were increased with 18 and 19%, respectively, after rpST treatment.

From these figures it was calculated that the excretion of N into the environment over the weight range 58-110 kg was reduced with 21% after rpST treatment; for P was the reduction in excretion 16%. The main uncertainty regarding the extent of the effect of rpST on N excretion is the lack of knowledge on the dietary levels of protein/amino acids needed to sustain the extremely high (approximately 210 g/day) protein deposition in rpST-treated pigs. The experimental data obtained sofar give no indications of a dramatic increase of these requirements in rpST-treated pigs.

Keywords: somatotropin, swine, environment, pollution.

Introduction

More than ten years ago rather heavy and confusing discussions already arose on the subject of the efficiency of animal production, especially with regard to the low efficiency of protein conversion in monogastric animals. That discussion was initiated by the well-known report of the "Club of Rome" dealing with the limited world resources for all kinds of raw materials, including components for human food. In an E.C.-workshop in 1981, in which another category of hormones, the anabolic steroids, was discussed, I showed some figures of output-input relations for protein, calculated by Van Es in 1978 (Table 1).

Table 1. Efficiency of protein conversion (output/input)

broiler	0.40
laying hen	0.40
fattening pig	0.34
veal calf	0.33

From these figures it is clear that the efficiency of protein conversion in monogastric farm animals is in the order of 1/3, with 2/3's being excreted via faeces and urine.

Whereas in the seventies the discussions were almost exclusively focussed on the term "inefficient production of animal protein, competition between animal and man for the scarce sources of (plant) protein", the impact of this inefficiency, such as the big losses of protein and the polluting effect of the excreted nitrogenous compounds (mainly urea), attracted hardly any attention. However, in the past ten years the situation, at least in the Netherlands, has completely turned around: There is no longer any discussion on the loss of valuable protein in the animal production cycle but only complaints on the environmental pollution with N and also P caused by "bioindustry". This drastic change is not illogical when realizing the heavy concentration of farm animals in the Netherlands. Especially the numbers of pigs increased considerably during the last years; in 1980 15.6 millions were slaughtered, and in 1987 it has increased to more than 22 millions. One must also realize that the pig and poultry industry in the Netherlands is not spread evenly over the country but is specifically concentrated the southeastern part. Whereas some years ago the concern was mainly on the pollution of the surface water by P orginating from the animal industry, recently the attention has been focussed more on the pollution of the groundwater with nitrate and the pollution of the air with ammonia. Especially since observations on the rising levels of nitrate in wells used for the water-supply and the serious effects of ammonia on the vitality of forests, serious discussions are underway aimed at how the N load in these regions can be diminished, including suggestions in parliament to force the animal industry to drastically reduce the numbers of animals.

Ways to reduce pollution

The total output of N and P in the Netherlands originating from the three main categories of farm animals was estimated some years ago by Jongbloed et al. (1985). The figures are given in Table 2.

Table 2. Estimated output of N and P in the Netherlands (1984) (in 1000 kg per year).

	Cattle	Swine	Poultry
N	440,000	120,000*	53,000
P	56,000	32,000	15,500

* in 1987 estimated at 160,000 tons N.

Whereas the numbers of cattle and poultry are rather stable (poultry) or slightly going back (cattle), by 1987 the number of pigs has increased considerably.

Besides, cattle are rather uniformly spread over the country in relatively low concentrations, whereas the other categories are together much more concentrated in certain areas.

Reduction via the feed

Considering the problem described above, the question now arises: which measures, apart from a reduction in the number of animals, can be taken to bring the environmental pollution by animal industry back to acceptable levels. Research sponsored by the government, together with the mixed feed industry, was started some years ago to study the possibilities of reducing the N and P output of poultry and swine by changing feeding systems, diet compositions and other measures involving the animals.

In Table 3 a rough calculation regarding the importance of the two main routes of N excretion of a fattening pig over the range 20-110 kg is given.

Table 3. Routes of N excretion in a fattening pig (20-110 kg live weight)

Input of total N (270 kg feed x 16% crude protein) =	7.0 kg
Input of faecal digestible N(digestibility N = 85%) =	6.0 kg
N in 110 kg pig(protein content 15%)	2.5 kg
1) Output of faecal N =	1.0 kg
2) N in urine	3.5 kg
(Input of faecal digestible N - N in body at 110 kg)	

The figures for feed conversion (3.0), dietary protein content (16%), digestibility of the protein (85%) and protein content in the slaughter pig (15%) are estimations based on present-day practical situations in the Netherlands.

From these figures it can be deducted that the efficiency of N deposition, expressed as a percentage of intake of total N, over this weight range is approximately: $36\% \frac{(2.5 \times 100)}{7.0}$.

It is clear that the main route of N excretion is via the urine; therefore in the research programme aimed at reducing N output in pigs, the main emphasis is on this aspect.

Faecal N output can in theory be reduced by a lower dietary N content or an increased digestibility of dietary N. A higher N digestibility can be attained by a choice of highly digestible feed components or by technological measures to increase digestibility of lower digestible feed components, for example via enzymes.

Urinary N output can be reduced via dietary measures by optimally balancing the amino acid composition of the diets in such a way that the requirements of the animal for maintenance and production are adequately covered and no surpluses of amino acids are present. The potentials in this direction are considerable; however, progress is limited by a lack of knowledge of the exact requirements of amino acids other than lysine and methionine + cystine (threonine, tryptophan, isoleucine). The first goal of a research project, in which ILOB and State institutes are cooperating, is to determine these requirements. In theory substantial reductions in the protein contents of pig diets are possible by supplementing low-protein basal diets with the relevant amino acids. The practical application will be mainly dependent on the availability of those fermentatively produced amino acids and on the price level of these amino acids in comparison with the protein-bound amino acids in natural feedstuffs.

It was recently estimated (v. Weerden, 1988; Jongbloed et al., 1985) that a reduction of urinary N output in the order of 20% may be practically possible.

Reduction via the intermediary metabolism

A second potential way to reduce urinary N output is the intervention in the intermediary N (amino acid) metabolism via application of hormones or hormone-like compound. Examples are the anabolic steroid and related compounds, growth hormone or somatotropine (ST) and, to a certain extent, the β-agonists. The potent zoötechnical effects of the three categories of agents, all acting via a shift of the energy deposition in the body from fat to protein, have been extensively discussed in a number of conferences (Lu and Rendel, 1975; ASAS, 1987, 1988; Hanrahan, 1987).

Because these agents drastically improve the efficiency with which the protein in the feed is converted to protein in the body, it is evident that they will also affect urinary N excretion and in this way reduce pollution.

To quantify the effects of porcine somatotropine (PST) on N and P excretion, the results of a recent experiment carried out in a cooperation between the Agricultural University Wageningen and ILOB-TNO will be presented.

Short communications of the data obtained in this experiment have already been reported at the ASAS-meeting of this year (Huisman et al., 1988; Van der Hel et al., 1988).

In this experiment the effects of recombinant porcine somatropine (rpST) on N and P deposition were studied in crossbred (Dutch Landrace x Dutch Yorkshine, F1), Pietrain and Duroc pigs. The effects of rpST on N and P balance and on weight gain and feed conversion were of the same order

of magnitude in the three breeds. For the calculation of the effects of rPST on N and P excretion only the figures obtained in the F1-animals are used.

Twelve castrated male pigs of approximately 58 kg live weight were allocated to two groups of six animals each, a rpST group (dose, 4 mg per day) and a placebo group. The experiment was finished ten weeks later. During the last six weeks N balance was measured six times (P1-P6) during 6 days per period. P and Ca balance was measured only in test period P2.

The animals were fed at a restricted level of 260 kcal M.E. per kg^{*75}; in P1 the daily amount of feed supplied was approximately 2.4 kg, and in P6 2.9 kg. The diet contained 19.4% crude protein and 0.92% faecal digestible lysine, levels which are approximately 25% higher than in normal practical feed formulations.

The result for weight gain, N deposition, and efficiency of N retention in the different parts of the experimental period are presented in Tables 4 and 5.

Table 4. Weight gain and feed conversion in control and rPST group

Live weight	Control (kg)	(kg)	rPST (% of control)
at start of experiment	57.7	58.5	101
test period P1	80.7	83.7	104
test period P2	87.6	92.0	105
test period P3	93.6	98.1	105
test period P4	100.4	105.5	105
test period P5	107.4	113.6	106
test period P6	112.9	118.6	105
slaughter	119.5	126.1	106
P1 - P6, in g/day	924	1010.*	110
start-P6, in g/day	883	964.*	109
Feed conversion:			
P1 - P6, abs.	2.89	2.69*	93
start - P6, abs.	2.74	2.55*	93

* significantly different from control (P < 0.05).

Table 5. N balance and efficiency of N retention (as % of intake)

| Test period | N balance | | | Efficiency | |
	Control (g/day)	rpST (g/day)	rpST (% of control)	Control	rpST
P1	27.9	33.8	121	39.1	46.0
P2	30.4	36.4	120	40.1	46.2
P3	26.5	34.6	131	33.4	42.0
P4	26.1	34.5	132	31.3	39.9
P5	23.7	30.7	130	27.2	34.6
P6	23.7	31.0	131	26.5	34.6
mean	25.7	33.6*	131	32.9	40.6

* significantly different from control (P < 0.05)

Weight gain and feed conversion efficiency of the rpST animals from about 80 kg live weight onwards were significantly improved with 10% and 7% respectively compared to controls. N deposition was significantly increased with 31% and 7.7%, more of the dietary N being retained in the body of the rpST pigs.

As was to be expected, the effect of rpST on N balance was only on the excretion of N via the urine. Excretion via the faeces was the same in both groups (N digestibility in controls on average 82.5%, and in the rpST group 82.6%).

Results of the measurement of P and Ca balance during the test period P2 are given in Table 6. Both mineral balances were increased with 18 and 19%, respectively, in the rpST treated group; the efficiencies of P and Ca retention were increased by 4.8 and 4.6%, respectively.

Table 6. P and Ca balance in test period P2

	Control (g/day)	rpST (g/day)	(% of control)	Efficiency (% of intake) control	rpST
P balance	6.3	7.5*	118	34.0	38.8
Ca balance	8.7	10.3	119	30.2	34.8

* significantly different from control (P < .05) .

Calculation of reduction of pollution

From the results presented in Tables 4, 5 and 6 the effects of rpST on excretion of N and P were calculated. For these calculations different ways can be applied. First, one can base the estimations on an equal time period for the control and rpST group, for example P1-P6. However, at the end of test period P6 the rpST animals were approximately 7 kg heavier than the control pigs and, although the treated pigs are considerably less fat than the untreated ones, one may not assume beforehand that because of that, the growth hormone treated pigs will be slaughtered in practice at a heavier weight. It was therefore decided to estimaten and P excretions over a time period during which the animals reached a common slaughter weight.

In this case a rather practical final weight of 110 kg was chosen. Because N balance was only measured during the last 6 weeks of the ten-week's treatment period, the figure for the rpST effect on N retention during the first four weeks of the treatment period had to be approximated. We have assumed that the effect of rpST on N retention during the first four weeks was the same as during the last six weeks, i.e. as a percentage of N-intake, 7.7% higher. The results of the calculation are given in Table 7 for N and in Table 8 for P. To estimate the effect on P excretion, the figures measured in test period P2 were extrapolated to the whole ten week treatment period.

Table 7. Calculation of N excretion per animal

	Control	rpST
Weight range (kg)	57.7 - 110	58.5 - 110
Number of days	59	53
Feed intake (kg)	138	124
N intake (g)	4280	3845
Efficiency of N retention (% of intake)	32.9	40.6
N excretion (% of intake)	67.1	59.4
N deposition in body (g)	1410	1560
N excretion (g)	2870	2285
Difference (g)		- 585
Difference (%)		- 21

Table 8. Calculation of P excretion per animal

	Control	rpST
Weight range (kg)	57.7 - 110	58.5 - 110
Number of days	59	53
Feed intake (kg)	138	124
P intake (g)	950	855
Efficiency of P retention		
(% of intake)	34.0	38.8
P excretion (% of intake)	66.0	61.2
P deposition in body (g)	325	330
P excretion (g)	625	525
Difference (g)		-100
Difference (%)		- 16

The figures in Table 8 show that rpST application over the weight range from 58 to 110 kg reduced N excretion by approximately 21%. In this period P excretion was diminished by approximately 16%. When we assume that from the total amount of feed consumed by a fattening pig over the weight range 20-110 kg, approximately 70% is eaten in the range 60-110 kg (Jongbloed et al., 1985), then the reduction in N output of that fattening pig amounts to approximately 15% when rpST is applied in the second part of the fattening period.

The calculations given above refer to pigs fed on a restricted scale. European pigs are at present, however, fed for a considerable part on an item basis. Data obtained by Kanis et al. (1988) in pigs of the same breed fed ad libitum the same basal diet as in our experiment showed an effect of rpST treatment over the live weight range 60-100 kg of +6% on daily weight gain and -10% on feed conversion. Above 100 kg live weight the effects were greater. These data suggest that the effects of rpST on weight gain and feed conversion are of the same magnitude in restricted and ad libitum fed finishing swine. It is therefore likely, that the effects of rpST on N deposition and N excretion will also be of the same magnitude.

Discussion

The main uncertainty remaining for predicting more precisely the effect of PST treatment on N output is the lack of knowledge on the levels of protein/amino acids needed to sustain the extremely high (approx. 30% above "normal") protein depositions observed in PST-treated animals. In the "Wageningen-experiments", as well as in other studies reported, the protein/amino acid contents of the basal diets were considerably higher than normal in order to have a safety margin. At present, research is being carried out at different locations, and also in Wageningen, to find out whether or not the requirements for amino acids/protein for PST-treated animals are increased.

Considering former ILOB-results with veal calves implanted with an effective anabolic steroid combination (estradiol + trenbolone acetate) and fed diets with different milk protein contents (Van der Wal and Berende, 1983), we expect no dramatic increase in these requirements. The somewhat irregular weight gain response pattern of PST-treated ad libitum fed pigs given diets with different protein levels (Newcomb et al., 1988) seemed to agree with this supposition. Even if dietary protein levels appear to be somewhat increased in order to reach the maximum rpST-response, it is still questionable whether under these circumstances higher protein doses are economically justifiable.

In conclusion it can be stated that rpST is an effective tool in reducing N (and P) output of swine.

More experimental data are needed to calculate more precisely the extent of this effect on N (and P) pollution of the environment, but an improvement in the order of 20% N for growing-finishing swine in the live weight range of 60-110 kg seems a reliable estimate.

Literature

Anabolic Agents in Beef and Veal Production, 1981. Proceedings of a workshop held at Brussels, March 5th and 6th, 1981.

American Society of Animal Science, 1987. 79th Annual meeting 1987. Journal of Animal Science Vol. 65, Supplement 1 and Vol. 66, Supplement 1.

American Society of Animal Science, 1988. 80 th Annual meeting 1988. Journal of Animal Science Vol. 65, Supplement 1 and Vol. 66, Supplement 1.

Hanrahan, J.P., 1987. Beta-agonists and their effects on animal growth and carcass quality. Elsevier, Londen and New York.

Huisman, J., E.J. Van Weerden, W. Van der Hel, M.W.A. Verstegen, E. Kanis and P. Van der Wal, 1988. Effect of rpST treatment on rate of gain in protein and fat in two breeds of pigs and as crossbreds. J .An. Sci 66, Suppl. 1, 254-255.

Jongbloed, A.W., A. Steg, P.C.M. Simons, W.M.M.A. Janssen, N.P. Lenis, J.A.C. Meys and K. Vreman, 1985. Mededelingen IVVO no. 3.

Kanis, E., K.H. de Greef, W. Van der Hel, J. Huisman, R.D. Politiek, M.W.A. Verstegen, P. Van der Wal and E.J. Van Weerden, 1988. Interactions of recombinant porcine somatotropin (rpST) treatment with genotype and slaughter weight for production traits for growing pigs. J. An. Sci. 66, Suppl. 1, 29 6.

Lu, F.C. and J. Rendel, 1975. Anabolic Agents in Animal Production. FAO/WHO Symposium Rome, March 1975. Georg Thieme Publishers Stuttgart, 1976.

Newcomb, M.D., G.L. Grebner, P.J. Bechtel, F.K. Mc Keith, J. Novakofski, D.G. Mc Laren and R.A. Ester, 1988. Response of 60 to 100 kg pigs treated with porcine somatotropin to different levels of dietary crude protein. J. An. Sci. 66, Suppl. 1, 281.

Van der Hel, W., M.W.A. Verstegen, J. Huisman, E. Kanis, E.J. van Weerden and P. van der Wal, 1988. Effect of rpST treatment on energy balance traits and metabolic rate in pigs. J. An., Sci 66, Suppl. 1, 255.

Van der Wal, P. and P.L.M. Berende, 1983. Effects of anabolic agents on food producing animals. Anabolics in Animal production. Symposium held at OIE, Paris, 15-17 February 1983 : 73-115.

Van Es, 1978. The future of beef production in the European Community. Martinus Nijhoff Publishers, The Haque/ Boston/ London.

Van Weerden, E .J., 1988. Beperking mineralenemmissie via veevoeding. Themadag Ede, 19 januari 1988, 34-43.

ADOPTED CONCLUSIONS OF SESSIONS

Conclusions from sessions as proposed by the chairmen and moderators; discussed and adopted in the plenary session at the end of the symposium.

Implications for the production system

Effect on requirements and wellbeing of the target animals

Consumer aspects

Environmental and economic impact

IMPLICATIONS FOR THE PRODUCTION SYSTEM

Chairman: R.G. Zimbelman
American Association of Animal Science, Bethesda MD, US

The undisputed improvement in increasing protein deposition and decreasing fat deposition from injections of RPST were markedly consistent across breeds, nutritional level, sexes and various management schemes in North America, Europe and China. The magnitude of response varied, but even the lowest responses were striking. The results were evident from visualization of carcass as well as from numerical data.

Also consistent was a reduction in feed intake as well as increased feed efficiency. Magnitude of increase cannot be expressed specifically because of several factors: 1) no hard data on optimum dosage, 2) the apparent interaction of dose with nutrition, i.e. higher protein deposition from higher doses may require altered composition of diet whereas more minimal responses may not; studies presented varied in length of treatment, dosage used, and initial and ending weights.

The potential for an acceptable product will largely depend on a practical slow release delivery system. Several companies may be successful to varying degrees, a generic description of efficacy may be virtually impossible slight modifications in chemical structure or conformation of PST. Prolonged release devices or formulations will likely sacrifice some efficacy and cost benefit considerations may influence the usage decision by different producers.

Grading systems and processing industry needs are quite complex and require serious consideration. There are a number of concerns, including pork belly thickness, processing procedures, as well as intramuscular fat levels, which may not be optimal with markedly decreased fat levels. Some of these may be aided by increasing slaughter weight, but that would be resisted for certain fresh cuts or current products.

An in depth study of how to react to extremely lean pigs is thoroughly needed in both the United States and various European markets. Results of research from pigs in the United States or from pigs which are not very lean may not apply to European programs in which lean pigs are already prevalent. Research in those situations is needed to assess whether benefits occur as well as whether there are currently undetected disadvantages in relation to meat quality or processing characteristics.

Genome modification is progressing at an amazing speed in terms of developing theoretical approaches to achieving and controlling gene insertion. The advantage of gene insertion over PST administration by injection may be greatest in pigs which already have some desirable traits, such as high prolificacy. In these pigs growth and carcass improvements would come from added PST or GRF genes. On the other hand it is likely to be many years (at least 8 to 10) before a useful breeding animal results. It is most probable that the progenitor transgenic will have a single gene insertion controllable by some feed or cheap input compatible with commercial production.

The breeding of that animal after puberty to a large group of mates suggests a requirement for a male, the subsequent mating of his offspring to achieve homozygosity. This will require considerable time. Finally, a "performance" test long enough to allow time for expression of undesirable traits prior to widespread introduction into the gene pool would be prudent. This would be costly in resources and time; therefore society should develop mechanisms, such as patents, to allow investors a reasonable return on their very risky and substantial investment if this technology is to proceed to commercialization.

Whether PST usage would require modification of testing and selection procedures used for genetic improvement depends on whether there is an interaction of PST usage with other desirable traits than performance and carcass characteristics.

One serious consideration is whether the most lean animal should be the objective. The specific description of fatty acid composition changes in PST or transgenic pigs should be a high priority.

Some caution in applying these new exciting technologies might be very prudent. Enhancing our understanding of how effects are achieved will be quite essential in chasing a "moving target".

REQUIREMENTS AND WELL BEING OF THE TARGET ANIMAL

Chairman: P.R. Wiepkema
Wageningen Agricultural University, The Netherlands

Animals maintain internal and external homeostasis by means of well-balanced, complex and interwoven regulatory systems. Many of the environmental parameters involved are controlled actively by the animal.

When changing relevant production traits of domestic animals the balance of existing homeostatis requires attention. For meeting requirements and well-being of the target animals, the main and side effects of novel technology need adequate clarification.

Campbell showed that PST treatment presumably effects fat reduction and protein increase not to the same extent. For this latter effect an adequate amount of protein should be available in the diet. The two effects interact with dosage of PST and with breed, sex and live weight.

A decreased feed intake, observed in trials, up to 100 kg body weight is associated with a significant decrease in fat deposition and increased protein accretion. The related impact on amino acid, fatty acid and glucose metabolism asks for further elucidation.

Verstegen showed, that PST treatment increased heat production, reflecting a higher metabolic rate. This increase may stem from a higher maintenance requirement or/and a reduced efficiency of energy utilization above maintenance level.

Curtis calculated the potential impact of the reduced thickness of the subcutaneous fat layer on the thermoregulatory capability of the PST treated pigs. It may lead to a narrowing of the thermoregulatory zone at the upper and under limits. For this reason effects on thermoregulation of the animals require determination of optimum temperatures for PST animals.

Information on the behaviour (social organization, feed and water intake, rest, etc.) of group housed and PST treated pigs is required, in order to evaluate a priori problems, that may arise under practical and intensive husbandry conditions. The reaction of PST treated pigs to being transported to the slaughter house, when high demands are made upon the pigs thermoregulatory capacity, requires special attention.

Kelley emphasized the positive role of PST under normal conditions with respect to activating the immune system (macrophages). Whether PST treatment may benefit the health of the pigs involved cannot be stated at the moment.

Day showed that PST when used before puberty does not disturb reproductive processes taking place some weeks after the end of the treatment. PST treatment during oestrus led to contradictory results.

CONSUMER ASPECTS

Chairman: B. Hoffmann
Justus Liebig University, Giessen, Germany

As was layed out by Norcross, U.S.D.A., in the U.S.A. well established regulatory procedures allow an adequate risk-benefit assessment concerning the use of drugs in food animals. As a product of recombinant DNA-technology PST falls within the responsibility of the F.D.A.; F.D.A. has allowed the use of PST for efficacy in research studies under the NIDA-regulations without a withdrawal period; similarly no withdrawal period is necessary for milk concerning the use of BST under similar conditions.

Some still open questions - eg. the relevance of altered IGF-1 levels for consumer safety - request to be answered prior to a final approval. According to Norcross other regulatory procedures are available to deal with approval of transgenic animals. Norcross strongly endorsed communication and exchange of views and data between regulatory agencies and others concerned with these problems.

It was made clear during the discussion that, different to the U.S.A. adequate and efficient regulatory pathways have evolved in Europe only since the late sixties (U.K.) and late seventies (F.R.G.) or they are still being established in other E.E.C.-member states.

According to Schams, who presented data on PST and IGF-1 from a collaborative study, base-line levels in blood plasma are reached within 26 hours for ST and within 4 days for IGF-1 following treatment with PST. Preliminary data on ST and IGF-1 in muscle have been presented indicating that no residues are present 4 days after treatment. No data concerning IGF-1 levels in liver and kidney are available and further information on the break down of IGF-1 and the formation of fragments likely to be bioactive is necessary.

Prusa and Demeyer in their presentations confirmed the general trend of leander carcasses and decreased intramuscular fat following treatment with PST; however, apparent breed differences have to be taken into account. Although measurable differences in nutritional composition and sensory quality between PST-treated and untreated animals have been reported, no major concerns are evident. Protein and moisture contents of muscle increased slightly similarly as polyunsaturated fatty acid contents in raw pork and cholesterol in cooked pork; thiamine contents were reported to decrease slightly. Overall sensory quality was not altered, though some deviations from the control groups have been reported.

The possibility to reduce fat and caloric intake from pork by application of PST has been discussed as one form to improve human nutritional quality.

From the consumers point of view Graham requested open communication. Perception by the consumers relates to more than safety, it includes other ethical matters, e.g. animal welfare. The modern consumer, who is able to handle computers and other sophisticated instruments, wants to be consulted, he further is able to be educated, i.e. he will be able to deal with information from industry and science. In this sense Graham discussed the problem of labelling of certain products as to their origin; she further disagreed in calling products to increase efficiency health products.

The still open questions, however, are who is the consumer and on what platform he can be met and how to spread solid information.

Dantzer, who presented a philosophical approach to the problem, referred to the normative type of the process in establishing ethical values. In order to forward certain ideas at the level of society, the potential impact of biotechnology on the socio-economic structure of animal production should be addressed. Although biotechnology has great potential for improving the efficiency of animal

production, a thorough consideration of ethical issues raised by their introduction is necessary for their understanding and acceptance by society.

ENVIRONMENTAL AND ECONOMIC IMPACT

Chairmen: K. AIBARA and G. VAN DIJK
Food and Drug Safety Research Center, Kanagawa, Japan, Wageningen Agricultural University, The Netherlands

The introduction of recombinant porcine somatotropin (rpST) in pig production will depend on a number of factors, most of which are now being quantified. Among these are farm economics, effects for the market chain, consumer acceptance, impact on the physical environment, government attitudes and ethical considerations.

Farm economics

Hayenga has made clear that cost advantages will induce a high adoption rate - all under the assumption that there will be no severe restrictions because of consumer acceptability. His figures indicate rates of 50-60% in 2-3 years. rpST will result in lower costs and hence early adopters will see their profit margins increased. This situation is not a stable one, however. After some time competitors will force laggards to adopt and profit margins down as prices in this industry have the tendency to equal long run average costs. Eventually consumers will benefit most persistently. Under European conditions also the processing and marketing industries will be able to secure part of the share. Pease suggests that the processing industry could take a "substantial" share. It seems that this statement is essentially valid for the short run. In the longer term similar conditions apply as to the farming sector.

Nevertheless part of the profit will remain in the farming and processing sectors.It is basically via new technologies that general growth in income and parity with general economic growth is achieved in those industries. This is normal.

The market effect

There will be little growth in demand, apart from substitutes effects. There is also little trade from Europe, US, Japan. Increasing islamic proportions of demographic changes makes the international pork market more of a stable nature than are, potentially, the prospects for beef, for example.

Steele and discussants pointed out that lower prices for pork will stimulate substitution of beef by pork. However, little quantitative information on elasticities of substitutions - assuming substantial price changes - is available. Studies are underway (Hayenga).

As regards the effects of introducing rpST on processing practices McKeith reported that there are hardly such effects. In any case such effects occur normal technology would easily master them. rpST has positive influence with regard to the environmental constraints. Van Weerden showed that per kg product there will be a decrease in polluting emissions (of N and P) ranging from -15 to -20%. No doubt these effects are substantial if not decisive for the Netherlands. The economic effects and valuation of the ecological argument, however, are still to be quantified. Assuming the installment of restrictions on P and N emission are forced by law, the introduction of rpST can be regarded as an important instrument in addition to other measures to diminish polluting effects. As a whole measures for environmental protection will lead to changes in production systems.

Consumer acceptance is not a datum. It can be changed via marketing and promotion or brand-policies. Progress in this respect has been very modest so that pork still has the status of a bulk product. Changing marketing policies however now seem underway. In such a development producers will be more integrated in the entire market channel. This may result in contract

production and vertical quality management. Under those conditions the consumer acceptance issue is dealt with in the normal way: quality is not perceived automatically by consumers and consumer's trust has to be won.

Government policies may resist to the introduction of rpST because of social and economic considerations. The structural implications in the country side may be substantial. rpST then could easily become an instrument for establishing ingingtrade barriers. However, in Europe this will gradually become less likely because of the consumer will obtain a more crucial position. Most of the discussants considered that big effects of location changes in pig production would occur because of the introduction of rpST.

Summarizing of effects interacting with economic impact:

farm economics   : stimulating for rpST introduction
ecological argument   : id.
consumer   : "you may convince me"
feed requirements/health : positive
tax payer   : (probably) neutral
target animal   : requires more in depth discussion

254

FRENCH RESUME

Scope of sympisium

Summeries of papers

Conclusions of sessions

BIOTECHNOLOGIES APPLIQUEES AU CONTROLE DE LA CROISSANCE ET DE LA QUALITE DU PRODUIT CHEZ LE PORC: IMPLICATIONS ET CRITERES D'AGREMENT

COMPTES-RENDUS DE

SYMPOSIUM

WAGENINGEN, PAYS BAS 12 - 14 DECEMBRE 1988

Sponsors:
Industrie des biotechnologies
Communauté Européenne
Wageningen Agricultural University

Editeurs:
P. van der Wal
G.J. Nieuwhof
R.D. Politiek

Co-éditeurs:
Chinois -   K.F. Fung
            S.Z. Qi
Français - A.A. Rérat
            R. Dantzer

CIP-data Koninklijke Bibliotheek, Den Haag

COMITE D'ORGANISATION:

Président: R.D.Politiek, Wageningen Agricultural University NL
Sécrétaire: P. Van der Wal Wageningen Agricultural University NL
Assistant: G.J.Nieuwhof

Membres: H.Karg München Technical University, DE
K.F.Fung South China Agricultural University Guangzhou, CH
R.G.Zimbelman American Association of Animal Science, Bethesda MD, US

PRESIDENTS ET MODERATEURS:

Président: R.D.Politiek, Wageningen Agricultural University NL
Sécrétaire: P. Van der Wal, Wageningen Agricultural University NL
K. Aibara Food and Drug Safety Research Center, Kanagawa, JP
L.L. Christian Iowa State University, Ames, US
G. Van Dijk Wageningen Agricultural University, NL
F. Ellendorff Institut für Tierzucht und Tierverhalten, Mariensee, DE
B. Hoffmann Justus Liebig University, Giessen, DE
R.L. Kline National Pork Producers Council, Des Moines IA, US
G.E. Lamming University of Nottingham, Sutton Bonington,GB
O.G. Pedersen Danish Bacon and Meat Council, Copenhagen, DK
A.A. Rérat Institut National de la Recherche Agronomique, Jouy-en-Josas, FR.
L. Reijnders Stichting Natuur en Milieu, Utrecht, NL
P. Wiepkema Wageningen Agricultural University

259

TABLE DES MATIERES

4: EFFETS SUR LES BESOINS ET LE BIEN-ETRE DE L'ANIMAL-CIBLE

MODE D'ACTION PHYSIOLOGIQUE
Mécanismes par lesquels l'hormone de croissance porcine (pGH) et les somatomédines (IGFs: Insulin-like growth factors) régulent les performances de croissance chez le porc: du récepteur à l'animal entier
T.D. Etherton

BESOINS NUTRITIONNELS ET CONDITIONS D'EXPLOITATION
Influence de la somatotropine porcine sur le métabolisme énergétique du porc
M.W.A. Verstegen, V. van der Hel et E.J. van Weerden

Répercussions des techniques biotechnologiques visant à la manipulation de la croissance et du développement des animaux sur les besoins nutritifs, tissulaires et alimentaires chez le porc
R.G. Campbell, R.J. Johnson et R.H. King

SANTE ET REPONSE IMMUNITAIRE
Effets de la somatotropine sur le système immunitaire
K.W. Kelley, C.K. Edwards

EFFETS SECONDAIRES
Effets secondaires potentiels de la somatotropine exogène chez le porc
S.E. Curtis

EFFETS SUR LA REPRODUCTION ET LA LACTATION
Répercussions des nouvelles technologies pour l'amélioration des performances de croissance sur la reproduction et la lactation chez le porc
B.N. Day, S. Terlouw et A. Rieke

5: ASPECTS INTERESSANT LE CONSOMMATEUR

SECURITE DES PRODUITS COMESTIBLES
Biotechnologies et contrôle de la croissance et de la qualité du produit chez le porc: sécurité des produits comestibles
M.A. Norcross, R.A. Carnevale, E.A. Brown et A.R. Post

Apparition potentielle de résidus après traitement des porcs avec de la somatotropine recombinante
D. Schams, E. Kanis et P. van der Wal

CARACTERISTIQUES NUTRITIONNELLES ET ORGANOLEPTIQUES
Caractéristiques nutritionnelles et organoleptiques de la viande de porcs traités par la somatotropine
K.J. Prusa

Effet de la somatotropine porcine recombinante sur la qualité de la carcasse et de la viande de porcs belges et hollandais
D.Demeyer, R. Verbeke, G. van de Voorde, J. Fabry, E. Deroover et R.H. et Dalrymple

L'OPINION DES CONSOMMATEURS
L'opinion des consommateurs sur les technologies et biotechnologies appliquées à l'alimentation
J. Graham

CONCLUSIONS

OBJECTIFS DU SYMPOSIUM

L'accès à des produit carnés de bonne qualité à des prix abordables est devenu un droit pour une partie de plus en plus importante de la population mondiale. La mise en pratique des connaissances acquises dans le domaine de la recherche animale a permis de répondre à cette demande des consommateurs. Le perfectionnement des "outils" scientifiques, grâce au développement des biotechnologies est une étape probablement essentielle pour faire face aux demandes futures tout en tenant compte des contraintes grandissantes dans le domaine de la production.

La superficie des cultures destinées à l'alimentation animale est limitée et la capacité d'absorption par l'environnement des excreta polluants a déjà été dépassée dans de nombreux endroits. Le maintien du système de production animale actuel ne peut donc plus être garanti. Les exigences quant à la qualité et la sûreté d'utilisation des produits sont maintenant définies de façon précise. De même, le bien-être des animaux demande à être mieux pris en compte.

Les progrès en biotechnologie ouvrent des perspectives de plus en plus larges pour permettre de répondre à ces exigences avec efficacité. Des améliorations significatives de l'efficacité et de la qualité de la production animale deviennent possibles. L'objectif de ce symposium est l'étude, dans un contexte général, des possibilités et des contraintes des nouvelles technologies pour le contrôle de la croissance et de la qualité des produits et dans les réponses apportées aux exigences des consommateurs, de l'animal et de l'environnement.

Priorités pour l'amélioration de la production animale

L'amélioration de l'efficacité de la conversion de l'aliment en viande est certainement la perspective la plus prometteuse pour le maintien à long terme du système de production animale. Elle permet de réduire la superficie des cultures destinées à l'alimentation animale et d'abaisser le prix de la viande. Enfin, elle constitue le facteur le plus efficace pour diminuer la pollution de l'environnement liée aux excreta animaux.

Depuis qu'il devient évident qu'un excès d'apport calorique est nuisible à la santé de l'homme, un produit de bonne qualité doit être plus maigre et moins gras. La sécurité d'utilisation du produit ainsi que son goût et sa tendreté sont aussi des paramètres prioritaires.

Le bien-être des animaux, à savoir leur santé et leur comportement, peut être mieux appréhendé par les progrès réalisés en physiologie animale, en éthologie et en immunologie.

Les nouvelles biotechnologies

Diverses technologies appliquées en physiologie et potentiellement à même de combiner rentabilité et sécurité ont été sélectionnées afin d'être analysées lors de ce symposium. Ces technologies se refèrent à "l'axe somatotrope".

La croissance des espèces animales productrices d'aliments est contrôlée par le génome qui exprime ses potentialités dans le système d'interactions entre somatocrinine (GRF: somatotropin releasing factor) - somatostatine - somatotropine - somatomédines.

Depuis 6000 ans, l'homme est intervenu sur ce système en modifiant progressivement le génome des animaux par la sélection systématique afin d'adapter la production animale à la demande.

Ces 10 dernières années, ce processus a été accéléré de façon considérable grâce à l'insémination artificielle et la transplantation embryonnaire alors que d'autres technologies de pointe faisaient leur apparition.

En effet, une modification plus sélective du génome a été récemment apportée par l'insertion de gènes contrôlant la croissance dans le patrimoine héréditaire des animaux producteurs d'aliments.

Une intervention encore plus sélective sur le système physiologique contrôlant la croissance a consisté à modifier le niveau de ses différents constituants. Cela a pu être réalisé, par exemple, en

administrant directement de la somatotropine et de la somatocrinine (GRF: growth hormone releasing factor).

La dernière acquisition permettant d'intervenir sur l'axe somatotrope provient des techniques d'immunisation. La potentialisation de l'effet de la somatotropine et la neutralisation de l'effet de la somatostatine ont été rendues réalisables grâce aux anticorps.

Evaluation des critères de sécurité et de rentabilité

Le mode d'action commun de ces technologies conduit de plusieurs façons à des effets comparables sur les animaux cibles, leurs produits et l'environnement. Il paraît donc justifié de les étudier dans leur ensemble pour leurs dénominateurs communs.

Durant ces dernières années, les biotechnologies ont permis de fournir à la recherche zootechnique les différents éléments clefs de l'axe somatotrope, de façon séparée, ce qui a conduit à une meilleure compréhension de leurs effets.

L'accumulation rapide de nouvelles données scientifiques augmente les possibilités d'analyse des implications potentielles des trois types de technologies nouvelles impliquées dans le contrôle de la croissance, qui ont été mentionnées dans le paragraphe précédent.

L'introduction d'innovations dans le domaine de la production animale a déjà montré par le passé et de façon répétée que leur réalisation conduit facilement à de profondes divergences d'opinion quant à leur agrément. Leur innocuité pour le consommateur a été un objectif primordial pendant longtemps. Plus récemment leur innocuité pour l'animal cible, l'impact sur l'environnement et les répercussions sur les structures de système de production ont aussi été pris en considération.

Les questions concernant le seuil d'admissibilité des nouvelles technologies ont souvent été définies assez tardivement au cours de leur évolution. Le manque d'attention sur la nature de ces questions a empêché leur prise en compte effective dans les protocoles experimentaux. Le résultat en a été que les réponses adéquates ont été apportées avec retard et à un coût plus élevé que nécessaire.

Pour une meilleure concertation entre recherche et réglementation des applications de ces technologies, l'organisation régulière de consultations internationales réunissant les diverses parties impliquées de la communauté scientifique paraît absolument nécessaire. Une telle consultation a été réalisée lors de ce symposium.

L'état des connaissances actuelles est passé en revue et les priorités de la recherche future sont définies par la confrontation entre scientifiques des universités, groupes de recherche de l'industrie, et institutions impliquées dans les problèmes de réglementation. L'aide financière et la participation de ces 3 catégories illustrent bien la compréhension partagée de la nécessité d'une telle évaluation scientifique commune.

De plus, ce symposium pourrait contribuer également à l'harmonisation de l'implantation de ces technologies de pointe dans des secteurs géographiques stratégiques. Les conséquences néfastes des différences entre ces régions quant aux critères d'agrément et de réglementation n'ont pas besoin d'être énumérées pour démontrer l'urgence d'une évaluation scientifique commune.

RESUMES DES COMMUNICATIONS

(Tableaux et figures dans les rapports originaux)

BIOTECHNOLOGIE, COBPETITIVITE ET AGREMENT: l'ENJEU POUR L'EUROPE

Mark F. Cantley
Directeur de L'Unité de Concertation pour la Biotechnologie en Europe (CUBE: Concertation Unit for biotechnology in Europe) Commission des Communautés Européennes

(Les opinions exprimées n'engagent que l'auteur. Aucun énoncé de la politique de la Commission n'est clairement exposé, si ce n'est ce qui fait référence à des documents officiels).

Résumé

L'auteur n'est pas un spécialiste en biologie, mais il est impliqué dans la conception et l'application d'une stratégie des biotechnologies en Europe. Les questions concernant les implications et les critères d'agrément ont été à l'ordre du jour depuis quelques années, particulièrement en ce qui concerne les applications à l'agriculture des progrès récents de la recherche en biologie et des biotechnologies.

La stratégie communautaire est présentée dans ses grandes lignes: la compétitivité à l'échelon international en est son orientation principale, ce qui permet de renforcer la poursuite des objectifs plus vastes du traité de la CEE. Les critiques publiques et politiques des biotechnologies ajoutent d'autres dimensions à cette notion, telles que l'écologie, les impacts economico-structurels sur l'agriculture, le bien-être de l'animal, les aspects éthiques, les droits et la sécurité des consommateurs. Ceux qui se sentent menacés ou outragés pour un de ces points cherchent des alliés parmi les autres.

Dans ce vaste contexte, les problèmes liés à cette prise de conscience générale et aux critères de valeur sociaux ou culturels compliquent les priorités généralement accordées à la compétitivité économique, sans toutefois nier les bienfaits de l'innovation et de la compétition au sein d'une structure globale commune basée sur une perception partagée des intérêts communs - que ce soit dans un système mondial de commerce libéral sous le contrôle du GATT ou bien avec des contraintes acceptées au bénéfice général de l'écosystème (cf. les limitations maintenant admises au plan international de la production des chlorofluorocarbones).

Il est de l'intérêt public que la communication entre les différentes parties intéressées soit la plus efficace possible afin d'obtenir un meilleur partage de ces opinions et d'élever le débat public et politique

Mots clefs: biotechnologie, Communauté Européenne, compétition de marché, agrément, porc.

LES "OUTILS" BIOTECHNOLOGIQUES DE REGULATION DE LA CROISSANCE CHEZ LE PORC

R. Dean Boyd and Diane Wray-Cahen
Department of Animal Science
Cornell University, Ithaca NY 14853-4801

Résumé

La croissance est un processus parfaitement orchestré qui implique une multitude d'hormones et nécessite des quantités importantes de nutriments. La somatotropine (ST) est une hormone qui régule le métabolisme et qui joue un rôle primordial dans le déterminisme de la répartition postnatale des nutriments absorbés. Chez le porc en croissance, l'administration de ST exogène altère de façon notoire la vitesse et le mode de croissance tissulaire en redistribuant les nutriments vers les tissus spécifiques, et ce, de façon hautement coordonnée. Un accroissement sans précédent dans la production de tissu maigre a pu être mené de pair avec une diminution de la rétention lipidique. Les stratégies qui permettent d'augmenter la concentration sanguine de ce polypeptide naturel vont fournir aux producteurs de porcs la possibilité d'augmenter de façon spectaculaire leur rendement de production, tout en procurant aux consommateurs un produit alimentaire vraiment maigre. Les récentes innovations dans le domaine de la biologie ont fait naître de nouveaux "outils" qui vont permettre aux scientifiques d'employer un grand nombre de méthodes pour réguler la croissance des animaux. Dans cette revue, nous allons discuter de 5 techniques potentielles qui sont actuellement à l'étude, c'est-à-dire l'administration de a) ST exogène, b) secretagogues de la ST, c) somatomédine C (IGF-1 - Insulin-like growth factor 1), d) les manipulations immunologiques de la sécrétion ou de l'activité biologique de la ST, e) l'insertion de gènes ou la régulation de l'expression du génome (i.e. ST, CRF). Dans un futur "proche", l'accélération de la croissance sera réalisée grâce à l'administration de ST exogène, de secretagogues de la ST, ou grâce à l'emploi d'anticorps spécifiques permettant la potentialisation de l'activité biologique de la ST endogène. En ce qui concerne la somatomédine C, de nombreuses questions d'ordre scientifique ne sont tojours pas résolues, ce qui ne permet pas son emploi à des fins commerciales. Dans un futur plus "lointain", il est fort concevable que les manipulations génétiques de l'axe somatotrope seront en première ligne, dans la mesure où les techniques du génie génétique fournissent des méthodes spécifiques et sophistiquées permettant le contrôle de l'expression génétique (i.e. amplification du gène) ou l'insertion de gènes (amélioration génétique - ST, GRF). Nous pouvons d'ores et déjà penser que les manipulations de l'axe somatotrope seront d'envergure suffisante pour permettre le contrôle de la répartition des nutriments et vaincre les réticences du public quant à l'emploi de certaines technologies pour la production de viande. Finalement, l'intérêt dominant de la ST réside dans le fait qu'elle est devenue une "sonde" inestimable pour mieux comprendre les mécanismes de la croissance post-natale et la régulation du métabolisme.

Mots clefs: biotechnologie, régulation de la croissance, répartition des nutriments, somatotropine, somatomédine C (insulin-like growth factor), insertion de gène, porc.

BIOTECHNOLOGIES APPLIQUEES AU CONTROLE DE LA CROISSANCE ET DE LA QUALITE DU PRODUIT CHEZ LE PORC: REGLEMENTATION ET AGREMENT DU PUBLIC.

P. van der Wal

Wageningen Agricultural University, Wageningen, Netherlands.

Résumé

Le contrôle de la croissance et de la qualité du produit chez le porc peut être réalisé par diverses manipulations sur l'axe somatotrope, c'est-à- dire l'administration de ses différents constituants, la modulation de leurs effets par les techniques d'immunisation, l'insertion des gènes en question dans le génome de l'animal.

Les réglementations concernant ces trois technologies diffèrent selon le type de technologie, et selon les pays. Néanmoins, elles exercent un effet comparable sur les aspects de rentabilité et de sécurité d'utilisation par leur mode d'action commun.

L'harmonisation des critères d'admissibilité de ces technologies est essentielle si l'on veut effectivement préserver la sécurité des consommateurs, de l'animal et de l'environnement, tout en créant des objectifs bien définis pour la recherche et le développement. Cet enjeu sans précédent dans le domaine des sciences animales et des aliments nécessite une coopération internationale, en particulier dans le domaine de la recherche. Seuls des efforts communs peuvent permettre de répondre aux problèmes généraux de sécurité et de rentabilité posés par ces technologies. Ces problèmes n'ont pas de spécificité géographique et ils nécessitent une mise en oeuvre de moyens scientifiques et d'expertises spécifiques, qui ont bien sûr leurs limites, où que ce soit.

La coopération internationale en matière d'expertise dans ces domaines devrait permettre l'harmonisation des réglementations internationales et prévenir ainsi toute possibilité de mésentente commerciale au plan international.

Les caractéristiques communes des technologies appliquées à l'axe somatotrope répondent aux préoccupations primordiales de la réglementation en vigueur:

L'efficacité, caractérisée par l'amélioration des rendements de production et de qualité du produit, résulte d'une augmentation de la rétention de protéines et d'une diminution du dépôt de gras.

La sécurité du produit, est garantie par la nature protéique des constituants de l'axe somatotrope, ce qui les rend plus sensibles à la dégradation par l'intestin ou l'environnement.

L'agrément du public concernant ces technologies nécessite une information générale tant sur leurs contributions potentielles quant au coût et à la qualité des aliments que sur la sécurité d'utilisation pour les consommateurs, l'animal et l'environnement.

Un système de réglementation puissant et bien structuré est absolument nécessaire pour obtenir l'agrément des consommateurs. La crédibilité du système dépend de l'amélioration des directives et des procedures permettant l'application des décisions réglementaires.

Mots clefs: contrôle de la croissance, somatotropine, agrément, porc, réglementations.

RENTABILITE DE LA PST EN AMERIQUE DU NORD: CRITERES D'EXPLOITATION ET AVANTAGES.

N.C. Steele, R.G. Campbell, T.J. Caperna, J.P. McMurtry et M.B. Solomon
U.S. Department of Agriculture, Agricultural Research Service, Beltsville Agricultural Research Center, Nonruminant Animal nutrition Laboratory and Meat Science Research Laboratory, Beltsville, MD 20705 USA and Animal Research Institute, Werribee, Victoria 3030 Australia

Résumé

Diverses technologies permettent actuellement de modifier la croissance et la composition corporelle des animaux, en particulier en intervenant sur un des maillons de l'axe somatotrope, modifiant ainsi la production, la sécrétion ou le métabolisms de l'hormone de croissance (GH). Les techniques sont les suivantes: traitement des animaux par une GH exogène, spécifique de l'espèce, administration de somatocrinine (GHRF) et autoimmunisation par la somatostatine. L'administration de GH ou somatotropine porcine exogène (PST) produit des effets marquants sur la croissance et le mode de développement du porc en augmentant le dépôt de tissu maigre avec un dépôt de tissu gras minimal. L'intérêt modial que suscite ce type de technologie est basé sur la présomption de sa rentabilité sans vraiment tenir compte des systèmes d'exploitation en place. Dans le domaine de l'industrie porcine, les systèmes d'exploitation européens favorisent des facteurs comme l'alimentation restreinte, la commercialisation de porcs entiers, les mélanges alimentaires composés de protéines provenant de sources hétérogènes, la répartition de la production porcine pour un marché de porcs lourds ou légers, etc. A l'opposé, le type de production pratiqué en Amérique du Nord est en faveur d'une alimentation ad libitum, de la commercialisation de jeunes truies et de mâles castrés, d'une consommation élevée de protéines de bonne qualité, enfin d'un marché de porcs lourds exclusivement. Dans des expériences récentes, les critères d'exploitation affectant la rentabilité de la PST ont été évalués. Selon les résultats obtenus, la PST semble être absolument indispensable au développement de tissu maigre aussi bien chez le jeune porc que chez le porc à l'engrais. De plus, la prise alimentaire, plus particulièrement la consommation d'énergie peuvent limiter la réponse à la PST. Cependant, l'administration de la PST provoque les mêmes effets dans les 2 sexes, c'est-à-dire que les truies et les porcs castrés répondent à la PST par des taux de rétention protéique comparables à ceux des mâles entiers. Les résultats des recherches en cours semblent indiquer que les technologies liées à la PST sont adaptées aux systèmes d'exploitation actuels, mais que le type d'exploitation du porc pratiqué en Amérique du Nord semble particulièrement propice à son application. Ceci implique que la production de porcs pour l'exportation sur le marché mondial deviendra de plus en plus compétitive puisqu'il existe maintenant des moyens d'uniformiser la production de porc maigre de haute qualité.

Mots clefs: porc, hormone de croissance, composition corporelle, systèmes d'exploitation.

UTILISATION DE LA SOMATOTROPINE PORCINE RECOMBINANTE (rPST) EN EUROPE: ACQUIS ET PERSPECTIVES DE LA RECHERCHE

Vernon R. Fowler[1] and Egbert Kanis[2]

[1] *Rowett Research institute and Schoole of Agriculture, University of Aberdeen, Scotland.*
[2] *Wageningen Agricultural University, The Netherlands*

Résumé

La production porcine en Europe se situe dans un contexte particulier sur le plan agricole, social et scientifique. Depuis plusieurs années, d'énormes efforts ont été fournis pour produire des porcs qui aient une bonne efficacité alimentaire et qui puissent aussi répondre aux normes de qualité fixées par le transformateur. Le problème majeur est de déterminer si l'utilisation de rPST améliore de façon significative la rentabilité dans les conditions de production qui prévalent en Europe.

Les expériences menées dans les élevages européens dans différents centres des Pays Bas, d'Allemagne de l'ouest et du Royaume Uni (Ecosse), ont montré clairement que l'utilisation de rPST améliorait considérablement la vitesse de croissance, l'efficacité alimentaire et particulièrement la teneur en tissu maigre des carcasses. L'augmentation la plus spectaculaire a été celle du taux de dépôt de tissu maigre et de la rétention quotidienne d'azote. Ces faits ont été constatés pour toutes les catégories de poids entre 35 et 140 kg et dépendent de la période et de la dose administrée.

Dans le travail réalisé en Ecosse, où les traitement ont été appliqués entre 35 et 95 kg de poids vif, pour une dose très élevée de 7 mg rPST/jour et un apport de protéines de 19Og/kg, le gain moyen quotidien du groupe traité était de 20 % supérieur à celui du groupe témoin, et la teneur en azote de la carcasse augmentée de 10 %" Dans l'étude effectuée en les Pays Bas sur les bilans azotés en alimentation restreinte, l'accroissement du gain moyen quotidien était de plus de 10 %, l'augmentation du gain protéique quotidien d'environ 30 % et la diminuition du dépôt quotidien de gras d'environ 10 %, même chez le Piétrain. Dans l'ensemble, l'administration de rPST a entraîné une réduction de l'ingestion spontanée d'environ 5 % sauf dans l'expérience Néerlandaise menée en conditions d'alimentation ad libitum, où l'ingestion spontanée était augmentée de 8 % dans le cas des porcs Piétrain ou des porcs croisés, pour la période 100-140 kg de poids vif.

La teneur en protéines des régimes s'est révélée être un facteur important pour que les effets de l'administration de rPST sur le dépôt de protéines puissent pleinement s'exprimer. Il existe maintenant d'immenses possibilités de réalisation d'expériences modèles permettant de trouver la meilleure combinaison possible entre génotype, régime, poids à l'abattage et administration de rPST, afin de tirer les meilleurs avantages de cette nouvelle technologie pleine de promesses.

Mots clefs: somatotropine, porc, qualité de carcasses, vitesse de croissance, efficacité alimentaire, Europe.

PERSPECTIVES D'UTILISATION DE LA SOMATOTROPINE PORCINE POUR LES PORCS CHINOIS

K.F. Fung et S.Z. Qi
South China Agricultural University, Canton, China
Beijing Agricultural University, Beijing, China

Résumé

La somatotropine porcine a été administrée à 44 porcs chinois de race Large Black-White et croisés Landrace dans la province de Guangdong. Les effets sur le gain moyen quotidien ont été plus importants en F1 (+15,3 %) qu'en F2 du croisement d'absorption (+11,3 N). Cependant, ce dernier groupe présentait beaucoup moins de lard dorsal (-19,2) et beaucoup plus de tissu maigre (+17,0%) que le premier groupe (-10,7 % et + 9,8 %).

La somatotropine porcine a également été administrée à Beijing à 48 porcs de race Beijing Black, en cours de finition tardive. Les porcs dont les régimes étaient composés de 18 % de protéines brutes ont présenté un gain moyen quotidien, un indice de consommation et un dépôt de tissu maigre plus importants que ceux qui recevaient des régimes à 16 % ou 14 % de protéines brutes.

Les résultats semblent projeter un nouvel éclairage sur les races chinoises qui pourraient, grâce à l'administration de somatotropine porcine, accroître leur gain de poids quotidien, leur indice de consommation, la teneur corporelle en tissu maigre et réduire l'épaisseur de leur lard dorsal.

Mots clefs: somatotropine, porc, vitesse de croissance, efficacité alimentaire, Chine.

MODIFICATION DIRECTE DU GENOME ANIMAL

Thomas E. Wagner, Ph.D. Director
Edison Animal Biotechnology Center, Ohio University, Athens, Ohio 45701 U.S.A.

Résumé

Les méthodes actuelles utilisées pour l'introduction de gènes dans les lignées germinales d'animaux de laboratoire ou d'intérêt zootechnique sont passées en revue. Les méthodes comprennent le transfert direct de gènes par microinjection dans le pronucleus des oeufs fertilisés, l'infection des embryons par les retrovirus vecteurs, et la production d'animaux à partir de cellules souches embryonnaires multipotentes en culture continue. Bien que des animaux transgéniques (porcs) n'aient été obtenus de nos jours qu'à l'aide de la méthode de microinjection dans le pronucleus, l'utilisation d'une lignée de cellules-souches embryonnaires de porc qui permettrait la production de porcs transgéniques ou clonés, est envisagée. Les caractères phénotypiques des porcs transgéniques exprimant l'hormone de croissance sont discutés en détail, que ce soient les caractères positifs, liés à la réduction de 50% ou plus de la graisse corporelle ou l'amélioration de 30% ou plus de l'indice de consommation, ou les caractères négatifs dûs à des inconvénients plus marqués de structure et à la plus grande sensibilité au stress. Les effets négatifs de l'expression de l'hormone de croissance chez les porcs transgéniques pourraient être surmontés si la période d'expression de l'hormone de croissance était limitée dans le temps à une partie de la vie de ces animaux. Avec cet objectif à l'esprit, des chimères de gènes contenant le promoteur de la P-enolpyruvate carboxykinase (PEPCK) lié au gène de structure de l'hormone de croissance bovine (bGH) ont été introduites dans des lignées germinales de souris et de porcs. Les résultats confirment que l'expression de l'hormone de croissance chez ces animaux ne se produit pas pendant le développement embryonnaire et qu'elle peut être contrôlée par le régime alimentaire. Ainsi, chez la souris, des régimes riches en glucides réduisent de 5 % la concentration sérique en bGH par rapport aux taux de base, alors que la reingestion d'un régime riche en protéines mais dépourvu de glucides augmente de 20 fois la bGH sérique en l'espace d'une semaine. Les études de l'impact du régime alimentaire sur l'expression de la bGH sont en cours chez le porc, mais il semblerait que les porcs transgéniques exprimant le PEPCK/bGH ne présentent pas les mêmes inconvénients que les porcs transgéniques exprimant l'hormone de croissance sous le contrôle d'un promoteur constitutif.

Mots clefs: Transfert de gènes, croissance, porc, régulation, promoteur

TECHNOLOGIES UTILISANT LA SOMATOTROPINE: IMPLICATIONS EN SELECTION PORCINE

Egbert Kanis

Wageningen Agricultural University, Department of Animal Breeding, P.O. Box 338, 6700 Wageningen, The Netherlands

Résumé

L'emploi de techniques biotechnologiques actuelles et futures pour le contrôle de la croissance et de la composition corporelle des porcs aura des répercussions importantes sur les programmes de sélection. Cela est en particulier le cas des technologies faisant appel à la somatotropine, cette hormone ayant des effets positifs considérables sur l'indice de consommation et la composition corporelle des animaux. L'effet de l'administration de somatotropine porcine (PST) et l'utilisation d'animaux transgéniques pour le gène de la somatotropine, vont être traités dans ce rapport.

L'administration de PST à grande échelle peut avoir des conséquences indirectes sur l'intensité de sélection et la réponse génétique. Les caractéristiques génétiques recherchées et leurs valeurs économiques doivent être réévaluées. Dans le cas d'interactions entre le génotype et l'administration de PST, il est recommandé d'administrer la PST aux animaux reproducteurs de base lors du contrôle de performances. Les paramètres génétiques et phénotypiques (héritabilités et corrélations) devraient être réestimés.

La PST offre de nouvelles possibilités d'introduction de races (chinoises) hautement prolifiques en tant que lignées maternelles dans les programmes de sélection. L'influence négative des génotypes chinois sur la composition des carcasses peut être contrebalancée par l'utilisation de PST. L'administration de PST conduit à une augmentation du poids optimum à l'abattage et à une diminution du nombre de porcs à produire par an dans le cas d'une production fixe de viande de porc. Il en résulte que le nombre de truies diminue ainsi que le coût de production.

Le transfert du gène de la somatotropine dans la lignée germinale chez le porc pourrait avoir les mêmes répercussions sur la croissance et la composition corporelle que l'administration de PST. Cependant, il faut signaler que l'emploi de porcs transgéniques aura des conséquences énormes sur la stratégie de sélection dans les troupeaux de base. La variation entre les animaux souches transgéniques créés risque d'être élevée et beaucoup d'animaux vont être réformés à cause de caractéristiques négatives. Les transgéniques restants devraient être utilisés de façon très intensive pour la reproduction, ce qui sera à l'origine de problèmes de faible taille de population. La recherche d'homozygotie dans le produit fini commercial et l'introduction ou non d'autres gènes étrangers dans des lignées déjà transgéniques pour le gène de somatotropine, déterminent la stratégie optimale de sélection.

En conclusion, soulignons que le développement et l'introduction des transgéniques dans le noyau d'un programme de sélection porcine revêt une importance capitale et demande une recherche intensive. Une telle entreprise ne peut être menée à bien que si les organisations d'élevages réunissent leurs efforts dans une action commune.

Mots clés: Somatotropine, transgéniques, sélection porcine

IMPLICATION DE LA SOMATOTROPINE DANS L'INDUSTRIE DE LA TRANSFORMATION DE LA VIANDE PORCINE

F.K. McKeith, P.J. Bechtel et J. Novakovski
University of Illinois, Urbana, IL U.S.A.

Résumé

L'industrie de la transformation de la viande de porc comprend l'abattage ainsi que la découpe et le toilettage des carcasses, la préparation des morceaux de viande fraîche et des viandes salées ainsi que la fabrication de saucisses. Nos études ont montré que la somatotropine conduira à une réduction du gras et à une augmentation de la proportion de maigre chez les porcs en finition. Cette évolution de la composition corporelle pourrait affecter certains ou tous les secteurs de l'industrie de la viande de porc. Les problèmes potentiels associés à la méthode d'abattage et de toilettage impliquent une augmentation de la masse de sous-produits, des difficultés d'écorchage, une modification du taux de refroidissement des carcasses et du ressuyage lors du refroidissement. Les problèmes potentiels associés à la préparation de pièces ou de morceaux de gros comprennent les difficultés de découpe des tissus maigres mous et pliables, la séparation des muscles ou des groupes musculaires lors de la préparation des morceaux à détailler et les difficultés rencontrées lors de l'écorchement des morceaux en évitant d'exposer la surface musculaire. La proportion accrue de masse maigre affectera la teneur en eau et exigera un changement dans le traitement des produits afin d'atteindre les ovectifs recherchés de composition et de conservation à l'étalage. L'évolution de la composition et de l'épaisseur de la poitrine de porc aura des conséquences pour les fabricants de viandes salées, en particulier de bacon (surtout pour le marché Américain). De même, le pourcentage de protéines extraites pour la production de jambon sans os devrait être reévalué. Les fabricants de saucisses seront concernés par les changements potentiels dans les propriétés de la viande telles que la pigmentation, le rapport humidité/protéines, la rétention d'eau, le pH, la teneur en protéines myofibrillaires et la composition du gras.

Il existe un grand nombre de données sur la croissance et la composition corporelle de porcs traités à la somatotropine, mais les renseignements concernant les produits de transformation sont limités. Selon ces données, les procédures d'abattage et de toilettage des porcs ainsi traités ne posent pas de problèmes. Cependant, seulement un nombre très faible de ces porcs ont été soumis à des abattages industriels à grande vitesse. Plusieurs équipes de chercheurs ont examiné les propriétés de transformation des carcasses; l'amélioration du rendement à la découpe ainsi que de la composition des morceaux a été mise en évidence. Nous ne disposons d'aucune information sur des problèmes potentiels à l'abattage tels qu'une incidence accrue de PSE (pale soft exsudative meat). Les problèmes de salaison et de fabrication de saucisses n'ont pas été étudiés directement; cependant, les questions relatives au pH, à la couleur de la viande, à la teneur en gras, aux rapports entre humidité et protéines et aux caractéristiques de poitrine ont été examinées et peu de problèmes ont été notés. La seule exception concerne l'épaisseur de poitrine qui est en corrélation directe avec l'épaisseur du lard dorsal.

Même si l'utilisation de la somatotropine va conduire à des changements pour les producteurs et les transformateurs de viande de porc, nous ne pensons pas qu'elle sera la cause de difficultés insurmontables et les problèmes peuvent être traités par la technologie actuelle.

Mots clés: Somatotropine, rendement à la découpe, transformation, viandes salées, porc

MECANISMES PAR LESQUELS L'HORMONE DE CROISSANCE PORCINE (pGH) ET LES SOMATOMEDINES (IGF's: Insulin-like growth factors) REGULENT LES PERFORMANCES DE CROISSANCE CHEZ LE PORC: DU RECEPTEUR A L'ANIMAL ENTIER.

T.D. Etherton

Department of Dairy and Animal Science, University Park, PA 16802 U.S.A.

Résumé

La GH porcine est une hormone naturelle qui présente une large panoplie d'effets chez le porc. Le traitement des porc en croissance par l'hormone de croissance porcine (pGH) augmente de façon spectaculaire les performances de croissance de l'animal (i.e. gain moyen quotidien, indice de consommation, composition des carcasses). Les actions biologiques de la pGH peuvent schématiquement être classées en 2 catégories, somatogéniques ou métaboliques. Dans ce chapitre, je discuterai de quelques mécanismes par lesquels la pGH affecte la croissance et le métabolisme. La discussion aura pour thèmes 1) les effets de la pGH sur la croissance et le métabolisme du tissu adipeux 2) le rôle de la pGH et de la somatomédine C (IGF-1) sur la stimulation de la croissance musculaire 3) les mécanismes impliqués dans l'hyperglycémie et l'hyperinsulinémie des porcs traités de façon chronique par la pGH 4) les arguments en faveur d'un double rôle des protéines liant les IGF-1 (IGF-BP,): transport des IGF, dans la circulation générale, mais aussi modulation de leur activité biologique et 5) la signification de la séquence d'acides aminés récemment établie à partir de clones d'ADNc qui codent pour les récepteurs de la GH de l'homme et du lapin.

Bien qu'il soit évident à l'heure actuelle que la pGH modifie la composition corporelle des animaux, les mécanismes biologiques par lesquels elle opère ne sont toujours pas élucidés. Il existe peu d'informations quant à la façon dont le récepteur de la pGH génère des signaux chimiques et sur la nature des molécules qui servent de médiateurs intracellulaires pour l'expression des effets biologiques de la pGH. Dans la mesure où notre compréhension des mécanismes d'interaction entre pGH et son récepteur s'affine, il devrait bientôt être possible d'établir quels sont les acides aminés de la pGH qui permettent sa liaison à son récepteur. Cette information permettrait de "créer" des analogues de la pGH qui auraient une plus grande activité biologique. Ainsi, les effets constatés à l'heure actuelle quant au traitement des porcs par la pGH exogène ne représentent en fait que la première étape d'une série de démarches qui conduiront à des moyens économiques et rentables de manipulation des performances de croissance.

Mots clefs: somatotropine, somatomédines (insulin-like growth factors), croissance, régulation, porc

INFLUENCE DE LA SOMATOTROPINE PORCINE SUR LE METABOLISME ENERGETIQUE DU PORC

M.W.A. Verstegen, W. van der Hel, E.J. van Weerden
Agricultural University Wageningen and Institute of Animal Nutrition and Physiology, ILOB, Wageningen, The Netherlands

Résumé

L'administration à des porcs de somatotropine exogène a été étudiée pour ses effets sur le dépôt de protéines et de gras et sur le taux métabolique. La rPST a été appliquée pendant 10 semaines à 3 génotypes de porcs (Piétrain, Duroc et croisés Landrace Neerlandais x Yorkshire Neerlandais), à partir de 55 kg. Les animaux ont tous reçu le même niveau d'alimentation (2.6 fois le niveau d'entretien). Comparés aux animaux témoins, le gain de poids corporel était augmenté d'environ 100g/jour. Le gain protéique augmentait de 40g/jour/animal et le gain de gras diminuait de 40 g/jour/animal.

L'administration de rPST conduisait à une augmentation du taux métabolique de 46 KJ/kg0.75/jour (7.7%). Divers aspects de cette augmentation ont été discutés. Si l'efficacité partielle de synthèse des protéines et de la matière grasse à partir de l'énergie métabolisable n'était pas modifiée, les dépenses d'entretien (EMe: énergie métabolisable pour l'entretien) en présence de rPST augmentaient de 393 à 451 KJ d'énergie métabolisable (EM) par kg0.75.

Quand l'augmentation du taux métabolique était associée à une diminution de l'efficacité énergétique partielle de synthèse des protéines (kp) et non à l'entretien, l'efficacité énergétique du gain protéique diminuait de:

kp = 0.59 (animaux témoins) à
kp = 0.48 (animaux traités par PST)

Une troisième possibilité d'augmentation du taux métabolique aurait pu être celle qui est associée à la rétention de gras. En supposant qu'il n'y ait pas d'effet sur l'entretien et la synthèse protéique, l'efficacité énergétique partielle pour le gras (kf) serait alors de:

kf = 0.68 (animaux traités)
kf = 0.77 (animaux témoins)

Les conséquences de l'augmentation du taux métabolique pour les dépenses thermiques, ont également été discutées. Une diminution de l'adiposité corporelle aurait pour résultat un amincissement de la couche de gras sous-cutané et une moindre isolation thermique. Il est indispensable d'évaluer quelle pourrait être l'importance des conséquences de ces effets combinés (augmentation de la production de chaleur et diminution de l'adiposité) sur les limites inférieures de thermoneutralité. Un taux métabolique plus élevé diminuerait la limite supérieure de la tolérance thermique. De plus amples investigations devront être menées afin de déterminer les conséquences nutritionnelles des modifications des dépôts de gras et de protéines.

Mots clefs: somatotropine porcine, taux métabolique, entretien, efficacité partielle, porc.

REPERCUSSIONS DES TECHNIQUES BIOTECHNOLOGIQUES VISANT A LA MANIPULATION DE LA CROISSANCE ET DU DEVELOPPEMENT DES ANIMAUX SUR LES BESOINS NUTRITIFS TISSULAIRES ET ALIMENTAIRES CHEZ LE PORC.

R.G. Campbell, R.J. Johnson et R.H. King
Animal Research Institute, Werribee, Victoria 3030, Australia

Résumé

L'administration de somatotropine porcine exogène (PST), de facteurs de libération de la somatotropine, mais aussi probablement d'IGF-1 augmente les taux de dépôts protéique et minéral, ce qui a pour résultat un développement plus rapide du squelette, une amélioration des performances de croissance et une diminution de la teneur en gras de la carcasse. Cependant, les effets de ces technologies sur les besoins alimentaires chez le porc en croissance restent obscurs. Pour des porcs de 30 à 60 kg, l'administration de PST exogène augmente la rétention protéique de 25 à 40 %. Cependant, du fait de l'amélioration de l'efficacité d'utilisation des acides aminés par des mécanismes demeurés inconnus, le traitement a peu de répercussions sur les niveaux de protéines et d'acides aminés alimentaires nécessaires pour permettre des performances de croissance presque maximale. Par contre, l'administration de PST à des porcs entre 60 et 100 kg de poids vif augmente la rétention protéique de 50 à 80 % (selon le sexe de l'animal) avec une augmentation concomitante de 30 à 45 % du niveau de protéines (acides aminés) alimentaires nécessaires à des performances de croissance presque maximales. La stimulation du métabolisme protéique induite par la PST se fait par l'intermédiaire de IGF-1 qui sert de médiateur et résulte de l'augmentation des taux de synthèse et de dégradation des protéines. Cependant, pour pleinement évaluer quelles sont les répercussions de la PST, et des technologies qui lui sont rattachées,sur les besoins en nutriments, des informations supplémentaires sont indispensables sur l'amplitude de l'augmentation des taux de rétention protéique et minérale qui peut être obtenue avec ce type de technologie et sur les modifications associées du métabolisme intermédiaire minéral et celui des acides aminés.

Mots clefs: somatotropine, porc, besoins nutritifs, protéines, substances minérales.

EFFETS DE LA SOMATOTROPINE SUR LE SYSTEME IMMUNITAIRE

Keith W. Kelley et Carl K. Edwards, III

Laboratory of Immunophysiology, Department of Animal Sciences, 162 ASL, 1207 West Gregory Drive, University of Illinois 61801 U.S.A.

Résumé

Il a longtemps été suggéré que la somatotropine affectait les cellules du système immunitaire. On sait maintenant qu'elle accroît la taille du thymus, qu'elle augmente certaines activités des cellules lymphoïdes, qu'elle amorce la libération des dérivés oxygénés actifs des macrophages et qu'elle augmente la différenciation des neutrophiles et des érythrocytes. La somatotropine est même synthétisée par les cellules lymphoïdes. Ces découvertes récentes suggèrent qu'en plus de l'augmentation de la vitesse de croissance et de la production laitière, la somatotropine module aussi les activités fonctionnelles des lymphocytes et des macrophages.

Mots clefs: somatotropine, lymphocytes, macrophages, granulocytes.

EFFETS SECONDAIRES POTENTIELS DE LA SOMATOTROPINE EXOGENE CHEZ LE PORC

Stanley E. Curtis

Animal Sciences Department, University of Illinois, Urbana IL 61801, U.S.A.

Résumé

Deux aspects spécifiques à la nature du porc et qui pourraient être modifiés par la somatotropine exogène sont respectivement sa thermorégulation (et donc les exigences thermiques pour son environnement) et son comportement alimentaire (c'est-à-dire l'aménagement des porcheries et des systèmes d'alimentation). L'administration de somatotropine exogène à un porc de 75 kg aurait pour effet net une augmentation de 6oC de la température minimale critique effective de son environnement et une diminution de plusieurs degrés de sa température critique maximale. Ainsi, le porc serait plus sensible aux limites thermiques à la fois supérieures et inférieures de son environnement. La réduction importante de la consommation de nourriture chez les porcs traités par la somatotropine exogène pourrait être due au stress thermique, aux problèmes sociaux ou à la mauvaise adaptation de l'accès à la nourriture. Ces différents aspects devraient être examinés afin de trouver les moyens d'y remédier.

Mots clefs: porc, somatotropine, environnement thermique, environnement social, amènagement des systèmes d'alimentation, consommation de nourriture.

REPERCUSSIONS DES NOUVELLES TECHNOLOGIES POUR L'AMELIORATION DES PERFORMANCES DE CROISSANCE SUR LA REPRODUCTION ET LA LACTATION CHEZ LE PORC

B.N. Day, Steve Terlouw et August Rieke

Department of Animal Science, University of Missouri-Columbia, Columbia, MO 65211 U.S.A.

Résumé

De nouvelles biotechnologies sont apparues dernièrement et se sont révélées des moyens efficaces pour modiner considérablement la croissance et la composition des carcasses des porcs en croissance-finition. Les récents progrès dans le domaine de l'insertion des gènes ont abouti à la production d'animaux transgéniques utilisés pour la reproduction; des descendants ont ainsi été produits. Cependant, des problèmes majeurs ont été observés concernant la reproduction des verrats et des jeunes truies transgéniques exprimant l'hormone de croissance humaine, y compris l'anoestrus et l'absence de libido. Il existe peu de données suggérant que la courbe de lactation des truies puisse être modifiée et la production laitière augmentée par le traitement à l'hormone de croissance porcine hypophysaire (pCH) ou à l'hormone de croissance porcine recombinante (rPST).

Des troubles de la reproduction, y compris une puberté retardée et des follicules kystiques, se sont produits quand les jeunes truies ont été traitées quotidiennement par la pGH à une période proche du démarrage de la maturité sexuelle, ou durant la phase de prooestrus du cycle oestrien. Par contre, il ne s'est pas produit d'effet négatif sur l'intervalle entre présentation au verrat et oestrus, l'âge de la puberté, la proportion des jeunes truies atteignant la puberté avant un âge de 240 jours, ou le taux de gestation, quand les jeunes truies ont été traitées par injection quotidienne de somatotropine porcine recombinante (rPST) pendant la phase croissance-finition (50 à 110 kg de poids corporel). De même, le taux de gestation et le nombre moyen d'embryons au 25e jour de gestation n'ont pas été modifiés par l'administration de rPST entre le 4e et le 18e jour de gestation. Ces résultats indiquent que les performances de reproduction des jeunes truies suivant l'administration de rPST durant la phase croissance-finition ne sont pas affectées.

Mots clefs: porc, reproduction, hormone de croissance.

BIOTECHNOLOGIES ET CONTROLE DE LA CROISSANCE ET DE LA QUALITE DU PRODUIT CHEZ LE PORC: SECURITE DES PRODUITS COMESTIBLES

H.A. Norcross, R.A. Carnevale, E.A. Brown, A.R. Post
United States Department of Agriculture, Food Safety and Inspection Service, Washington, D.C. 20250

Résumé

Bien que la plupart des pays développés jouissent d'une alimentation riche en protéines, la nécessité de technologies qui améliorent la qualité et la quantité des protéines alimentaires est ressentie par une partie importante de la population mondiale. L'utilisation des produits pharmaceutiques visant à accélérer la croissance et améliorer l'efficacité alimentaire, conjointement à l'amélioration des facteurs génétiques et nutritionnels, a permis de fournir de plus importantes quantités de protéines alimentaires à un nombre d'individus plus grand que jamais. Les anabolisants, malgré une publicité parfois défavorable, ont été particulièrement avantageux pour améliorer l'indice de consommation des animaux.

La synthèse protéique et sa régulation ont fait l'objet de recherches intensives en génétique, tant au plan biochimique que moléculaire. La corrélation qui existe entre les produits de gènes spécifiques, tels que les somatotropines, et l'augmentation de la vitesse de croissance, de l'efficacité alimentaire et de la répartition matières grasses/protéines a suscité un grand intérêt comme représentant une possibilité de contrôle artificiel de la synthèse protéique chez les animaux d'élevage. La somatotropine, et les composés afférents, c'est-à-dire les somatostatines, somatomédines, et somatocrinines (growth hormone releasing factors), sont les premiers produits de la technologie des DNA recombinants qui pourraient être économiquement rentables pour augmenter le rendement de production agricole nationale et mondiale.

Si de tels produits doivent être employés aux Etats-Unis, une approbation doit être obtenue de la FDA (United States Food and Drug Administration). La sécurité et la rentabilité de ces produits doivent être démontrées par des études scientifiques bien contrôlées et bien conçues.

La somatotropine, la somatomédine et d'autres facteurs, en particulier les facteurs de libération ont été employés dans de nombreux protocoles expérimentaux et soumis à l'approbation de la FDA comme étant de nouveaux produits pharmaceutiques à l'étude pour la production animale. La réglementation de l'emploi de ces nouveaux agents dans le cadre d'une étude pharmacodynamique et une surveillance continue après approbation doivent constituer une protection suffisante pour la santé publique et garantir la bonne adaptation des produits à l'utilisation proposée ainsi que leur efficacité chez les espèces animales considérées.

Mots clefs: biotechnologies, somatotropine, santé publique, rentabilité, réglementation.

APPARITION POTENTIELLE DE RESIDUS APRES TRAITEMENT DES PORCS AVEC DE LA SOMATOTROPINE RECOMBINANTE

D. Schams[1], E. Kanis[2] et P. van der Wal[2]

[1]*Institut für Physiologie, Technische Universität München 8050 Freising- Weihenstephan, FRG and*

[2] *Animal Science Departments, Agricultural University of Wageningen, Netherlands.*

Résumé

Ces dernières années, la somatotropine porcine recombinante (rPST) s'est montrée particulièrement rentable pour l'amélioration des caractéristiques de croissance telles que le gain moyen quotidien, l'efficacité alimentaire et la faible adiposité des animaux traités. Cette étude rend compte de la première tentative d'évaluation des concentrations sanguines et tissulaires de PST, ainsi que des concentrations sanguines d'IGF-1 avant et au moment de l'abattage des porcs traités à la rPST.

Dans l'essai no1 (94 porcs), cinq paramètres ont été examinés: trois races (Piétrain, Duroc et F1 de Great Yorkshire x Landrace Neerlandais) quatre portées par race; deux sexes (mâles castrés et jeunes truies); deux traitements (rPST et placebo); deux poids à l'abattage (100 kg et 140 kg). Le traitement (bihebdomadaire, 14 mg de rPST dissous dans un tampon arginine HCl en injections intramusculaires) commençait à 60 kg de poids vif. Le sang de la veine jugulaire était collecté à l'abattage, 4 jours 1/2 après la dernière injection. Dans l'essai no 2, 36 mâles castrés de trois races différentes (Piétrain, Duroc et F1) ont été traités de 60 à 120 kg de poids vif par de la rPST deux fois par semaine à raison de 14 mg par injection i.m. Le sang de la veine jugulaire était collecté dans l'heure suivant la dernière injection et 26 - 27 h après, à l'abattoir. En outre, du tissu musculaire provenant de l'épaule droite de 10 porcs (7 traités, 3 placebo) a été collecté, afin d'être analysé pour sa teneur éventuelle en résidus de PST.

La somatotropine porcine et l'IGF-1 ont été évalués par RIA.

Dans l'essai no1, 4 Jours 1/2 après la dernière injection de rPST, les concentrations sanguines de PST chez les animaux traités étaient similaires à celles des animaux témoins, ou significativement plus basses dans les races Piétrain et Duroc. Dans l'essai no 2, dans l'heure suivant la dernière injection, il y avait une augmentation moyenne spectaculaire des concentrations sanguines de rPST de 2 ng/ml jusqu'à 240-321 ng/ml. Vingt-six à vingt-sept heures après, les valeurs trouvées chez les animaux traités avaient déjà diminué jusqu'au niveau des valeurs témoins. Les concentrations tissulaires n'étaient pas significativement différentes et étaient inférieures à 5 ng/g tissu humide. Les concentrations sanguines d'IGF-1 n'étaient pas significativement différentes entre animaux témoins et animaux traités, dans l'essai no 1 et dans l'essai no 2 dans l'heure suivant la dernière injection. Par contre, les concentrations étaient significativement plus élevées 26 - 27 h après. En conclusion, aucun résidu mesurable de la PST ou de l'IGF-1 n'a été trouvé dans le sang ou le muscle des animaux traités à la rPST, 4 à 5 jours après la dernière injection.

Mots clefs: somatotropine, insulin-like growth factors, résidus, porc.

CARACTERISTIQUES NUTRITIONNELLES ET ORGANOLEPTIQUES DE LA VIANDE DE PORCS TRAITES PAR LA SOMATOTROPINE

K.J. Prusa

DepartemEt of food and nutrition, Iowa State University, Ames, Iowa 50011 U.S.A.

Résumé

Bien qu'il existe des différences mesurables dans la composition nutritionnelle et la qualité organoleptique de la viande de porcs qui ont été traités ou non par la somatotropine, aucun problème majeur n'a été mis en évidence. Selon plusieurs études, la teneur en matière grasse intramusculaire est abaissée par l'administration de somatotropine porcine (PST). Une teneur intramusculaire en matières grasses de moins de 1 % due au traitement par la PST a même été signalée. Dans les études qui décrivent une diminution de la graisse musculaire, les contenus protéiques et hydriques du tissu musculaire sont légèrement augmentés. Par contre, aucune différence n'a été notée dans les profils d'acides gras ou dans la teneur en cholesterol du muscle long dorsal chez les animaux traités jusqu'au jour de l'abattage. Toutefois, la teneur en acides gras polyinsaturés de la viande de porc crue et la teneur en cholesterol de la viande de porc cuite se sont avérées un peu plus élevées chez les animaux dont le traitement avait été suspendu 7 jours avant l'abattage. Les concentrations tissulaires en thiamine avaient une tendance à diminuer légèrement en réponse au traitement par la PST. Plusieurs études ont signalé que l'administration de PST n'avait pas d'effet néfaste sur la qualité organoleptique du muscle long dorsal. Par contre, il a été noté une diminution minimale de la tendreté du muscle, de sa succulence et de l'intensité de sa saveur après un traitement par de la PST à concentration élevée.

Mots clefs: somatotropine, composition nutrtionnellle, qualité organoleptique, porc.

EFFET DE LA SOMATOTROPINE PORCINE RECOMBINANTE SUR LA QUALITE DE LA CARCASSE ET DE LA VIANDE DE PORCS BELGES ET NEERLANDAIS

D. Demeyer[1,2], R. Verbeke[1], G. van de Voorde[1], J. Fabry[3], E.Deroover[4] ,R.H. Dalrymple[5]

[1] *University of Ghent, Ghent, Belgium;*

[2] *University of Brussels, Belgium;*

[3] *Agricultural Resarch Centre, Gembloux, Belgium;*

[4] *Cyanamid Benlux NV, Mont-Saint-Guibert, Belgium;*

[5] *American Cyanamid Company, Princeton, New Jersey, U.S.A.*

Résumé

Les résultats illustrant les effets de la somatotropine porcine recombinante (rPST) sur la qualité de la carcasse et de la viande de porcs belges et neérlandais sont publiés en détail ailleurs et résumés ici. Des porcs belges en fin de croissance (60 à 120 kg environ) ont été traités par 4 concentrations de rPST (O; 1,5; 3 et 6 mg/jour) en irvections quotidiennes. Ils ont été nourris ad libitum avec un régime à base de céréales et riche en protéines (expérience no1). Les porcs neérlandais nourris de la même façon, sur une période de croissance-finition similaire, ont été traités avec 0 ou 14 mg de rPST, en injections bihebdomadaires (expérience no2). Dans chaque expérience, des données ont été collectées concernant les rendements de carcasse et d'organes, la qualité des carcasses le rendement à la découpe, la qualité organoleptique de la viande, la composition globale et la composition des muscles (expérience no2 seulement).

Le traitement par la rPST a entraîné une diminution légère des rendements de carcasse, associée à une augmentation de poids du coeur, du foie et des reins. La qualité de la carcasse a été considérablement améliorée, comme il ressort de la diminution des différentes mesures de gras de la carcasse et de l'amélioration de sa classification. Les rendements en viande de la carcasse ont été améliorés, avec des réductions concomittantes des morceaux de gras et du toilettage. Aucune différence significative n'a été observée en ce qui concerne la baisse des valeurs de pH musculaire, mais il semble que les températures aient été plus élevées peu de temps après la mort. Les valeurs de pH tardives étaient légèrement, mais significativement, augmentées. Les diverses mesures concernant la texture, la couleur et la capacité de rétention d'eau de la viande ont montré que le seul effet statistiquement significatif était une couleur légèrement moins rouge. La composition en protéines myofibrillaires et la longueur des sarcomères du muscle long dorsal n'ont pas été modifiées, mais la teneur en protéines brutes était légèrement plus élevée.

Ces études ont montré que l'utilisation de différentes concentrations de rPST peut augmenter le rendement en viande et diminuer le gras de carcasse, même chez des races sélectionnées pour une composition de carcasse supérieure, et cela sans effet néfaste sur la qualité organoleptique de la viande.

Mots clefs: somatotropine, qualité de carcasse, qualité de viande, poids d'organes, porc

L'OPINION DES CONSOMMATEURS SUR LES TECHNOLOGIES ET BIOTECHNOLOGIES APPLIQUEES A LA PRODUCTION DES ALIMENTS

Janet Graham

Consumers in the European Community Group (CECG), London, United Kingdom

Résumé

Ceci est le point de vue d'un consommateur britannique. Il n'est pas spécifique à la PST, puisque la prise de conscience du consommateur pour ce produit et son application fait encore défaut. Neanmoins, la recherche au CECG sur la BST et les autres technologies alimentaires modernes nous ont permis de tirer certaines conclusions en ce qui concerne l'opinion du consommateur sur ces nouvelles techniques et leurs applications.

Les consommateurs se sentent de plus en plus concernés par les méthodes modernes en agriculture qui reposent sur l'utilisation d'antibiotiques, d'hormones, de pesticides, de protéines obtenues par génie génétique, telles que la BST (somatotropine bovine); la PST (somatotropine porcine) est donc susceptible de subir un examen semblab)e en temps utile. Quelques-unes des réalisations citées ci-dessus ont contribué à nous approvisionner copieusement et de façon attrayante en aliments de plus en plus variés mais les progrès ont aussi conduit à une aliènation des consommateurs qui ont l'impression que leur nourriture n'est plus "naturelle".

Il est nécessaire d'établir des critères permettant de juger ces nouveaux procédés, basés également sur une estimation des besoins des consommateurs. Ceci revient à examiner si un progrès particulier dans ces domaines pourrait être bénéfique au consommateur. Autrement dit, un produit sera-t-il plus sûr, moins cher, plus varié, plus facilement disponible, plus durable, mieux adapté, mieux conditionné ? Sera-t-il accepté immédiatement, ou va-t-il rencontrer la suspicion des consommateurs, conduisant à leur réticence? Si, ce qui semble probable, quelques nouveaux développements ou percées scientifiques ont quelque avantage et quelque répercussion pour les consommateurs, alors les aspects positifs et négatifs devraient être éclaircis afin que le public puisse prendre une décision.

Les droits des consommateurs dans nos sociétés d'abondance comprennent celui très important de pouvoir choisir la nourriture que nous mangeons et de pouvoir faire ce choix après ample information: nous ne souhaitons pas que ce choix soit réduit à néant par ceux qui voudraient bannir de principe les nouvelles réalisations. De même, pour que ce choix soit circonstancié, les instances impliquées dans la production alimentaire et la commercialisation, depuis la recherche jusqu'à la vente finale, doivent être mieux préparées à la diffusion d'une information utile et utilisable.

Mots clefs: biotechnologie, alimentation humaine, consommateurs, opinion, porc.

ASPECTS ETHIQUES RELATIFS A L'UTILISATION DES BIOTECHNOLOGIES POUR LE CONTROLE DE LA CROISSANCE ET DE LA QUALITE DU PRODUIT CHEZ LE PORC

R. Dantzer

INRA-INSERM U.259, rue Camille Saint-Saëns, 33077 Bordeaux Cedex

Résumé

Le développement des nouvelles biotechnologies pour l'amélioration des performances de croissance et de la qualité du produit dans l'industrie du porc suscite de nombreux problèmes, dont certains ont des implications éthiques très importantes. Les considérations éthiques quant à l'utilisation des biotechnologies pour la production animale doivent être appréhendées à plusieurs niveaux. Au niveau de l'animal, deux questions se posent: l'une concerne la perception de l'aspect artificiel, et l'autre est liée à l'influence négative possible du traitement sur la santé de l'animal. Au niveau professionnel, l'emploi croissant des biotechnologies semble favoriser la subordination des chercheurs dans le domaine animal et des vétérinaires à des intérêts économiques, aux dépens de leur rôle plus traditionnel de soins à l'animal. Au niveau des consommateurs, le point de vue éthique fait appel non seulement à l'éducation mais aussi à la protection et à la liberté de choix. Au niveau de la société, les répercussions potentielles des biotechnologies sur les structures socio-économiques de la production animale doivent être évaluées. Bien que les biotechnologies représentent un grand potentiel pour l'amélioration de la rentabilité de la production animale, une analyse approfondie des problèmes éthiques posés par leur introduction dans l'agriculture est nécessaire pour les comprendre et les faire accepter par la société.

Mots clefs: biotechnologie, porc, somatotropine, porc transgénique, éthique.

REPERCUSSIONS ECONOMIQUES DE L'UTILISATION DE SOMATOTROPINE PORCINE SUR L'INDUSTRIE DU PORC

M. Hayenga. B.Buhr, K, Skold, S. Johnson, E. Grundmeier
Iowa State University, Ames, Iowa, United States

Résumé

Cette étude fournit une analyse complète des impacts de l'utilisation de la PST dans le domaine de la production porcine; elle tente également d'expliquer toutes les répercussions économiques dynamiques de l'introduction de la PST. Cependant, il faut rappeler que les résultats obtenus grâce à ce travail sont limités par les hypothèses utilisées dans l'analyse, et par la disponibilité limitée des données sur la PST.

L'impact le plus percutant de la PST est la diminution du coût associée à une meilleure production de maigre par porc. L'augmentation de la rentabilité qui résulte de l'adoption de la PST par les producteurs entraîne une augmentation rapide de la production. Cette augmentation provoque une baisse des prix à la fois au niveau de la ferme et de la vente au détail. Du fait de la diminution des coûts de production, les producteurs qui adoptent la PST immédiatement récoltent des profits plus importants, mais l'industrie dans son ensemble réalise des recettes moins conséquentes à mesure que la production accrue fait baisser les prix à la ferme. Du point de vue de la rentabilité, l'adoption de cette nouvelle technologie est stimulante pour les producteurs de porcs pour deux raisons: à court terme, accroissement des profits; à long terme, avantages compétitifs dans l'industrie du porc pour les adoptants comparés aux non-adoptants. De plus, les producteurs de porcs regagnent ainsi une partie du terrain cédé aux avancées technologiques dans le domaine de la production avicole, durant ces trente dernières années; ils deviennent aussi des interlocuteurs plus compétitifs pour le budget du consommateur. Ainsi, les transformateurs et les consommateurs bénéficient d'une production plus élevée associée à une baisse des prix, alors que les adoptants tardifs se trouvent dans un "cercle vicieux technologique". Les profits globaux des producteurs de porc changent très peu à long terme, comme on aurait pu s'y attendre dans une industrie compétitive de libre échange. Les producteurs de céréales sont affectés alors que les producteurs de soja ne le sont pas.

Néanmoins, plusieurs problèmes concernant les répercussions de la PST sur la production ainsi que les réponses à apporter aux consommateurs n'ont pas encore été résolus. Avant que les répercussions à long terme sur la production, et les effets secondaires éventuels soient appréhendés avec une certitude raisonnable, l'adoption à grande échelle de la PST ne se produira pas. L'agrément du consommateur pour de la viande provenant de porcs traités par la PST reste un problème important qui peut avoir une influence considérable sur l'adoption de la PST.

Plusieurs paramètres qui n'ont pas été considérés dans ce travail comprennent:

Le potentiel de conversion des conditionneurs de viande, c'est-à- dire la potentialité d'accorder leur préférence à des porcs de boucherie plus lourds, du fait de carcasses plus maigres, et les répercussions éventuelles.

Les implications éventuelles de l'ajournement des réglementations internationales sur l'utilisation nationale de PST et sur les restrictions quant aux importations dans les pays producteurs et consommateurs de viande de porc les plus importants.

Les avantages des transformations technologiques en compétition (par exemple les autres promoteurs de croissance, les béta-agonistes) sur les industries du porc, du boeuf et de la volaille.

De tels paramètres pourraient intensifier ou diminuer de façon spectaculaire les changements que nous envisageons actuellement en conséquence de l'introduction de PST. A mesure que nous

possèderons plus d'informations, nous serons mieux à même d'appréhender de façon plus précise les impacts économiques probables de la PST.

Mots clefs: somatotropine porcine, biotechnologie, impact économique, porc.

CONTROLE DE LA CROISSANCE DES PORCS DANS LA CEE: EFFETS SUR LA COMPETITIVITE DE LA VIANDE DE PORC ET DES INTERVENANTS DANS LA FILIERE PORC.

A.H.R. Pease
GIRA S.A.*, Geneva, Switzerland

Résumé

Le bénéfice total de l'utilisation de PST dans la production porcine est estimé à 31 ECU/porc. Pour les premiers porcs abattus, 20% de ce bénéfice iront aux fournisseurs de PST, 50% aux producteurs de porcs (y compris EUROPA grading premia) et 30 % aux bouchers-charcutiers.

La viande extra-maigre qui apparaîtra sur le marché fera baisser les prix, si bien qu'en l'espace de quelques semaines ou de quelques mois, le bénéfice sera réparti différemment: 20% aux fournisseurs de PST et 80 % aux consommateurs.

Mots clefs: somatotropine, répercussions économiques, Europe, porc.
* Actuellement avec Strategic Animal Systems Research and Consultancy

EFFECTS DE LA SOMATOTROPINE PORCINE (PST) SUR LA POLLUTION AZOTEE DE L'ENVIRONNEMENT

E.J. van Weerden et M.W.A. Verstegen

TNO Institute of Animal Nutrition and Physiology, ILOB department, Wageningen, The Neth rlands. Department of Animal Nutrition, Agricultural University, Wageningen, The Netherlends.

Résumé

Des porcs mâles castrés croisés (Landrace Neerlandais x Yorkshire Neerlandais) ont reçu 4 mg/jour de somatotropine porcine recombinante (rPST) à partir de 58 kg de poids vif et pendant 10 semâines. Un groupe placebo non traité a servi de témoin. Les animaux ont été nourris 3/4 fois par jour à un niveau restreint de 260 Kcal d'énergie métabolisable/kg de poids corporel.

Les paramètres mesurés étaient les suivants: bilan azoté pendant 6 périodes expérimentales durant les 6 dernières semaines de traitement, gain de poids et indice de consommation.

Le bilan azoté augmentait de façon significative de 31%; 7,7% supplémentaires d'azote alimentaire était retenu par l'organisme des animaux traités à la rPST. La vitesse de croissance était augmentée de 10% et l'indice de consommation amélioré de 7% chez les porcs traités par la rPST.

Les bilans de P et de Ca augmentaient respectivement de 18% et de 19% après le traitement à la rPST.

Ces valeurs ont permis de calculer que l'excrétion d'azote dans l'environnement pour des porcs de 58 à 110 kg était réduite de 21% après traitement; par ailleurs, la réduction de l'excrétion de P était de 16%.

La grande incertitude quant à l'étendue de l'effet du rPST sur l'excrétion azotée réside dans le manque de connaissances des niveaux alimentaires de protéines/acides aminés nécessaires pour couvrir le dépôt protéique extrêmement élevé (approximativement 210 g/jour) chez les porcs traités. Les données expérimentales obtenues jusqu'à présent ne donnent aucun indice d'une augmentation spectaculaire des besoins nutritionnels chez les porcs traités à la PST.

Mots clefs: somatotropine, porc, environnement, pollution

291

CONCLUSIONS DES SESSIONS

Conclusions, telles qu'elles ont été proposéees par les présidents
et lesmodérateurs, discutées et adoptées en session plénière
à la fin du symposium.

IMPLICATIONS POUR LES SYSTEMES DE PRODUCTION

Président: R.G. ZIMBELMAN

Les progrès indiscutables apportés par les injections de somatotropine porcine recombinante (rPST) pour augmenter le dépôt protéique et diminuer le dépôt de gras ont été considérables quels que soient les races, le niveau d'alimentation, le sexe ou les différents systèmes d'exploitation en Amérique du Nord, en Europe et en Chine. Bien entendu, il existe des variations dans l'amplitude des réponses, mais même la réponse la plus faible est saisissante. Les résultats sont évidents qu'ils soient basés sur l'examen des carcasses ou sur les données numériques.

La diminution de la consommation d'aliments ainsi que l'augmentation de l'efficacité alimentaire ont également été significatifs. L'amplitude de cette augmentation ne peut être exprimée de façon spécifique pour plusieurs raisons: 1) Le manque de données strictes quant aux doses optimales employées 2) L'interaction apparente entre dose et nutrition, i.e. pour que de fortes doses entraînent un dépôt protéique plus élevé, la composition du régime doit être modifiée, ce qui n'est pas le cas pour des réponses moins importantes; dans les études présentées, il existait des variations sur la durée du traitement, les doses employées et enfin le poids initial et final des animaux.

Les conditions pour que le produit soit acceptable dépendront largement de la mise au point d'un système pratique permettant la diffusion lente du produit dans l'organisme. Plusieurs firmes peuvent réussir plus ou moins bien dans cette voie, compte tenu de l'impossibilité virtuelle de décrire de raçon générique l'efficacité du produit en raison de légères modifications dans la structure chimique ou la conformation du rPST. Les techniques et les préparations à effet prolongé seront probablement un peu moins efficaces et les considérations quant au bénifice économique devraient influencer le choix des différents fabricants.

Les exigences des systèmes de classification des carcasses et de l'industrie de la transformation sont assez complexes et méritent d'être sérieusement considérées. Il existe de nombreux problèmes à savoir l'épaisseur de la poitrine de porc, les méthodes de transformation, mais aussi la teneur en graisse intramusculaire qui pourrait ne pas être optimale avec des niveaux de gras très réduits. Certains de ces facteurs pourraient être améliorés par l'augmentation du poids à l'abattage, mais ceci peut ne pas être valable pour certains morceaux de viande fraîche ou pour des produits courants.

Une étude approfondie de marché sur la façon de réagir à des porcs extrémement maigres s'avère nécessaire à la fois aux Etats Unis et en Europe. Les résultats de la recherche sur les porcs aux Etats Unis ou sur des porcs qui ne sont pas très maigres pourraient ne pas être applicables aux programmes Européens, dans lesquels les porcs maigres prédominent déjà. Une recherche réalisée dans ce type de situation est donc nécessaire afin de déterminer si un bénéfice peut se produire et s'il existe des inconvénients non détectés en routine concernant la qualité ou les caractéristiques de transformation de la viande.

Les techniques de modifications du génome progressent à une vitesse surprenante, en particulier le développement des approches théoriques pour la réalisation et le contrôle de l'insertion des gènes. Les avantages de l'insertion de gènes par rapport à l'administration de rPST par injection devraient être plus importants chez les porcs qui présentent déjà des caractères desirables tel qu'une prolificité élevée. Chez ces porcs l'amélioration de la croissance et de la carcasse proviendrait plutôt de l'insertion des gènes de la somatotropine ou de la somatocrinine (GRF).

Neanmoins, il faudra probablement de nombreuses années (au moins 8 à 10) avant d'obtenir des résultats utilisables chez les animaux reproducteurs. Il est plus que probable que l'animal transgénique géniteur aura une insertion de gène unique, qu'on pourra maîtriser par un apport alimentaire à bon marché qui soit compatible avec la production commerciale.

295

La nécessité d'accouplements avec un grand nombre de partenaires après la puberté pour un tel animal suggère que ce soit un mâle, l'homozygotie étant obtenue par accouplement avec sa progéniture. Cela prendra énormément de temps. Finalement, il serait prudent de réaliser un test de performances sur une période assez longue pour permettre l'expression de caractères indésirables avant l'introduction à grande échelle de rPST dans la banque de gènes. Cela sera onéreux et prendra du temps; c'est pourquoi la societé devrait développer des mesures telles que le dépôt de brevets pour rendre aux investisseurs le bénéfice de leurs investissements risqués et substantiels si cette technologie doit être destinée à la commercialisation. Il reste à déterminer si l'utilisation de rPST nécessiterait des modifications des procédures de testage et de sélection utilisées pour l'amélioration génétique. Ceci dépend de l'interaction éventuelle de l'utilisation de rPST avec d'autres caractères désirables que ceux ayant trait aux caractéristiques des performances et de carcasse.

Il faut reconsidérer très sérieusement la question de savoir si l'obtention d'un animal le plus maigre possible est un objectif en soi. La description spécifique des variations dans la composition en acides gras des porcs traités par le rPST ou transgéniques devrait être une priorité.

Il semble avisé de prendre des précautions quant à l'application de ces nouvelles technologies passionnantes. Une meilleure compréhension de leur mode d'action sera relativement indispensable pour partir à la chasse d'une "cible mobile".

REPERCUSSIONS SUR LES BESOINS ET LE BIEN-ETRE DE L'ANIMAL-CIBLE

Président: P.R. WIEPKEMA

Les animaux maintiennent une homéostasie interne et externe au moyen de systèmes de régulation bien équilibrés, complexes et étroitement liés. Un grand nombre des paramètres liés à l'environnement sont contrôlés activement par l'animal. Quand on modifie les caractères de production des animaux domestiques, l'équilibre de l'homéostasie existante doit être pris en considération. Les effets principaux et secondaires des nouvelles technologies doivent être mis en évidence afin de satisfaire les besoins et le bien-être de l'animal-cible.

Campbell a montré que le traitement par la somatotropine porcine recombinante (rPST) aurait pour effet une diminution du gras et une augmentation de la rétention protéique, mais selon des proportions différentes. En particulier, pour le dernier effet cité, il est nécessaire que le régime alimentaire contienne une quantité adéquate de protéines. Les deux effets interagissent avec la dose de rPST et avec la race, le sexe et le poids vif.

La diminution de l'ingestion alimentaire observée dans les essais jusqu'à 100 kg de poids corporel est associée à une diminution significative du dépôt de gras et une augmentation de la rétention protéique. Les répercussions sur le métabolisme des acides aminés, des acides gras et du glucose demandent à être mieux élucidées.

Verstegen a montré que le traitement par le rPST augmente la production de chaleur, ce qui reflète un taux métabolique plus élevé. Cette augmentation provient probablement d'un besoin d'entretien plus élevé ou bien d'une moindre efficacité de l'utilisation énergétique au dessus du niveau d'entretien.

Curtis a calculé les répercussions éventuelles de la réduction de l'épaisseur de la graisse sous-cutanée sur les capacités de régulation thermique des porcs traités à la rPST. Cela pourrait conduire à un rétrécissement de la zone de thermorégulation par rapprochement de ses limites. Pour cette raison, les effets du traitement des animaux par la rPST sur leur thermorégulation nécessitent la détermination des températures optimales pour leur élevage.

Des informations sur le comportement (organisation sociale, ingestions alimentaire et hydrique, repos, etc.) des porcs logés en groupe et traités par la rPST sont nécessaires afin d'évaluer a priori les problèmes qui peuvent surgir en pratique dans des conditions d'élevage intensif. Il faut ainsi être particulièrement attentif aux réactions des porcs traités à la rPST lors de leur transport à l'abattoir quand leur capacité de thermorégulation est très sollicitée.

Kelley a insisté sur le rôle positif normalement joué par la somatotropine dans l'activation du système immunitaire (macrophages). A l'heure actuelle il est difficile d'établir quels pourraient être les bienfaits du traitement par la rPST sur la santé des porcs.

Day a montré que l'utilisation de rPST avant la puberté ne perturbe pas les processus de reproduction qui se déclenchent quelques semaines après l'arrêt du traitement. L'administration de rPST durant l'oestrus fournit des résultats contradictoires.

LE POINT DE VUE DES CONSOMMATEURS

Président: B. HOFFMANN

Comme cela a été montré par Norcross (USDA) aux Etats Unis, des procedures bien établies de réglementation permettent une estimation adéquate des risques et bénéfices en ce qui concerne l'emploi de produits pharmaceutiques chez les animaux destinés à la consommation. Etant un produit de la technologie liée aux ADN recombinants, la somatotropine porcine re des Etats Unis, des procédures réglementaires efficaces n'ont été mises en place en Europe que depuis la fin des années 1960 (GB) et 1970 (DE) ou qu'elles sont toujours en cours d'établissement dans d'autres pays membres de la Communauté Européenne.

Il est nécessaire de répondre à des questions qui restent ouvertes, comme par exemple l'innocuité pour la santé des consommateurs des modifications de concentrations de somatomédine C (Insulin-like growth factor 1, IGF-1), avant une autorisation définitive. Selon Norcross, d'autres procédures réglementaires restent disponibles pour traiter l'autorisation de mise sur le marché des animaux transgéniques. Norcross souscrit fortement à toute communication, échanges d'opinions et de données entre toutes les instances concernées par les problèmes de réglementation.

Il est apparu clairement pendant la discussion qu'à la difference des Etats Unis, des procédures réglementaires efficaces n'ont été mises en place en Europe que depuis la fin des années soixante (GB) et soixante-dix (DE), ou qu'elles sont toujours en cours d'établissement dans d'autres pays membres de la Communauté Européenne.

Selon Schams, qui a présenté des données provenant d'une étude en collaboration sur la rPST et l'IGF-1, les concentrations basales sanguines de somatotropine et d'IGF-1 sont atteintes respectivement après 26 h et 4 jours de traitement par la rPST. Des résultats préliminaires présentés lors de ce symposium ont montré qu'il n'y avait pas de résidus de rPST et de IGF-1 dans les muscles après 4 jours de traitement. Il n'existe pas de données concernant les concentrations hépatiques et rénales d'IGF-1 et il est de plus nécessaire d'obtenir de plus amples informations quant à la dégradation de l'IGF-1 et à la formation de fragments susceptibles d'être biologiquement actifs.

Prusa et Demeyer dans leurs présentations ont confirmé la tendance générale selon laquelle le traitement par rPST conduit à l'obtention de carcasses plus maigres et à une diminution du gras intramusculaire; néanmoins, il existe des différences entre races qui doivent être prises en compte. Bien que des différences mesurables aient été constatées dans la composition nutritionnelle et la qualité organoleptique entre animaux traités ou non par le rPST, aucun problème majeur ne ressort avec évidence. En effet, les concentrations protéiques et hydriques augmentent légèrement, de façon similaire à la teneur en acides gras polyinsaturés de la viande de porc crue et de celle en cholestérol de la viande de porc cuite; par contre la teneur en thiamine diminue, elle, légèrement. La qualité organoleptique globale n'est pas altérée bien que quelques déviations par rapport au groupe témoin aient été rapportees.

La possikilité de réduire l'ingestion de matières grasses et de calories à partir de la viande de porc grâce à l'emploi de rPST a été discutée comme étant une des façons par lesquelles la qualité de la nutrition humaine peut être améliorée.

Graham s'est fait le porte-parole des consommateurs en demandant l'ouverture du débat. Leurs opinions concernent plus que des problèmes d'innocuité, elles comprennent aussi d'autres paramètres éthiques, comme le bien-être de l'animal. Le consommateur moderne, qui est capable de manipuler les ordinateurs et d'autres instruments sophistiqués, désire être consulté; de plus il est capable d'être éduqué, c'est-à-dire qu'il sera capable de traiter les informations apportées par l'industrie et la science. C'est dans cette optique que Graham a discuté des problèmes de label d'origine de certains produits; en outre, cet auteur s'est montré en désaccord avec l'appellation "produits diététiques" pour des produits qui sont destinés au profit commercial.

Les questions qui demeurent sans réponse concernent l'identité du consommateur, le terrain d'entente, la diffusion d'une information fiable; Dantzer a présenté une approche philosophique du problème dans laquelle il faisait référence aux aspects normatifs du processus en faisant ressortir les valeurs éthiques. Afin de faire avancer quelques idées au niveau de la société, les répercussions potentielles des biotechnologies sur les structures socio-économiques de la production animale devraient être mises en valeur. Bien que les biotechnologies représentent un potentiel important pour l'amélioration de la rentabilité de la production animale, il est nécessaire de considérer sérieusement la portée éthique de leur mise en pratique pour qu'elles soient comprises et acceptées par la société.

REPERCUSSIONS SUR L'ENVIRONNEMENT ET L'ECONOMIE

Présidents: K. Aibara et G. van Dijk

L'introduction de la somatotropine porcine recombinante (rPST) dans la production porcine dépend de nombreux facteurs dont la plupart ont été répertoriés. Parmi ceux-ci, on peut citer l'économie de l'exploitation, les effets sur la chaine commerciale, l'agrément du consommateur, les répercussions sur l'environnement physique, les attitudes gouvernementales et les considérations éthiques.

L'économie de l'exploitation:

Hayenga a exposé clairement que les avantages économiques entraînent un taux élevé d'adoption de l'utilisation du rPST à la condition qu'il n'y ait pas de réserves notables liées aux critères d'agrément des consommateurs. Ses données indiquent des taux de 50 - 60% en 2 - 3 ans. L'emploi de rPST conduira à une diminution du coût et de ce fait ceux qui auront adopté cette technique très tôt, verront leur marge de profit augmenter. Toutefois, ce type de situation n'est pas stable. Après quelque temps, la compétition forcera les retardataires à adopter ce type de technique et les marges de profit baisseront puisque les prix pratiqués dans cette industrie ont tendance à s'égaliser avec les coûts moyens à long terme. Ce seront éventuellement les consommateurs qui seront les bénéficiaires les plus durables. Dans les conditions européennes également, les industries de transformation et de commercialisation seront à même de s'assurer une marge bénéficiaire. Pease suggère que l'industrie de transformation pourrait prendre une quote-part substantielle. Il semblerait que cette constatation soit valable essentiellement pour le court terme. A long terme, les conditions seront les mêmes que dans le secteur des exploitations agricoles. Neanmoins, une partie du profit restera dans les secteurs d'élevage et de transformation. Il semble normal que ces nouvelles technologies soient à la base d'une égalisation entre augmentation générale des revenus et croissance économique globale.

L'effet de marché

Il y aura peu d'augmentations de la demande, à moins d'effets de substitution. Il y a d'ailleurs peu d'échanges commerciaux entre l'Europe, les Etats Unis et le Japon. Les changements démographiques, avec l'accroissement de la proportion de la population islamique, rendent le marché international du porc de nature plus stable que ne pourraient le laisser prévoir potentiellement les perspectives pour le marché du boeuf par exemple.

Steele et les participants à la discussion ont fait remarquer que la baisse des prix de la viande de porc favorisait le remplacement de la viande de boeuf par le porc. Néanmoins, peu de données quantitatives sont disponibles quant aux paramètres d'élasticité de telles substitutions, présumant de variations de prix considérables. Des études sont en cours (Hayenga). Quant aux répercussions de l'introduction de rPST dans les pratiques de la transformation, McKeith souligne qu'il n'y en a pas. A chaque fois que de telles répercussions se produiraient, la technologie normale pourrait les maîtriser facilement. Par contre, le rPST a une influence positive en ce qui concerne les contraintes liées à l'environnement. Van Weerden a montré qu'il y aura une diminution de 15 à 20% des émissions polluantes (d'azote et de phosphore) par kg de produit. Il n'y a aucun doute que ces effets sont importants à défaut d'être décisifs pour les Pays Bas. Toutefois, les répercussions économiques et la validation de l'argumentation écologique sont toujours à quantifier. Même si la loi imposait des restrictions quant aux émissions de N et de P, l'introduction de rPST pourrait être considérée

comme un moyen important ajouté aux autres mesures visant à diminuer les effets polluants. Au total, les mesures pour la protection de l'environnement conduiront à des changements dans les systèmes de production. L'agrément du consommateur n'est pas une donnée inamovible.

Elle peut être modifiée grâce à la commercialisation, la promotion et les campagnes publicitaires. Les progrès dans ce domaine ont été si modestes que la viande de porc est toujours considérée comme un produit de masse. Il semblerait malgré tout que des modifications de la politique de commercialisation soient en cours. Dans une telle évolution, les producteurs seront mieux intégrés dans l'ensemble de la chaîne commerciale.

Cela devrait déboucher sur une production contractuelle et une gestion verticale de la qualité. Les problèmes liés à l'agrément du consommateur sont alors traités de façon normale dans ces conditions: en effet, la qualité n'est pas perçue automatiquement par les consommateurs et la confiance des consommateurs doit être gagnée.

Les raisons pour lesquelles les politiques gouvernementales résistent à l'introduction de rPST sont probablement liées à des considérations sociales et économiques. Les conséquences quant aux structures nationales peuvent être très importantes. La rPST pourrait alors devenir facilement un instrument pour établir des barrières commerciales. Toutefois, ceci deviendra de moins en moins possible en Europe, du fait que le consommateur obtiendra une position plus décisive. La plupart des participants à la discussion ont considérés que l'introduction de rPST aurait des répercussions importantes liées aux modifications géographiques de la production porcine.

Résumé des paramètres d'interaction à impact économique:

économie de la ferme:	favorable à l'introduction de rPST
argumentation écologique:	idem
consommateur:	"demande à être convaincu"
besoins nutritifs/santé:	avis favorable contribuable: (probablement) neutre
animal-cible:	nécessite une discussion plus approfondie

CHINESE RESUME

Scope of sympisium

Summeries of papers

Conclusions of sessions

最新资料

应用生物技术控制猪的生长和产品质量：意义和可接受性

国际专题讨论会论文集

荷兰，Wageningen，1988年12月12日－14日
编者：P. VAN DER WAL, C. J. NIEUWHOF 和
R. D. POLITIEK

在畜牧生产中，通过动物的生长激素轴生理地控制动物的生长和产品质量。

生物技术提供了影响生长激素轴的许多途径。直接投给生长激素，免疫技术和基因插入可能成为有效的生物技术手段。更有效的利用饲料，更瘦的肉和较少的环境污染可能被做到。

这些技术被管理机构和公众的接受取决于它们的生产效益和对消费者，目的动物和环境的安全性。

专题讨论会根据现行规章的要求讨论了这些技术的前景。

欧洲共同体，美国和西太平洋地区的研究提供了分析问题的材料依据。

目录见背面

出版者

| P.O.Box 4 |
| Pudoc 6700AA Wageningen |
| Netherlands |

请向您通常购书的书店或出版者定购

目 录

应用生物技术控制猪的生长和产品质量：
意义和可接受性

专题讨论会论文集
荷兰，瓦格廷根
1988年12月12日－14日

编者：
P.Van der Wal
G.J.Nieuwhof
R.D.Politiek
副编者：
中文：冯淇辉
　　　齐顺章
法文：A.A.Rerat
　　　R.Dantzer

发起者：
生物技术行业
欧洲共同体
瓦格廷根农业大学

印 于 荷 兰 。

组织委员会:

主席:	R.D.Politiek	Wageningen农业大学,	荷兰
秘书:	P.Van der Wal	Wageningen农业大学,	荷兰
助理:	G.I.Nieuwhof		
委员:	H.Karg	慕尼黑技术大学,	西德
	冯淇辉	华南农业大学,	中国
	R.G.Zimbelman	美国畜牧学会,	美国

主席和讨论主持人:

K.Aibara	食品和药物安全研究中心,	日本
L.L.Christian	Iowa 州立大学,	美国
G.Van Dijk	Wageningen 农业大学,	荷兰
F.Ellendorff	动物饲养及行为学研究所,	西德
B.Hoffmann	Iustus Leibig大学,	西德
R.L.Kline	国家猪肉生产者理事会,	美国
C.E.Lamming	Nottingham 大学,	英国
O.G.Pedersen	丹麦熏猪肉和肉类理事会,	丹麦
A.A.Rerat	国家农业研究所,	法国
L.Reijnders	自然与环境基金会,	荷兰
P.Wiepkema	Wageningen 农业大学,	荷兰

目　录

对加工业的意义

生长激素对猪肉加工业的意义
F.K.McKeith,P.J.Bechtel 和 J.Novakofski

4.对受试动物的需求和健康的影响

生理作用方式

猪生长激素(PGH)和胰岛素样生长因子(IGFs)调控猪生长
性能的机制：由PGH 和 IGF受体到整体动物的探讨
T.D.Etherton

营养和管理的需求

猪生长激素对猪能量代谢的影响
M.W.A.Verstegen, W. Van der Hel 和 E.J.Van Weerden

操纵动物生长和发育的生物技术对猪组织和饲料营养
物需求的影响
R.G.Campbell, R.J.Johnson 和 R.H.King

健康和免疫反应

生长激素对免疫系统的影响
K.W.Kelley, C.K.Edwards

副作用

外源性生长激素对猪的可能的副作用
S.E.Curtis

对生殖和泌乳的影响

促进生长的新技术对猪生殖和泌乳的影响
B.N.Day, S.Terlouw 和 A.Rieke

5.消费者方面

食用产品的安全性
使用生长激素后的猪肉在营养和感官上的特征
K.J.Prusa

I　专题讨论会的目的

专题讨论会的目的

以买得起的价格得到优质肉类产品是世界人口中增长部分的公认的权利。利用畜牧科学的成就已可能满足消费者对这些动物产品的需求。然而在克服日益增长的生产紧张状态的同时，为了满足进一步的需求，大概必须开发新的生物技术作为锐利的科学工具。

种植动物饲料的土地面积是有限的，而且在有些地区已超出了环境承受污染性排泄物的能力。因此，不能再想当然的认为动物生产必定受到支持。对产品质量和安全性的要求规定的更为苛刻。对动物的健康也要求更高的重视。

生物技术的进展为有效地满足这些需求展现了日益广阔的前景。显著提高动物生产的效率和产品质量已是指日可待。这次专题讨论会的目的是在全球范围内探讨控制动物生长和产品质量的新技术，在满足消费者、动物和环境的需求方面的潜力和受到的限制。

改进动物生产方面需要优先考虑的问题

提高饲料转变为肉的效率在许多方面为长期维持动物生产体系提供了最有希望的前景。它减少种植动物生产所需饲料作物的耕地面积，并降低肉类成本。最后但并非不重要的一点，它是减少动物排泄物污染环境的最有效的途径。

在产品质量方面必须考虑到对更多瘦肉和较少脂肪的要求，这是由于人们越来越认识到摄入过多的能量对人的健康有害。产品的安全性以及味道和嫩度也是需要高度重视的。

以健康和行为作为指标的动物良好生存状况可用动物生理学，行为学和免疫学的进展进行更有效的研究。

正在出现的生物技术

在这次专题讨论会中，选择性地分析了证实既有效而本质上又安全的与生理学有关的技术。这些是与生长激素轴有关的技术。

食用动物的生长是由基因组调控的，它的潜力通过生长激素释放因子（GRF）－生长激素抑素－生长激素－生长调节素这个相互作用的体系而表现出来。

6000年来，人类用系统的选种和育种方法逐渐修饰动物的基因组以影响这个轴，其目的是使动物生产符合人类的需求。

在过去的几十年中，通过人工授精和胚胎移植显著地加快了这一进程。然而，与此同时其他的先进技术也正在出现。

最近通过向肉用动物基因组中插入控制生长基因，使基因组的修饰更具有目的性。

一个更具有目的性的能对控制生长的生理轴发生影响的方法是改变上述各种信使的含量。这是通过直接投给生长激素和生长激素释放因子实现的。

最近在影响生长激素轴成分的技术中又增加了免疫技术。已证明用抗体增强生长激素的效应和结合生长激素抑素的方法是可行的。

对安全和功效的评价

这些技术的作用方式相同，所以它们对受试动物，动物产品以及对环境的影响在许多方面类似。因此可以把它们放在一起研究它们的共同特性。

由于生物技术能够提供生长激素轴中控制生长的各种关键成分，并可分别用这些成分进行动物试验，因而近年来对它们的作用有了更好的认识．

随着科学数据的迅速聚累，越来越有可能分析上述三种相关的控制生长的新技术的潜在作用和可接受性方面的问题．

在动物生产中引进早期的革新已经反复表明，这些成就易于引起对它们的可接受性方面的长期的意见分歧．长时期争议的中心问题是消费者的安全问题．最近还注意到了受试动物的安全，对环境的影响和对生产体系结构的冲击．

新技术可接受性方面的问题常常是在技术开发的后期才被确定． 对这些即将来临的问题的本质没有充分的认识， 防碍了在实验设计中及时地把它们结合进来进行研究．其结果是对这些问题做出恰当回答的时间比较晚，并且要付出较高的代价．

为了给研究工作以及应用这些技术的管理工作提供适当的指导，有关的科学团体之间及时地举行国际磋商是非常有益的．这次专题讨论会就体现了这种磋商．

在来自大学，工业研究团体以及负责制定规章制度的机构的科学家们之间的相互探讨中，检阅技术的现状和确定进一步研究的重点．由这三方面提出倡议并参加这次专题讨论会，说明大家都认识到这种联合的科学评议是有用的．

这次专题讨论会还可进一步协调相关地区的技术研究．不需详加说明这些地区在认可和规章制度方面的分歧即已表明举行联合科学评议的紧迫性．

<div align="right">（齐顺章 译）</div>

II 提交的论文摘要

〔表和图见英文全文〕

1.挑 战

生物技术，竞争性和可接受性：对欧洲的挑战

Mark F. Cantley

欧洲共同体，欧洲生物技术协作组（CUBE）委员会主任
（本文只是作者个人意见，除了明确引用官方文件者
外，不是委员会政策的说明。）

摘　　要

作者不是生物学家，但参与欧洲生物技术战略的制定
和贯彻。近年来关于生物技术的意义和可接受性已成为引
人注目的问题，尤其关于生物学知识和生物技术的新进展
在农业中的应用更是如此。

共同体战略的纲要已经制定，其基本方向是国际竞
争，设想是为了支持欧洲经济共同体条约中更为广泛的目
标的追求。对生物技术的公众和政治评议的范围扩大了，
其中包括生态学，对农业经济结构的影响，动物的良好生
存，伦理问题，消费者的权利和消费者的安全等。在一个
方面觉察到威胁或感到损害的人们便想在其他方面的批评
者中寻求问题。

在此更加广泛的范围中，全球责任和社会的或文化的
价值的争论使通常强调的经济竞争变得更为复杂。但并不
否定革新的利益，也不否定以分享共同利益的观念为基础
的全球范围内的竞争。这种竞争可按GATT条例在自由世界
贸易系统中同时进行，或者在为了全球生态系统的利益所
达成的约束下进行。（参看，现在国际上已同意的对氟氯
化碳生产的限制。）

为了发扬这些共同观念和提高公众和政治评议的水
平，必须促进有关团体之间的更为有效的交流。

关键词：生物技术，欧洲共同体，市场竞争，可接受
性，猎。

（尹德中　译，　齐顺章　校）

2．概　述

用生物技术"工具"调控猪的生长

R.Dean Boyd 和 Diane Wray-Cahen
康乃尔大学畜牧系，Ithaca NY 14853-4801

摘　要

　　生长是涉及多种激素高度协调的过程，并且需要足量的营养物质。已证明生长激素（ST）有调节代谢的作用。它在确定出生后动物吸收的营养物质如何分配方面起主导作用。投给外源性ST通过以高度协调的方式把营养物质导向特异的组织或者由特异组织输出的作用，显著改变生长期猪组织的生长速度和状况。已发现ST在显著加快瘦肉组织增长的同时减慢脂类的沉积。提高血液中此天然多肽激素的浓度给养猪业者提供了良机，他们可用此法使生产效率发生显著的改进，同时又可提供给消费者以确实是瘦肉的食物。最近的生物学创新产生了新的生物学"工具"。这些工具使美国科学家能够采用不同的方法达到ST的效应。在这篇综述中讨论了5种可能的方法，目前这些方法都在系统的研究中。讨论的技术是：（a）外源性ST，（b）ST的促分泌物，（c）胰岛素样生长因子（IGF-I），（d）ST分泌或效力的免疫操纵，和（e）基因的插入或基因表达的调控（例如ST,GRF）。在不久的将来，可用外源性ST，适当的ST释放促进物，或用增强内源性激素生物学活性的位点特异性抗体等来达到ST的效应。还有许多重要的生物学问题需要解决，然后科学家们才能确定IGF-I媒介的ST效应是否适合商业开发。从长远的观点看，随着遗传改进技术的发展成为控制基因表达（即基因放大）或基因插入（即基因的最佳化—ST,GRF）的尖端的和特殊的方法，可以认为能用遗传学手段操纵ST"轴"。我们期待对操纵ST"轴"进行充分广泛的研究，以便在消除公众反对在肉用动物生产中使用某些技术的疑虑的同时，做到定向的营养物分配。最后，ST的最重要性在于它已成为研究出生后动物生长和代谢调控机制的宝贵"探针"。

　　关键词：生物技术，生长调节，营养物分配，生长激素，胰岛素样生长因子，基因插入，猪。

<div align="right">（齐顺章　译）</div>

用生物技术控制猪的生长和产品质量的
规章限制和公众认可

P. VAN DER WAL
荷兰　Wageningen农业大学

摘　要

　　通过生长激素轴可调控猪的生长和产品质量．其途径有，投给生长激素轴的各种成分，用免疫法影响这些成分以及在动物基因组中插入有关基因．

　　这三种技术的管理依技术类型和地区的不同而各异．然而它们的作用方式相同，因而在效能和安全方面产生的影响也类似．为了更有效地维护消费者、动物和环境的安全，也为了有效地为研究和开发制定一个较明确的目标，有必要协调这些技术能够得到批准所需要的条件．

　　动物及食品科学的空前挑战需要在科研上进行国际合作．这种通力合作是能够充分妥善处理这些技术在安全和效能方面的一般问题的．这些问题没有地区差别，它需要研究力量和专门知识．而这种专门知识在任何地区都是有限的．

　　在这些领域中，专门知识的国际性联系将有利于国际管理的协调，这是防止国际贸易中分裂性争执的关键．

　　对管理的核心问题来说，与生长激素有关的各种技术都是相同的．

　　在效能方面，影响生产效率和产品质量（由增加蛋白质的聚存和减少脂肪的沉积所引起）是它们的共同特点．

　　在产品安全方面，由于生长激素轴的各种成分都是蛋白质，它们在肠道和环境中易于降解，从而提供了良好的前景．

　　在公众对这些技术的认可方面，至关重要的是要有充分的很好权衡这些技术对成本，肉品质量，以及消费者、动物和环境安全诸方面的可能利益的资料．

　　还没有一个强有力的人员配备充足的管理体系为消费者的接受创造坚强的基础．这个体系的信誉取决于方针和手续的尽可能的充善，并能确保按章办事．

　　关键词，生长控制，生物技术，生长激素，认可，猪，管理．

<div align="right">（尹德中　译，齐顺章　校）</div>

3．对生产体系的意义

PST在北美的效应：经营管理上的不同和优点

N.C.Steele, R.G.Campbell, T.J.Caperna
J.P.McMurry, 和 M.B.Solomon
美国，马里兰州，Beltsville 城，美国农业部，农业研究
服务站，Beltsville 农业研究中心，非反刍动物营养
实验室和肉类科学研究实验室
澳大利亚，维多利亚州，Werribee 城，动物研究所

摘　要

现有的改变家畜生长和组成的各种技术，特别是用外源种属特异性的生长激素，生长激素释放因子处理和生长激素抑素自身免疫，都是作用于生长激素轴的某个环节，以改变此激素的产生、分泌和代谢。投给外源性猪生长激素对猪的生长和发育状况有明显的影响，有利于瘦肉组织的增长和脂肪沉积的减少。全世界对这项技术的应用都感兴趣是因为推测在任何饲养管理条件下都同样有效。欧洲对猪的饲养管理喜欢用限制饲喂。非阉割公猪的交易。异源性饲料蛋白源的混合，用于销售的轻型猪和重型猪的分开饲养以及诸如此类的条件。西半球的生产实践与北美相似。明显喜欢用自由采食，用青年母猪和去势公猪，较高的摄入优质蛋白和专一的重型猪市场。在最近完成的几项试验中，对影响猪生长激素作用的不同管理条件进行了评估。结果表明，猪生长激素对幼猪和育肥阶段的猪的瘦肉增长都是主要的生理控制因素。同时，饲料摄入量，特别是能量摄入量能够影响动物对猪生长激素的反应。然而猪生长激素的效应实际上不受性别影响。母猪和去势公猪对生长激素的反应与非去势公猪具有相似的蛋白增长率。当前的研究结果表明，猪生长激素技术在现行的管理体系下是适用的，而北美对猪饲养管理的特点更有利于这项技术的应用。这意味着，由于现在有了更为一致的生产高质量瘦肉的技术，以向全球市场出口为目的的猪肉生产将变得更有竞争性。

关键词，猪，生长激素，组成，饲养管理。

（张永清　译，　齐顺章　校）

重组猪生长激素(rPST)在欧洲的应用:
研究的体会和展望

Vernon R.Fowler(1) 和 Egbert Kanis(2)
(1). 苏格兰,阿伯丁大学,Rowett 研究所和农学院
(2). 荷兰,Wageningen 农业大学

摘要

在欧洲,养猪业是在一个有特色的农业、社会和科学的环境中进行的。许多年来,专家们致力于培育饲料利用效率既高,又符合加工业者制订的评定标准的猪种。在欧洲盛行的生产条件下,重组猪生长激素的应用是否能明显提高效益,仍是主要争议的问题。

在荷兰,西德和联合王国(苏格兰)的实验中心,用重组猪生长激素对欧洲猪进行的所有实验都清楚的表明,应用重组猪生长激素能够非常显著地提高生长速度,饲料利用率,尤其是使胴体瘦肉增多。提高最显著的是瘦肉组织的沉积速度和每日氮的沉积。在体重35-140公斤范围内的所有体重情况下都取决于给药时期和剂量。在苏格兰,用体重35-95公斤的猪,喂给蛋白含量为190克/公斤的饲料,每天给予重组猪生长激素7毫克的高剂量,实验组的日增重比对照组高20%,胴体的氮含量比对照组增加10%以上。在荷兰用定量喂给饲料所做的氮平衡实验表明,甚至皮特兰猪(Pietrain)的日增重也提高10%以上。日蛋白增加约提高30%,日脂肪沉积降低约10%。一般说来,重组猪生长激素能使自由采食量降低约5%。只有在荷兰进行的自由采食实验在这一点上是个例外。皮特兰猪和杂交猪由100公斤长至140公斤体重时,其饲料摄入量增加约8%。

饲料中的蛋白含量对重组猪生长激素充分发挥其对蛋白质沉积方面的效应很重要。很明显,当前是确定基因型、饲料、屠宰重和重组猪生长激素剂量之间的最佳结合,以便按其模式进行,从而由这项新的令人振奋的技术中得到最大收益的良好时机。

关键词:生长激素,猪,胴体品质,生长速度,饲料利用率,欧洲。

(张永清 译,齐顺章 校)

中国猪应用猪生长激素的前景

冯淇辉
中国，广州，华南农业大学
齐顺章
中国，北京，北京农业大学

摘　　要

　　在广东省将猪生长激素投给４４头中国大花白猪和Landrace的杂交猪，对 F_1 平均日增重的作用 (+15.3%) 比级进二代 F_2 (+11.3%) 更显著。但后者的背膘降低 (-19.2%) 和瘦肉增加 (+17.0%) 比前者 (-10.7%和+9.8%) 要显著的多．

　　在北京将猪生长激素投给了育肥后期的北京黑猪．喂给含 18%粗蛋白饲料的猪比喂给含16%和14%粗蛋白饲料的猪的平均日增重提高的更多；饲料利用率更好和瘦肉产量增加的更多．

　　看来这些结果使人们对中国猪种有了新见解，即用猪生长激素能够提高猪的日增重，饲料利用率和瘦肉产量并降低背膘．

　　关键词：生长激素，猪，生长速度，饲料利用率，中国．

<div align="right">（齐顺章 译）</div>

直接修饰家畜的基因组

Thomas E. Wagner
哲学博士，主任
美国，Ohio 大学，Edison 动物生物技术中心

摘要

本文综述了当前将基因引入实验动物和家畜种系中的方法．这些方法包括受精卵原核微注射的直接基因转移法．反转录病毒载体感染胚胎法和全能胚胎干细胞连续培养培育动物法．虽然迄今只有用原核微注射法获得了基因转移家畜（猪），但已报导了一种从猪胚胎细胞得到的胚胎干细胞系可用于培育基因转移猪或克隆猪．本文详细讨论了能表达生长激素的基因转移猪的表型特征．其中包括体脂降低50%或更多，饲料利用率提高30%或更高等有利特征，以及动物骨架发育的困难增大和应激的敏感性增高等不利特征．已提出将生长激素在基因转移猪中的表达控制在其生长期的一定时期内，能够克服生长激素的表达所带来的不利作用．为达到此目的，将磷酸烯醇式丙酮酸羧激酶（PEPCK）的启动子与牛生长激素（bGH）的结构基因连接起来形成嵌合基因，并将此基因引入小鼠和猪的种系中．结果证明在这些动物的胚胎发育期生长激素不表达，而且它的表达可用饲料来调控．用高糖饲料可使小鼠体内bGH的浓度降至基础水平的5%．当再喂给高蛋白并且无糖的饲料时，一周内其血清中的bGH增高20倍．虽然用饲料调控bGH在猪体内表达的研究还在进行中，但PEPCK/bGH基因转移猪没有出现各种残疾，而在用组成型启动子控制生长激素表达的基因转移猪则出现这些残疾．

关键词：基因转移，生长．猪，调控，启动子．
（朱宝利　译，齐顺章　校）

与生长激素有关的技术：对猪育种的意义

Egbert Kanis

荷兰，Wageningen 农业大学动物育种系

摘要

现在和将来的生物技术在调控动物的生长和机体组份方面的应用对猪的育种方案具有重要意义。这一点可特别寄希望于和生长激素有关的技术，因为生长激素对饲料转化率和机体组份有明显的正效应。本文探讨了猪生长激素（PST）的投给和生长激素基因转移猪的意义。

猪生长激素（PST）的大量使用对选择强度及遗传反应可能有间接效果。必须对育种的目标性状及其经济价值进行重新评价。假如PST的使用与基因型之间有相互作用的话，建议仅在做生产性能测定期间，给核心群猪使用PST。遗传参数和表型参数（遗传力和相关系数）应做重新估计。

在繁殖育种的方案中，PST给引进高繁殖率的（中国）品种作为母系提供了新的可能性。中国品种猪的表型在胴体组成上的不利影响会被PST的使用所抵消。由于PST能增高最佳的屠宰体重，因而如果猪肉的总产量固定的话，就可减少猪的年出栏数。其结果是商品母猪的需要数量减少，生产成本亦即降低。

将生长激素基因成功地转移到猪的种系之中将对生长和机体组份产生与使用PST类似的效果。此外，基因转移猪的利用无论如何会将对核心猪群的育种策略产生巨大影响。可以预料所获得的基础群基因转移猪之间的差异将是很大的。许多猪会因它们的不利特征而被淘汰。剩下的基因转移猪将被用来作高强度的繁殖，因而带来群体含量小的问题。最佳的育种策略取决于纯合性猪是否是所希望的最后商业产品，以及在已转移生长激素基因的品系中能否继续导入其他外源基因。

最后的结论是，在一个猪育种计划的核心群中引入和发展基因转移猪是非常重要且需加强研究的。只有各育种组织共同冒险，联合努力才能成功。

关键词：生长激素，基因转移，猪育种。

（朱宝利 译，齐顺章 校）

生长激素对猪肉加工业的意义

F.K.Mckeith, P.J.Bechtel 和 J.Novakofski
美国，伊利诺州，伊利诺大学

摘　　要

　　猪肉加工业包括屠宰，胴体修整，鲜分割肉制备，腌肉和香肠生产。我们的研究表明，生长激素能使育肥猪脂肪降低，肌肉增加。这些大的组成变化可能会影响猪肉加工业的某些或全部过程。与屠宰和修整过程有关的潜在问题有，副产品增加，去皮困难，胴体冷却速度和冷缩程度改变。与切成批发分割肉有关的潜在问题有，切割柔软瘦肉组织的困难，在制备零售分割肉时肌肉或肌肉群分离的困难，以及在去皮时不使肌肉表面暴露的困难。瘦肉量的增加将影响含水量，因而可能需要改变操作程序以获得所期望的产品组成的终点值及货架寿命。腌肉加工者关心的是制作腌肉的腹肉组成和厚度变化（尤其对美国市场来说）。还有用于生产无骨火腿肉的蛋白渗出液特性也要重新评价。香肠制作者关心的是肉品性质的可能变化，其中有色素浓度，水分对蛋白质的比值，系水力，pH，肌纤维蛋白浓度和脂肪组成的变化。

　　关于生长激素处理猪的生长和组成方面已有相当多的资料。但对于其加工特点则资料很少。现有的少量资料还没有涉及到生长激素处理猪的屠宰和修整程度的问题。只有少数猪是用高速操作的商业法屠宰的。一些研究组评价了胴体的制作特点，并报导了在分割肉产率和分割肉组成方面的优点。可能出现的屠宰问题。如PSE肉的增加还未见报导。也没有直接提到腌肉和香肠制作方面的问题。然而对pH值，肉颜色，脂肪含量，水份对蛋白比值和腹肉特点已做了评价，并且没有发现什么问题。例外的是腹肉厚度。它与背膘厚度直接相关。

　　尽管生长激素的应用需要改进，以便生产者和加工者都能采纳，但我们相信，它不会引起不可克服的困难，用现有技术是能够解决这些问题的。

　　关键词：生长激素，分割肉产率，加工，腌肉，猪。

4．对受试动物的需求和健康的影响

猪生长激素（pGH）和胰岛素样生长因子（IGFs）调控猪生长性能的机制：由pGH和IGF受体到整体动物的探讨

T. D. Etherton
美国Park大学奶牛和畜牧系

摘　要

猪生长激素是一种天然存在的蛋白类激素，对猪有广泛的生物学效应。用猪生长激素（pGH）处理生长期的猪，能显著提高猪的生长性能（包括平均日增重，饲料利用率和胴体成分）。pGH的生物学效应大致可分为促生长效应和代谢效应两类。本文将讨论pGH影响生长和代谢的某些机制。讨论的内容包括：（1）pGH对脂肪组织生长和代谢的影响，（2）pGH和胰岛素样生长因子I（IGF-I）二者在促进肌肉生长中的作用，（3）长期使用pGH引起血中糖和胰岛素含量升高的因素。（4）关于IGF-I结合蛋白（IGF-BPs）不仅仅是在血液中运输IGFs，而且还对IGFs的生物学活性起调节作用的证据。（5）最近由克隆的cDNA序列确定的人和兔GH受体的氨基酸序列的意义。

虽然现在已经知道pGH能改变营养物质在肉用动物体内的分配，但对发生此种作用的生物学机制则不清楚。关于pGH受体怎样产生化学信号以及媒介pGH在细胞内的生物学效应的分子本质都一点也不知道。随着我们对pGH与其受体的相互作用的认识不断深入，很有可能确定出pGH中与pGH受体结合的氨基酸残基。据此，进而有可能设计出生物学活性更高的pGH类似物。因此，我们现在所见到的利用外源性pGH处理猪的效果，只不过是通向以经济、有效的提高肉畜生长性能方法的一系列进展中的第一步。

关键词：生长激素，胰岛素样生长因子，生长，调节，猪．

（张少英　译．齐顺章　校）

猪生长激素对猪能量代谢的影响

M.W.A.Verstegen, W.van der Hel, E.J.van Weerden
荷兰， Wageningen 农业大学和
动物营养与生理学研究所

摘　要

　　本文研究了施用外源性生长激素对猪蛋白质和脂肪增长以及代谢率的效应。分别给三种基因型的猪（Pietrain，杜洛克和荷兰长白与荷兰约克夏杂交猪）由55公斤体重开始注射rpST。持续10周。全部动物的饲料水平相同（相当于维持需要量的 2.6倍）。与对照组相比，受试动物的体重增长速率提高约100克/天。体蛋白增长速率提高40克/天/头，脂肪增长速率下降40克/天/头。

　　rpST引起的代谢率的提高为每天每公斤$^{0.75}$、46千焦耳（7.7%）。讨论了这种代谢率增高的各个方面。如果由可代谢能分别合成蛋白质和脂肪的效率不变，则rpST使维持能（MEm）由每公斤$^{0.75}$、393千焦耳增高至451千焦耳ME。

　　如果代谢率的提高是与蛋白质合成的能量效率（Kp）降低相联系，而与维持能量无关，则蛋白质增长的能量效率应从对照组的Kp=0.59下降至pST处理组的Kp=0.48。

　　代谢率提高的第三种可能性是与脂肪沉积有关。假如对维持和蛋白质合成没有影响，则pST处理猪的脂肪能量效率为Kf=0.68，而对照组猪为Kf=0.77。

　　本文还讨论了代谢率的提高可能引起的对温度需求的影响。体脂减少将导致皮下脂肪减少和绝热性能降低。需要研究的是，综合效应（产热增加，脂肪减少）将对等温区下限产生多大的影响。高代谢率将降低热耐受的上限。

　　脂肪和蛋白质沉积的改变所产生的营养方面的后果是什么，也需要进一步探讨。

　　关键词：猪生长激素，代谢率，维持，分效率（Partial efficiency）。猪。

（张少英　译，齐顺章　校）

操纵动物生长和发育的生物技术
对猪组织和饲料营养物需求的影响

R.G.Campbell, R.J.Johnson 和 R.H.King
澳 大 利 亚, Victoria 3030, Werribee, 动 物 研 究 所

摘　　要

　　给予外源性猪生长激素(pst), st释放因子, 可能还有 lgt-l, 能够提高蛋白质和无机盐的沉积速率, 从而加快骨骼发育; 改进生长性能和降低胴体脂肪含量. 然而, 这些技术对生长期猪的饲料营养需求方面的影响仍 不 清楚. 对于30－60公斤体重的猪来说, 投给外源性pst可使蛋白质沉积提高25－40%. 在还不知道对氨基酸利用的改进情况下, 看来, 对于维持接近最大生长性能的饲料蛋白和氨基酸需要水平方面没有影响. 与此相反, 将pst投给60－100公斤体重的猪可使蛋白沉积提高50－80%（取决于动物的性别）, 与此同时, 为了获得接近于最高的生长性能需要饲料蛋白（氨基酸）水平增加30－45%. pst对蛋白质代谢的促进作用是由lgt-l介导的, 并且是使蛋白质合成和降解的速率加快的结果. 但是, 为了充分了解pst以及与之相关的技术对饲料营养需求方面的影响, 需要有这些技术究竟能使蛋白质和无机盐沉积速率增高至多大以及有关氨基酸和无机盐中间代谢变化的进一步资料.

　　关键词: 生长激素, 猪, 营养需求, 蛋白质, 无机盐.

（张永清 译, 齐顺章 校）

生长激素对免疫系统的影响

Keith W.Kelley 和 Carl K.Edwards, III
美国，伊利诺州，伊利诺大学，
畜牧系，免疫生理实验室

摘　　要

　　长期以来，　一直认为生长激素能影响免疫系统的细胞．现在已知，生长激素能使胸腺增大，加强淋巴细胞和释放活性氧中间产物的幼巨噬细胞的许多活性，以及促进中性白细胞和红细胞（原文如此）的分化．生长激素甚至可由淋巴细胞合成．这些新近的发现揭示，生长激素除了提高生长速率和奶产量外，还能调节淋巴细胞和巨噬细胞的功能活性．

　　关键词：生长激素，淋巴细胞，巨噬细胞，粒性白细胞．

<div align="right">（张永清 译，齐顺章 校）</div>

外源性生长激素对猪的可能的副作用

Stanley E.Curtis,
美国， Illinois 大学，畜牧系

摘　　要

　　外源性生长激素可能影响猪两方面的性能，一是体温调节（并因而影响猪对环境温度的需求），二是采食行为（并因而影响猪舍和喂饲系统的设计）．外源性生长激素对一头７５公斤体重的猪的净作用大致是：使猪的低临界有效环境温度提高６摄氏度，高临界温度降低几度．因此，猪可能在温度范围的高低两端都对环境温度更为敏感．投给外源性生长激素的猪的饲料摄入量之所以显著减少，可能是由于热应激、群居问题或采食的机会不够充分之故．应该探讨这些可能性，并寻找方法以减轻任何已被证实的影响．

　　关键词：猪，生长激素，热环境，群居环境，饲养设计，饲料摄取量．

<div style="text-align:right">（齐顺章　译）</div>

促进生长的新技术对猪生殖和泌乳的影响

B.N.Day, Steve Terlouw 和 August Rieke
美国, Missouri-Columbia 大学, 畜牧系

摘 要

已证明是主要改变生长－育肥期猪的生长和胴体组成的有效措施的新型生物技术正在涌现出来. 最近在基因插入方面的进展已能获得基因转移动物, 这种动物可以用来育种, 并已产生了后代. 然而在表达人生长激素的基因转移公猪和小母猪上已观察到了严重的生殖方面的问题, 其中包括不动情和性欲缺乏. 报导的有限材料表明, 用猪垂体生长激素 (pGH)或重组猪生长激素(rpGH)处理可改变母猪的泌乳曲线和提高乳产量.

生殖方面的紊乱有: 在接近开始性成熟时每天投给和在动情周期中的动情前期投给pGH, 青年母猪出现动情期延缓和滤泡囊肿. 然而, 在生殖的生长－育肥期 (体重 50－110公斤) , 每天注射重组猪生长激素(rpST), 对小母猪的配种到发情之间的间隔、发情年龄, 发情年龄小于 240日龄的母猪的比例或怀孕率都没有不利的影响. 同样, 在妊娠的第 4－18天期间使用rpST也不影响怀孕率和怀孕 25天时的平均胚胎数. 这些结果表明, 在生长－育肥期使用rpST, 不影响这一时期以后母猪的生殖性能.

关键词: 猪, 生殖, 生长激素.

(齐顺章 译)

5．消费者方面

生物技术与控制猪的生长和产品质量：
食用产品的安全性

H.A.Norcross, R.A.Carnevale,
E.A.Brown, A.R.Post
美国农业部，食品安全监督局

摘　　要

　　尽管许多发达国家享有蛋白质丰富的食品供应，但很多国家需要提高蛋白质产量和改善其质量的技术．目前，与改进遗传特性和营养条件一起，也使用药物促进生长和提高饲料转化率．从而使得家畜给人类提供了比以往更多的蛋白质．尽管有时合成代谢剂的名声不好，但它在促进家畜的饲料转化率方面表现出特殊的优点．

　　蛋白质的合成及其调节已成为在生物化学和分子遗传学水平上深入研究的课题．象生长激素这类的基因产物，由于能促进生长和饲料的转化率，并且能使脂肪／蛋白质发生重新分配．激发了科学家们用以探讨人工调节家畜蛋白质合成的可能性方面的兴趣．重组DNA技术生产的首批产品为生长激素和与其有关的化合物，生长激素抑素、生长调节素及生长激素释放因子．用这些化合物提高家畜和世界农业的生产效率是经济可行的．

　　如果这些产品在美国使用，必须得到美国食品药物管理局的批准．这些产品的安全性和有效性必须用严格控制和适当设计的科学研究来证明．

　　有关生长激素，生长调节素以及包括释放因子在内的其它因子的试验情况，已经作为新的动物药物提交给食品药物管理局申请批准．通过销售前的批准和批准后的监督来管理这些新药物，必须有效地保护公众健康，必须保证产品的合理使用，并且必须保证对动物是有效的．

　　关键词．生物技术，生长激素，公共卫生，有效性，管理．

（肖运来　译，程金根　校）

施用重组生长激素后在猪体内残留的可能性

D. Schams[1], E. Kanis[2] & P. van der Wal[2]

[1] 西德慕尼黑技术大学生理研究所

[2] 荷兰瓦格廷根农业大学畜牧系

摘　　要

　　近年来证明，重组猪生长激素（rpST）能非常有效地改进动物的生长性能，例如，平均日增重，饲料转化率和瘦肉率。本研究的首要目的是测定rpST受试猪在屠宰之前及屠宰期间，rpST在血中和组织中的含量以及IGF-I在血中的含量。

　　在实验1中（94头猪）设五个因子。三个品种（皮特兰、杜洛克以及大约克夏与荷兰长白猪的F₁代杂交种），每品种四窝；两个性别(阉公猪和小母猪)；两种处理(rpST和没有药效的平行对照)；和两个屠宰体重(100公斤和140公斤)。由体重60公斤开始，肌肉注射溶解于Arginin盐酸缓冲液中的rpST 14毫克，每周两次。在最后一次注射rpST的4.5天后由颈静脉采取血样，随即屠宰。实验2从三个品种（皮特兰、杜洛克以及F₁代杂种）中挑选36头阉公猪，从体重60公斤直到120公斤每次肌肉注射14毫克 rpST，每周两次。在最后一次注射后的1小时内及 26－27小时以后从颈静脉采取血样，随即屠宰。此外从10头猪（其中7头处理，3头平行对照）的右肩部取肌肉组织样用于pST残留分析。

　　pST和IGF-I用RIA法测定。

　　实验1中，在最后一次注射 rpST后的 4.5天，受试动物血中的rpST水平与对照相似，或者在皮特兰和杜洛克品种中明显降低。在实验2中，最后一次注射后的一小时内，其血中的 rpST明显增加，从每毫升2纤克（ng）到240－321纤克不等。26－27小时后受试动物的rpST含量已恢复到对照的水平。组织中的含量没有明显差异，都低于每克新鲜组织5纤克。在实验1和实验2中，最后一次注射后的1小时内，对照和受试动物的血中，IGF-I的浓度没有明显差异。而26－27小时后其浓度明显增加。得出的结论是，在最后一次注射pST的4.5天后，在血液和肌肉中没有发现pST或IGF-I的可测量残留。

关键词：生长激素，胰岛素样生长因子，残留，猪。

（程金根　译）

施用猪生长激素后的猪肉在营养和感官上的特征

K.J.Prusa

美国衣阿华州立大学食品营养系

摘　　要

　　尽管已经报导了使用和未使用生产激素的猪肉之间在营养成分和感官品质方面有明显的差异，但没有引起重要的关注。已有几份报告指出，用pSt处理后，猪肌肉内脂肪含量降低。已报导其降低量不足1%。而在这些报导肌肉内脂肪含量减少的研究中，肌肉蛋白质和水分的含量略有升高。用 pSt 处理后，并在屠宰的当天停止用药，没有看到其背最长肌脂肪酸组成和胆固醇含量的变化。但据报导在屠宰前7天开始停止使用pSt的话，其鲜肉中的高度不饱和脂肪酸含量和熟肉的胆固醇含量略有上升。用 pSt 处理后，组织中的维生素B_1含量略有下降。据几个试验报导，使用 pSt 对猪背最长肌的感官品质没有不良影响。但据报导，用高剂量处理的猪其肌肉的柔嫩性，多汁性及风味略有下降。

关键词：生长激素，营养成份，感官，品质，猪。

　　　　　　　　　　　　　　　（侯保平　译，程金根　校）

335

重组猪生长激素对比利时和荷兰猪的胴体及肉品质的影响

D.Demeyer[1,2], R.Verbeke[1], G.Van de Voorde[1], J.Fabry[3],
E.Deroover[4], R.H.Dalrymple[5].

[1] 比利时Ghent大学；   [2] 比利时Brussels大学；
[3] 比利时农业研究中心； [4] 比利时Cyanamid Benelux NV；
[5] 美国Cyanamid公司；

摘　　要

　　本文总结了采用rPST对比利时和荷兰猪的胴体和猪肉品质的影响，其详细结果见其他刊物。实验1使用比利时育肥猪（60－100公斤），设四个处理（每天分别注射0、1.5、3和6毫克的rPST）。随意采食高蛋白，含谷物的饲料。实验2使用荷兰猪，设0和14毫克两个处理，每周注射两次，在育肥期使用与实验1相同的饲料饲喂。分析的数据有：胴体器官产量；胴体质量及分割肉产量；肉的感官品质；组份组成和肌肉蛋白组成（仅在实验2中）。

　　随着心、肝和肾的增大，胴体产率稍微降低。胴体中各种脂肪的减少明显改进了胴体质量，也提高了胴体的级别。由于脂肪块和板油的减少，胴体肉块产量得到提高。死亡后不久，肌肉pH值下降速率没有显著差异，只是体温高一些。最终pH值升高不多，但差异显著。对肉质、肉色和系水力的分析结果表明，肉的红色稍微减淡，这是统计学上唯一的显著差异。对肌原纤维蛋白成分和背最长肌的长度没有影响，只有粗蛋白含量略有升高。

　　本研究表明各种水平的rPST都能提高肉的产量，并降低胴体脂肪，既使使用胴体成分优良的品种也不会对肉质的感官品质有不良影响。

　　关键词：生长激素，胴体质量，肉品质，器官重量，猪。

<div align="right">（侯保平　译，　程金根　校）</div>

消费者对食品技术和生物技术的认识

Janet Graham,
英国伦敦欧洲共同体消费者协会（CECG）

摘　　　要

　　本文是英国消费者的观点。尽管必定要出现消费者对 PST及其应用的认识问题，但本文不是特别针对PST的。在CECG，对BST（牛生长激素）以及现代食品技术的其它进展的研究，使我们能够就消费者对某些新技术及其应用的认识得出一些结论。

　　由于抗生素、激素、农药和遗传工程蛋白制品的使用，例如BST（牛生长激素）的使用，消费者日益关注建立在其之上的现代农业方法。看来在适当的时候，对 PST（猪生长激素）也会进行详细研究。某些技术曾使我们得到种类繁多的食品的持续和充分供应，这是很吸引人的。但是这些进步也使人们感到他们的食品不再富有自然本色而对这些技术不感兴趣。

　　我们需要建立标准以判断新的技术进展，其中包括对消费者需求的评价。用这个标准来检查某项进展是否保证了消费者的利益。一种新的产品是否更安全、更便宜、花样更多、供应的范围更广、更容易保存以及更加方便和更好的包装？它是否需要很长的时间才被接受，以及它是否会引起消费者的怀疑而抵制？看来，如果某项新的进展或科学突破对消费者既有一些好处又有一些坏处的话，则应将其积极和消极的作用都向公众说清楚，以便他们去决择。

　　在富有发达的国家中，消费者有一项非常重要的权利，那就是有权挑选他们所吃的食物，以及在充分了解的基础上进行挑选；我们不希望我们的选择受到原则上禁止新技术发展的那些人们的限制。同样，为了我们的选择是有根据的，我们也希望从事食品生产和市场销售的人们，从研究到最后出售，都必须更积极地提供有用的和在形式上可以使用的信息。

　　关键词：生物技术，人类食品，消费者，认识，猪。

（程金根　译）

利用生物技术控制猪的生长和产品质量引起的伦理问题

R. Dantzer
INRA – INSERM U.259, rue Camille Saint – Saens,
33077 Bordeaux Cedex

摘　　要

　　在养猪业中促进猪的生长和改善产品质量的新型生物技术的发展，引起了许多值得关注的问题．其中有些具有强烈的伦理含意．在动物生产中应用生物技术的伦理观必须从几个层次上去考虑．就动物本身来说，有两个问题：一个是生物技术产品的非天然性；另一个是处理可能对动物健康有不利影响．从专业的层次来说，越来越多地使用生物技术会使畜牧学家和兽医学家服从于经济效益，从而其结果是传统的对动物的关切和管理会有所放松．从消费者的层次来说，道德问题不仅涉及教育问题，而且涉及保护问题和选择自由．对社会层次来说，必须提出生物技术对动物生产的社会经济结构的潜在影响的问题．虽然生物技术对改进动物生产的效率具有极大潜力，但是，必须全面考虑由于在农业上使用新技术而引起的伦理问题，以求得社会的理解和接受．

　　关键词：生物技术，猪，生长激素，基因转移猪，伦理．

（程金根　译）

6. 对环境和经济的影响

猪生长激素对养猪业的经济反响

M.Hayenga, B.Buhr,K.Skold,S.Johson,E Grundmeier
美国衣阿华州立大学

摘 要

本研究综合分析了pST对猪肉的影响，并试图全面地阐述应用pST对经济的动态影响。然而必须强调的是本研究所获得的结果是分析时所使用的假设和有限的资料为前提。

应用pST最大的影响是降低成本并且增加每头猪的瘦肉产量。 生产者采用pST收益甚丰，从而引起产量的迅速增加。 猪肉产量增加的结果导致牧场和零售的价格都下降。由于生产成本降低，生产者采用pST后立即获得较高的利润，但是随着产量增多而迫使牧场价格下降，整个产业的收益将下降。从受益的角度看来，由于短期内利润的增加和长期内采用者对不采用者具有竞争优势，因而明显鼓励猪肉生产者采用新的技术。此外，养猪业者还能夺回一些在过去三十年中由于养禽业的技术进步而丢失的阵地， 从而成为一个更能生存的行业， 以得到消费者对食品的花费。当晚期使用者也跟上来使用时，则高产量低价格将使加工业者和消费者受益。在长期经营中，因为可以预料在竞争行业中是可以自由加入的，生产者总的收益很少。饲料谷物生产者将受损失，而大豆生产者不受影响。

仍须回答几个与 pST对生产的影响以及与消费者的需要反应有关的问题。既使将来肯定地知道了长期的生产影响和任何可能的付作用，整个养猪业都采用pST也是不可能的。消费者接受注射过pST的猪肉仍然是一个重要问题，而这个问题将长期影响着pST的应用。

本文没有考虑的一些重要问题如下：

A)由于胴体较瘦而使罐头食品厂的老板更喜欢重型猪的可能性及其影响；

B)国际上对家畜使用 pST的不同规定以及猪肉主要生产国和消费国的进口限制的可能作用；

C）竞争性技术的改变（例如其它生长促进剂，Beta兴奋剂等等）在养猪、养牛和养禽业中的影响。

这些改变可能增强或消弱当前我们所表明的使用 pST所引起的某些变化。当我们掌握更多的资料以后，我们将在更好的情况下更准确地评价pST对经济的影响。

关键词：猪生长激素，生物技术，经济影响，猪。

（程金根 译，齐顺章 校）

在欧洲共同体中猪的生长促进，
对猪肉和各级生产者竞争地位的影响

A.H.R. Pease, GIRA S.A.

瑞士日内瓦

摘　　要

应用PST使猪肉生产所获得的经济效益每头猪约为31个欧洲货币单位。对第一批屠宰的猪来说，PST供应商能获得其中的 20％。养猪业者能获得其中的50％。屠宰者/分割肉制做者能获得其中的 30％。市场上瘦肉增多将会导致价格下降，因此几周或几个月以后，这些效益的20％将由PST供应商获得，而80％则为消费者所得。

关键词：生长激素，经济影响，欧洲，猪。

（程金根　译）

猪生长激素对环境氮污染的影响

E.J. van Weerden 和 M.W.A. Verstegen

荷兰瓦格廷根TNO动物营养和生理学研究所ILOB系；

荷兰瓦格廷根农业大学动物营养系。

摘　　要

　　去势的杂交公猪（荷兰长白猪×荷兰约克夏），从58公斤体重开始共十周每天注射4毫克重组猪生长激素（rPST）。对照组用不含rPST的试剂进行注射。限制饲养，其代谢能为每天每公斤体重3/4 260 kcal。

　　测量的参数有氮平衡值，增重和饲料转化率。氮平衡值在处理期的最后六周分六次进行测定。在rPST处理后，氮平衡显著增加31％，从日粮中沉积的氮增加7.7％。增重加快10％。饲料转化率增加7％。rPST处理后，磷和钙的平衡分别增高18％和19％。从这些数据可以算出 rPST 处理后，体重在58－110公斤的猪，排泄到环境中的氮减少了21％，磷减少了16％。在有关rPST对氮排泄所起的作用程度中主要没有解决的问题是，还不知道rPST处理后，为了维持非常高的蛋白质沉积（每 天大约210克），日粮中蛋白质/氨基酸的水平究竟需要多高。到目前为止，所掌握的试验资料未能指明，在 rPST 处理后猪对蛋白质/氨基酸的需要量发生明显的增高。

关键词：生长激素，猪，环境，污染。

（侯保平　译，程金根　校）

III   会 议 的 结 论

Ⅱ3到Ⅱ6的结论是由主席和讨论主持人提出，并在专题讨论会最后的全体会议上正式通过的．

概要和结论

对生产系统的意义

主席：R.G.ZIMBELMAN

注射重组猪生长激素（rpST)在增加蛋白质沉积和降低脂肪沉积方面的无可争议的促进作用，在北美、欧洲和中国的不同品种，营养水平和性别以及不同管理体制之间是明显一致的．效果的大小虽然不同，但即使最低的效果也很显著．由胴体的形象和数据都可明显地看出此种结果．

在降低饲料的摄取和提高饲料利用率方面也是 一 致的． 由于下列几个因素不能具体说明增加的数量；(1)没有最佳剂量的确切数据， (2)剂量和营养之间的明显相互作用，即用较高剂量得到较高的蛋白质沉积可能需要改变日粮的成分，而较低的效果可能不需要；提交给讨论会的研究工作在处理时间的长短，所用剂量以及开始和最后的体重都不一样．

令人满意的产品在很大程度上取决于一个实用的缓慢释放的释放体系．一些公司可能在不同程度上成功了，从效果上看一般不会发生rpST的结构和构象的轻微改变．延缓释放的装置或配方很可能使效果有所降低和成本有所提高，因而可能影响不同生产者是否使用．

评级系统和加工工业的需求是十分复杂的，而且需要认真的考虑．需要考虑的问题很多，其中有腹肉厚度，加工程序，以及肌肉内脂肪的含量（肌肉内脂肪含量显著降低未必最令人满意）等．在这些问题中有的可因屠宰重量的提高而得到弥补，但在制备某些新鲜分割肉或流行产品时则可能不受欢迎．

非常需要深入研究美国和各种不同的欧洲市场上对极

端瘦肉型猪的反应．对美国猪或其他不是很瘦的猪所做的研究结果不一定适用于欧洲，因为在欧洲瘦肉型猪已经很普遍了．在这种情况下需要研究的问题是评定有没有利益可图，以及有没有与肉的品质和加工特点有关的迄今尚未发现的缺点．

在基因组的修饰方面正在按照发展中的理论方法以令人惊奇的速度向前进展，以期做到和控制基因的插入．基因插入比给猪注射 rpST 的最大优点可能是在那些已具有诸如产仔率高等令人满意的品质的诸方面．在这些猪上有可能用加入生长激素或生长激素释放因子基因的方法促进其生长和改善胴体品质．另一方面，很可能要在许多年后（至少 8 到 1 0 年）才能得到实用的可以进行繁殖的猪．很可能原始的基因转移动物是插入了单个基因，并且此基因是能够用某种饲料或适合商业生产的便宜物品进行调控的．

将青春期后的这种动物培育成一个大的繁殖群体看来需要一头公畜与其后代交配，以达到纯合．这将需要相当长的时间．最后，比较明智的办法应该是，先做足够长时间的性能测定，以便那些不令人满意的性状能够充分表现出来，然后再确定是否广泛的引入基因库中．这样做在财力和时间方面的代价可能是很昂贵的．因此，社会应该有一些办法，例如专利法，以便在这种技术着手进行商业化时，能使投资者为他们非常冒险的和巨大的投资收回合理的利润．

rpST 的利用是否需要修改那些用于遗传改进方面的测定和选择方法，取决于 rpST 的使用是否与猪的性能和胴体特性以外的其他令人满意的品质之间有相互作用．

我们的目标是否是最瘦的猪？这是一个需要认真考虑的问题．需要高度重视使用 τpST的猪或基因转移猪在脂肪酸组成方面的变化，并对它们进行专门的描述．

在使用这些新的令人振奋的技术时持谨慎态度是明智的．增强对何以产生这些效应的理解，对我们追求新的目标是十分重要的．

（齐顺章 译）

概要和结论

对受试动物的营养需求和健康的影响

主席：P.R.WIEPKEMA

动物维持内部和外部的稳态是通过很好平衡的、复杂的和互相结合的调节系统实现的．动物主动地调控着许多有关的环境参数．在改变家畜的有关生产性状时需要注意已有稳态的平衡．为了满足受试动物的营养需求和健康，需要充分阐明新技术的主、付效应．

Campbell证明，投给重组猪生长激素(rpST)大概不会以相同的程度影响脂肪的减少或蛋白质的增加．需要由饲料提供足够的蛋白质才能有增加蛋白质的效应．减少脂肪和增加蛋白质这两种效应都与rpST的剂量以及动物品种、性别和活重有关．

在实验中观察到，直到100公斤体重时，在与显著降低脂肪沉积和增加蛋白质积存的同时都伴有饲料摄取量的减少．这种对氨基酸、脂肪酸和葡萄糖代谢的有关影响需要进一步阐明．

Verstegen提出，用rpST处理使产热量增高，反映了其代谢率较高．这种增高可能是由于维持需要量较高，或者由于超出维持水平之外的能量利用效率降低所引起．

Curtis计算了由于rpST处理猪的皮下脂肪层变薄而影响其体温调节能力的潜力．它可能使体温调节区变狭．由于rpST处理影响动物的体温调节，所以需要测定rpST处理动物的最适温度．

需要有关于群体圈养并用rpST处理的猪的行为（群体的组织状态，饲料和水的摄取，休息等）的资料，因为可用这些资料评价在实际的和集约的饲养管理条件下可能出现的重要问题．需要特别注意rpST处理猪在运送到屠宰间时的反应，因为此时要求猪有较高的调节体温的能力．

Kelley强调了在正常情况下生长激素有活化免疫系统（巨噬细胞）的作用．当前还不能说明rpST处理对猪的健康是否有利．

Day证明，在青春期之前使用rpST不干扰处理结束后几周发生的生殖过程，而在发情期间用rpST处理则可引起不良的结果．

<div align="right">（齐顺章 译）</div>

概要和结论

消费者方面

主席：B.HOFFMANN

正如美国农业部的Norcross所阐述的那样，在美国已建立好的规定程序中，允许在食用动物应用药物方面，做适当的风险－效益评估．作为重组DNA的产物，重组猪生长激素（rpST)属于食品药物管理委员会（FDA)的责任范围之内． FDA已经允许在符合NIDA规则情况下，为提高科学研究效率，可以没有停止用药期限的使用rpST；同样，在相似情况下使用牛生长激素进行牛奶生产也不需要停止用药期限．

仍然还有一些没有解决的问题．例如，与消费者的安全有关的胰岛素样生长因子I(IGF-I)水平的改变问题，要求在对此问题得到答案之后才能最后批准．据Norcross所述，在基因转移动物的批准方面也有其他的规定程序．他非常赞同制定规章的人员和其他与上述问题有关的人员之间进行交流，交换观点和资料．

讨论中清楚地表明，与美国不同，在欧洲，适当而有效的制定规章的途径只是从60年代末期（英国），70年代末期（西德）才开始出现，其他欧洲共同体成员国则正处于制定过程之中．

据 Schams介绍的有关rpST和IGF-I的合作研究结果，在使用rpST后，血浆中的生长激素在26小时内达到基线水平， IGF-I在4天内达到基线水平．他所提供的关于肌肉中的rpST和IGF-I的初步数据表明， 距给药4天后没有残留． 关于肝脏和肾脏中的IGF-I水平目前尚无资料，关于IGF-I的降解以及很可能有生物活性的片段的形成， 需要更多的资料．

Prusa和Demeyer在报告中证实了使用rpST后胴体更瘦和肌肉内脂肪含量降低的普遍趋势。但是，必须考虑到品种间的明显差异。尽管报道了rpST处理和未处理动物的产品在营养组成和感官特征上的明显差异，但没有给于重要的关注。肌肉中蛋白质和水份的含量略有增加，生肉中的高度不饱和脂肪酸和熟肉中的胆固醇含量也略有增加。据报道，维生素B的含量略有降低。尽管报道了与对照组相比在感官特征上有些差异，但总的感官特征没变。

会议还讨论了应用rpST后人类减少了从猎肉摄入的脂肪和能量，这可能是一种改进人类营养质量的方式。

Graham从消费者的观点出发要求公开交流。消费者们所关心的不仅仅是安全问题，还有其他伦理方面，如动物保护的问题。现代消费者能够使用电子计算机及其他先进仪器，他们要求磋商，并能从中得到教育，这就是说，他们希望有能力处理来自工业和科学的信息。 在此意义上Graham讨论了在某些产品上标明其来源的问题。她也不同意把增加效益的产品叫做健康产品的作法。

然而，尚未解决的问题是，谁是消费者？在什么地方能够和他会面？以及怎样传播可靠的信息？

Dantzer的报告讨论了问题的哲学方面， 谈到了建立伦理价值过程的规范形式。为了使某些观点达到为社会所认识的水平，必须把生物技术对动物生产的社会经济结构的可能影响向公众宣传。虽然生物技术在提高动物生产效率方面有很大潜力，但是由于这些技术的应用所引起的伦理问题需要周到的考虑，以得到社会的理解和接受。

（杨作民 译）

概要和结论

对环境和经济的影响

主席：K.AIBARA 和 G.VAN DIJK

在猪的生产上使用重组猪生长激素 (rpST) 取决于许多因素，其中大多数因素目前正在定量中。这些因素是农场经济，对市场链的效应，消费者的接受情况，对自然环境的影响，政府的态度和伦理方面的考虑等。

农场经济

Hayenga 指出，成本的降低将导致高采用率—其前提是假定没有由于消费者的接受问题而产生的严格限制。他的数字表明在 2-3 年内采用率可达到 50%-60%。rpST 能使成本降低，因此，早采用 rpST 的人们可以看到他们从成本和售价的差额中获得的利润增加。但是这种情况并不稳定。经过一段时间后，竞争者将迫使后觉者使用 rpST。由成本和售价之间的差额所获得的利润也降低了，因为在这种行业中，时间长了，价格总是趋于和平均成本相等的。结果最持久获利的是消费者。在欧洲条件下，加工业和营销业也能得到部分利润。Pease 认为，加工行业能够得到相当大的一部分好处。看来在短期内这种说法基本上是可靠的。但在较长时期内，其情况将和饲养业一样。

无论如何，饲养业和加工业总能得到部分利润。在这些行业中，主要通过应用新技术而取得收入的增加和由于总的经济增长而取得相应的好处。这是正常的。

市场效应

除了替代效应外，市场需求将不会增长．在欧洲、美国和日本的顾客不会有多大增加．在人口统计中伊斯兰教人口比例的增高使得国际猪肉市场可能比其他市场，例如牛肉市场的前景稳定。

Steele以及参与讨论者指出，较低的猪肉价格将刺激人们以猪肉代替牛肉．但是，假定价格的变化足够大的话，则取代的弹性尚无数量方面的资料．这方面的研究正在进行中(Hayenga)。

McKeith的报告认为，使用rpST对于加工行业几乎没有影响．如果出现任何这种影响，用常规技术都能很容易的得到解决．rpST的使用对环境条件的限制方面具有积极效应．Van Weerden指出，使用rpST可使每公斤产品的污染性排泄物（氮和磷）减少15－20%．无疑这些效应对荷兰来说即使不是决定性的，也是很重要的．但是，对于经济的效应和生态学论点的评价仍然需要数量化．假如用法律强制限制磷和氮的排放的话，则除了其他减少污染的措施外，使用rpST可被看作是一个很重要的途径．总而言之，环境保护的措施将导致生产系统的改变。

消费者的接受并不是一个定数．它可以通过销售，宣传或商标策略而引起变化．过去这方面的进展一直是很有节制的，所以猪肉仍具有作为大宗产品的地位．然而，销售策略看来正在改变．在这样的发展过程中，生产者将更紧密地结合到整个市场渠道之中．这将形成合同制生产和垂直的质量管理．在这些情况下，对消费者的接受问题将

按常规方式处理，消费者不能自动发觉质量的好坏，必须赢得消费者的信赖。

由于社会和经济的考虑，政府的政策可能抵制rpST的应用。应用rpST对农村结构的意义可能很大。因而，rpST可能很易变成设置贸易障碍的工具。然而，在欧洲由于消费者将会得到更为决定性的地位，这种可能性将逐渐变小。大多数讨论参加者都认识到，由于使用rpST，将对猪生产的区域性变化发生重大影响。

与经济效果相互作用的一些影响概括如下：

农场经济　　　　　　　　：刺激rpST的应用
生态方面的理由　　　　　：同上
消费者　　　　　　　　　："你可以说服我"
饲料需要量／健康　　　　：正效应
纳税人　　　　　　　　　：（可能）中立
目标动物　　　　　　　　：需要更深入的讨论

（杨作民　译）

本中文论文集能在两星期内顺利地翻译和打印出来，得：

感谢中华人民共和国农业部马晋辉处长给予的大力支持，

感谢中华人民共和国农业部程金根先生，北京农业大学齐顺章教授和张永清先生出色的组织工作。

一九八九年四月三十日
于中国北京

353