The Changing Market Structure For The American Beef Industry

by

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I. Introduction

*Change* is now a common everyday word in the beef marketing. Change spells out “Cattlemen Have A New Great Encore.” You and I are witnessing this encore as the beef industry divides into two distinctly different marketing systems based on two distinctly different production systems.

First, we have the traditional beef system producing and marketing *commodity beef*. Second, we have a *value-based beef* system producing and marketing high quality beef designed to meet tight consumer specifications. A critical decision that today’s beef cow producers have to make is to decide which system – commodity beef or value-based beef – they are going to target their production towards. The beef industry’s transition into value-based marketing is generating rapid change in today’s beef industry.

Today’s beef industry has roughly 800,000 beef cow producers marketing to 2100 feedlots; who in turn, are marketing to 4 major beef packers who are marketing to 250 million plus domestic consumers. In spite of the wide spread belief that agriculture in general, and the beef industry in particular, are different from other U.S. industries, today’s beef industry is also caught up in the U.S. economy’s overall drive for efficiency. Consumers are demanding value in anything and everything they purchase. He who can produce the beef that consumers want, in the form that they want it, when they want it, at the lowest price wins.

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A. Commodity Beef

By definition, commodity beef is a homogenous product with little or no product differentiation and there are no brand names associated with commodity beef. Commodity beef is priced based on averages. Average beef prices are public information reported daily by the USDA Agricultural Marketing Service. Since one beef producer’s commodity beef is about the same as another beef producer’s commodity beef, the primary way that commodity beef producers compete is through being a lower-cost producer.

Traditionally, research and extension educational programs have targeted their research and educational programs towards increased production efficiency of commodity beef. The operational assumption has been that the increased production efficiency implies lower costs of production, which in turn, implies higher profits. Research, however, is changing. Using this conference as a specific example, current research and extension programs are changing to a focus on the production and marketing of consumer determined value-added production. Change is everywhere.

Commodity beef producers are trying to lower costs of production by adopting new genetics, new production practices, and new management tools that will increase their individual herd’s production efficiency. Producers generally perceive that production efficiency is a sufficient condition for profitability (economic efficiency). This certainly has been true in past decades; but, once again, things are changing.

IRM (integrated Resource Management) data suggests that production efficiency is a necessary condition but production efficiency is not now a sufficient condition to guarantee economic efficiency. Since the mid 1980s, financial management has increased in importance in beef production. In today’s profitable beef production, economic efficiency now also requires financial efficiency. I find that some beef producers have made this transition to financial

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I have had senior ranchers talk to me about why the current generation “can not survive on the ranch that momma and I lived on for 40 years.” What these senior ranchers have not recognized is the change that has occurred in the ranching business. For the last 30 years, profit margins have decreased with each and every added cattle cycle. This drop in profit margins has been heavily related to the 30 year decrease in beef demand. I really think that most ranchers have no concept of what 30 years of decreasing beef demand had done to them and to their neighbors. The good news, today, is that demand is increasing (see section in this paper on changing demand).
efficiency very well while others are still struggling.

The traditional business model followed by most commodity beef producers is to produce commodity beef during those time periods that best fit their production resources. There is little or no focus in the typical commodity business model on year-around supply, seasonal production patterns, or seasonal market price patterns. Consumers are expected to consume whatever is the easiest for beef producers to produce; in fact, consumer demand is ignored in the commodity beef business model.

The rest of the marketing chain is considered the enemy. The enemy’s fight with ever decreasing beef demand is frequently interpreted as the enemy attempting to take advantage of beef cow producers. If prices are low, it must be the fault of the next participant in the marketing chain.

Commodity beef producers typically are going it alone and often view their neighbor as their competitors. The general practice in the commodity beef business model is to not share any production or financial performance data with other participants in the marketing chain and there even is a general reluctance towards sharing with fellow beef cow producers. The management power of sharing and benchmarking to increase beef cow profits is not possible due to non-standardized accounting systems and the reluctance to share.

A. Change Came Out Of The Financial Crisis Of The 1980s

Change came out of the agricultural financial crisis in the 1980s when many beef producers found out that high production, in itself, did not guarantee financial survival. In addition, most beef producers were let down by their on-farm, production and financial management information systems; in fact, bankers were called upon to determine when a business failed. By that time all equity had been used up.

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4Out of North Dakota’s 12,000 operations with beef cattle, 250 participate in CHAPS Herd Performance System, share data, and benchmark against each other. Another 180 participated in the North Dakota Farm Business Management System, share data, and benchmark against each other. The other 11,570 do not share data and can not practice benchmarking.

5A favorable observation in the 1990s is that some farmers and ranchers decided to get out of farming while there was still some equity left in the business. In the 1980s, if you had equity, you farmed or ranched one more year. There is nothing wrong with selling the business while you still have equity but you need the financial records to know how much equity you have and how fast it is changing.
In the late 1980s, a group of NCBA cattlemen came to the Cooperative Extension Service and requested help in designing a new management information system for commodity beef producers that integrated financial management and production management into a single management information system. This new management information system was called IRM -- Integrated Resource Management. IRM was conceived and driven by grassroots NCBA cattlemen who witnessed neighbors forced out of business during the financial crisis of the 1980s. These grassroots producers wanted to make sure that their ranch did not succumb to the next financial crisis in the 1990s.

Over the last 10-12 years a completely new IRM educational program has been launched by State Cooperative Extension Services, NCBA, and State Cattlemen’s Associations to change how ranchers and beef farmers manage their commodity beef production. NCBA launched its Cattlemen’s Colleges, State Cattlemen Associations launched their Cattlemen’s Colleges, and State Extension Services launched intensive IRM educational programs all based around one common set of Standardized Performance Analysis (SPA) Guidelines. Ranchers were taught the IRM way of integrating financial management into the production management of their beef cow businesses. Since IRM’s conception, almost every state in the Nation has launched an IRM educational program for their beef producers.

Profits can and are being made from producing commodity beef. In fact, low-cost commodity beef producers are currently making good profits. My IRM work identified the key Critical Control Points (CCP) for running a profitable beef cow herd is intensified management.

My Northern Plains IRM Database clearly indicates that the economic rewards from commodity beef production through intensified management are going to those that have the lowest unit costs of producing a hundredweight of calf (see Figure 1). For example, the average net income per cow for all IRM Cooperators in 1999 was $129 per cow. My highest profit herd in 1999 generated $281 net returns to unpaid labor, management, and equity capital per cow.

Figure 1: Unit Costs Of Production For Northern Plains IRM Database
cow with his 1999 calves. My low-cost IRM Cooperators have made a profit each and every year of the cattle cycle. Yes, IRM is changing the economics of producing commodity beef.

B. Value-Based Beef

Value-based beef, the newer production and marketing system, is being marketed based on selected quality factors targeted towards consumers’ expressed wants and desires. Value-based prices are based on a specified set of quality specifications implemented through some form of a grid pricing system. The largest example of value-based beef is Certified Angus Beef (CAB).\(^6\) CAB is one of the oldest (founded in 1978) and perhaps the best-known of all beef carcass alliances.\(^7\)

Today there are many alliances being offered to beef producers. As early as 1996, Kansas State University (Sartwelle, Marston and Bolze) listed and described 13 alliances in a paper.\(^8\) Each different value-based marketing program focuses on a different set of quality specifications. New value-based marketing programs are starting up every year. The challenge for today’s value-based beef cow producers is to match their herd’s genetic characteristics to a specific value-based marketing program.

CattleFax reported that 40-50 percent of the beef produced is now or soon will be marketed on some contract, grid, or formula price structure.\(^9\) While costs of production are still important in value-based beef production, value-based beef producers spend considerable management energy focusing on adding value to their beef production.

Value-based beef producers are recognizing that consumers have specific quality specifications for what they consume and that consumers will reward quality through paying a

\(^6\)I once mentioned to an Angus breeder that CAB was really taking off. His response was: “Well, it is about time! We have been working on this for over 20 years.” The message is that developing an effective alliance takes years.


\(^8\)See previous footnote.

premium for that *quality product*. On-the-other-hand, consumers will pay a discount through reduced consumption of those products that do not meet consumers’ quality specifications. In addition, consumers demand a year-around supply of that quality product leading producers to the recognition that producers have to band together in business relationships to meet year-around consumer demand.

Value-based beef is characterized by the fact that value is linked to the production practices at each and every level of the supply chain. As a result, a value-based marketing system has to focus on all producers in the supply chain. The marketing challenge is to make sure that the marketing program recognizes these linkages equitably. The marketing system needs to recognizes that what one producer does in the supply chain directly impacts other producers in that supply chain. Fellow participants in the total value-based beef supply chain are business partners -- not their competitors.

Retail value is the collective sum of all “value added” actions taken in the total *supply chain*. How the complete value-based beef *supply chain* is managed determines the overall marketing success of any value-based beef marketing program. Value-based beef producers need to carefully select their value-based marketing program with care as not all value-based beef marketing programs will survive.

The logical next step in value-based beef marketing will be the move to *branded beef*; but, that is a subject of another complete paper.

**Key Factors Underpinning Change In The Market Structure**

Key production, economic, and financial factors are underpinning the *change* in the beef marketing system. My goal in this section of this paper is to briefly discuss 6 of the key underpinnings. The six *key* underpinnings causing *change* are:

1. Cattle cycle and its resulting beef price cycles
2. Economic hurt in the mid-1990s
3. Increasing production per cow
4. Long-term decreasing demand for beef
5. The good news on the recent up-turn in beef demand
6. Ranchers are currently marketing on an up-market

**1. Cattle Cycle And Its Resulting Beef Price Cycle**

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The single most important economic underpinning of the beef marketing system is the cattle cycle and its resulting beef price cycle. Beef cattle prices tend to go in 10-year cycles that correspond to each decade. History demonstrates that we can expect a “U” or “V” beef price cycle during each decade. Cattle prices typically start the decade with high prices, move to low prices in the mid-decade, and increase again towards the end of the decade.

Figure 2 illustrates the “V” shaped price cycle generated in the decade of the 1990s. Price spreads between feeder calves, feeder cattle, and slaughter cattle started out the decade wide but narrowed in the mid-1990s. The magnitude of the price depression in 1996 is best illustrated by the fact that feeder calf prices per hundred weight went below the per hundredweight price of slaughter steers. Since 1996, the price spreads have been widening. This is the typical price pattern during a typical cattle cycle. Price spreads start out the decade wide, narrow in mid-decade, and widen again toward the end of the decade. Where, then, are we in the current cattle cycle?

a. Current Cattle Cycle implications

Cattle cycles can be divided into three phases – contraction, expansion and turn-around. We have completed the 1996 to 2000 contraction phase, now have completed the turn-around phase and are just now entering into the expansion phase. The expansion phase should last through 2003.

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10For 22 years and two complete cattle cycles I had talked about 1974 being a unique time in history when calf prices per hundred weight averaged below slaughter cattle prices per hundred weight. Twenty-two years and two cattle cycles later it happened again. In 1996, the average price of feeder calves went below the average price of slaughter cattle. Both record lows – the 1974 and 1996 lows – were accentuated by record feed grain prices.
Beef production peaked in year 2000 and is projected to decrease in 2001-2003 time period. As the increased heifer retention materializes in the expansion phase, beef production should start increasing once again in year 2004. This cycle’s peak beef prices are currently projected for year 2003. The next downturn in market prices is projected for 2004 through 2007. Prices are projected to increase towards the end of the decade (see Figure 3).

As beef cow producers decide to divert heifers from feeding to breeding, the supply of feeder cattle will be reduced. The expansion phase is characterized by a smaller supply of feeder cattle, excess feedlot capacity, excess packer capacity and by overall industry consolidations.11

CattleFax reports a 15 percent increase in feedlot capacity in the last 15 years.12 Feedlots, trying to utilize their excess feedlot capacity, will increase their competitive bid for feeder cattle. Existing feedlots will turn to added imported Mexican feeder cattle to try and utilize existing feedlot capacity. Due to higher feeder cattle prices, some feedlots will feed cattle to minimize feedlot losses rather than to maximize profits.

All of this suggests that the beef industry will see the cow calf producer move into the drivers seat with respect to feeder cattle sales. They will decide when they want to market their calf production -- at weaning, after backgrounding, or through retained ownership. As more beef cow producers sell at weaning, the popularity of retained ownership will decline. Reduced retained ownership will lead to more cattle owned directly by the feedlots.

Feedlots, trying to ensure a feeder cattle supply for their feedlot, will strive to develop

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11Topper Thorp, CattleFax at NCBA Annual meeting, San Antonio, Texas Feb 2001.

and expand business relationships directly with beef cow producers. Reduced feeder cattle supplies will change how beef cow producers interact with cattle feeders.

2. The Economic Hurt During The Last Cattle Cycle

The economic impact of the mid-1990’s price depression was devastating for many beef cow producers. Figure 4 presents the average profit per cow earned by North Dakota’s Farm Business Management Association Members during the 1990s.¹³

Profit per cow was high in the early part of the decade averaging $152 to $192 per cow. Nineteen-nine hundred and ninety-four signaled the beginning of the market downturn with a 74 percent drop in beef cow profits in that one year. Average profits went negative in 1995 and went even more negative in 1996. Average profits again turned positive in 1997, 1998 and 1999. Profits continued increasing in 2000 to $124 per cow. Clearly, better times are returning for cow calf producers.

An important point for this conference is that we recognized the fact that over the five-year period – 1994 thru 1998 – producers earned an average annual profit of only $3 per cow for this five year period. It appears that profit margins are getting smaller for each progressive cattle cycle.

A signal that beef cow profit margins are getting smaller and smaller is the fact that this 5-year $3 average in the decade of the 1990s compares to the 5-year average low of a positive $33 for the decade of the 1980s. In fact, none of the 1980 years averaged below zero while two years in the 1990s averaged below zero. Clearly, something was raising havoc with the beef

¹³Profit here is defined as the earned returns to unpaid family and operator labor, management, and equity capital. These are the three resources that a ranch family contributes to the ranch business.
industry! Research now suggests that something was decreasing consumer demand for beef. More on this in a later section of this paper.

3. Increased Beef Produced Per Cow

While the cattle cycle’s influence on cattle numbers is a primary factor determining beef supply, it certainly does not explain the total beef supply picture. Figure 5 illustrates the USDA All-Cattle Inventory numbers from 1960 through year 2000 via the dashed line measured on the right axis. You can see that cattle numbers peaked in the mid-1970s, again in the mid-1980s, and once again in the mid-1990s. You also see that the long run trend in cattle numbers from 1975 through year 2000 has been downward.

The dark line in Figure 5 presents beef production measured on the left axis. While beef production varies during each cattle cycle, the long-term trend in beef production since 1965 has been upward. I particularly call your attention to the 1980 through year 2000 time period. While the all-inventory numbers trended downward over this 20-year period, beef production trended upward over this same time period. In fact, beef production in 1998 exceeded the record beef production in 1975. How could this be? The beef industry has 34
million less cattle in year 2000 as compared to 1975?

One key reason for the upward trending beef production from less and less cattle is “increasing beef production per cow.” Over the last 30 years, beef production per cow has trended upward (see Figure 6). In 1980, each cow produced approximately 450 pounds of carcass beef per year. By 2000, production had risen to 620 pounds of carcass beef per cow per year. This 170 pound increase in a 20 year time span represents an average annual productivity gain of 1.8 percent.14

Several factors are responsible for this production increase including weaning weights. Figure 7 confirms that in the decade of the 1980s, North Dakota beef cow producers added an average of 10 pounds per calf weaned per year. This totals to 100 pounds added to weaning weights in the decade of the 1980s. I fully believe that this North Dakota increase in weaning weights is indicative of the U.S. beef industry in general. Canada, on the other hand, shifted to a higher percentage exotic breeding programs and, as a result, increased weaning weights even more than the U.S.

Certainly, genetic improvements in both countries have resulted in bigger and bigger

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14Ibid.
Another primary source of productivity gains is heavier carcass weights (see Figure 8). Over the past 20 years, while annual productivity gains have averaged 1.8 percent, weight gain has accounted for 1.1 percent of the total 1.8 percent growth per year. All other productivity increases have accounted for about 0.7 percent per year. These other productivity increases involve the ability to produce more calves from a given number of brood cows and include fewer non-productive cow days and higher calving rates.

Better husbandry practices have certainly contributed to this higher beef cow production as have improved health programs. The popularity of slaughtering veal calves has decreased so today the beef industry is taking a higher percentage of all calves to slaughter weights.

Finally, imports have also contributed to this increased production (see Figure 9). Cattle imports make up of all types of cattle – breeding, feeders, and slaughter. Most Mexican exports into the U.S. are feeder cattle while Canadian exports to the U.S. are processed meats, slaughter cattle, cull cows, and feeder cattle. In any case, U.S. imports add to the total beef supply produced in the U.S.

While the amount of beef produced per cow is rising at a rate of about 1.8 percent per year, domestic and foreign demand is only increasing at about 1.3 percent per year. This suggests that

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15 Assumed 36 million head slaughtered annually. 36 million times 100 pound increase comes to 3.6 billions added pounds of beef. Carcass weights have continued to increase for the last 30 years.

16 Ibid.
productivity growth will likely outpace demand growth, and as a consequence, brood cow numbers over the long-run will likely decrease over time.\textsuperscript{17}

Current beef cow numbers have also been dropping since 1995 and yet total beef production has continued to rise. This short-run increase in beef production primarily due again to short-run increases in carcass weights, increased feeder cattle imports, and lower veal calf slaughter.

4. Decreasing Demand For Beef

During the 1980s beef consumption in North America declined, in part, due to concerns about human health and grazing pressures on public lands. At the same time, poultry and fish enjoyed increases in consumption due to lower prices and alleged health advantages. With real incomes also declining in the 1980s, consumers became more cost conscious and began to pay more attention to the quality of meat obtained per dollar spent.

Decreasing demand for beef led to continual decrease in the real price of beef. While nominal steer prices trended upward since the early 1960s (see Figure 10), inflation drove the real price of slaughter steers ever downward (Figure 11). By 1995, the real steer price was one-half of the real steer price in 1979.

Most cattlemen do not appreciate the impact that 25 years of decreasing demand for beef and the continued drop in the real price of beef was

\textsuperscript{17}Kris Hurt, "Cycle Nears End Of Contraction" Livestock Outlook Web Page, http://web.aces.uiuc.edu/farm.doc/marketing/livestockoutlook/0700cattle_text.html.
having on the ranching industry. Over the last 25 years, ranch after ranch has been forced out of business by decreasing demand. Let’s look at some ranching changes driven by decreasing demand.

A. Producers Turn To Exotics – Consumers Heighten Demand For Quality Information

Generating the family living draw from beef cows was one of the more challenging implications of reduced real prices of beef. To remain in business, beef cow producers had to increase production efficiency in an attempt to maintain family living draw during these times of reducing real market prices. Increased production efficiency became about the only way for a ranch business to survive.

Consolidation of smaller beef ranches into larger, more efficient ranches was one way to reduce family living draw per cow. Ranch after ranch was sold and consolidated into a neighboring ranch operation. Each ranch consolidation meant one less family’s living draw had to be generated from beef cows.

Producers looked to the introduction of Continental European Breeds (exotics) for significant increases in size and cutability as a means of increasing production efficiency. The genetic drive of the 1970s and 1980s was to increase weaning weights, carcass weights and to produce beef more efficiently. Figures 7 illustrates the dramatic increases in weaning weights and Figure 8 illustrates the dramatic increase in carcass weights. Carcass weights are still trending upward.

B. More Select Beef and Less Choice Beef

This focus on increasing weaning weights and the larger carcass weights led to the rise in popularity of producing USDA Select quality grade beef. In 1986 USDA, under pressure from the cattlemen, changed the name of existing beef quality grade from Good to Select. The amount of beef graded Select has increased markedly since that time. For example, in 1986 only 1.3 million pounds per month of Select beef were graded as compared to 30.2 million pounds per month in 1999. During this time period, the production of Choice beef has remained relatively stable at around 46 million pounds per month.

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In a market of increasing differentiation, USDA beef quality grades played an important role in distributing quality throughout the marketing chain and should have provided signals to cattle producers of consumer desires at the retail level. Increased use of the USDA beef quality grading system reflected heightened consumer demand for quality information and segregation at the retail level. According to USDA data, over 90 percent of beef from steer and heifer slaughter was quality graded in 1999 as compared to just 67 percent in 1986. Consumers wanted quality information and quality segregation at the market.

C. Beef Demand Research Tells More Of The Story

Although the amount of beef graded has increased markedly, not much is known about the price sensitivity of the USDA beef quality grades or the substitutability between grades and other meat products. Recently published research has shed some added light on beef demand. For example, chicken is only a substitute for Select beef, not Choice beef. Thus, chicken may be substituted for low quality, but not high quality beef.

Research shows that the two beef quality grades are good substitutes for one another during the fall and winter; however, during the summer Select beef is not a substitute for Choice beef. Apparently, retailer demand for Choice beef cannot be met by changes in relative prices of lower quality beef during the cookout season. In addition, demand for both Choice and Select beef becomes much more inelastic (% change in quantity demanded verses % change in price is less than 1.0) during the spring and summer than during the fall and winter.

Increases in retail beef prices increases the amount of wholesale pork and poultry demanded by meat retailers. Increases in retail beef prices have as much, if not more, of an impact on wholesale pork and chicken demand than equivalent changes in wholesale pork and poultry prices.

A previously unreported result, presented in the above study, is the cross price elasticity between Choice and Select beef. Results indicate that a 1 percent increase in the price of Choice beef is associated with a 0.28 percent increase in the quantity of Select beef demanded. On-the-other-hand a 1 percent increase in the price of Select is associated with a 0.19 percent increase in the quantity of Choice beef demanded by meat retailers. Price changes in Choice

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\(^{19}\text{Ibid.} \)
have a larger impact on the quantity of Select demanded than the reverse.

The same pattern of beef demand may apply to producers marketing fed cattle. If these same seasonal fluctuations in beef demand are transmitted to the farm level, cattle producers, as a whole, may be able to benefit from timing the feeding of cattle. Feeding cattle to heavier weights during the summer and fall to achieve the Choice quality grade may prove to be a profitable strategy. However, if the seasonal pattern of beef demand is not transmitted to the farm level, packers may be capturing this economic surplus. Packers may be able to take advantage of changes in retailers’ demand for quality graded beef by increasing its margins through strategic seasonal cattle purchasing.


It appears that today’s beef industry is currently living with the genetics brought on board in the 1970s and 1980s. During the 1990s, the percent of the carcasses grading Choice went down (see Figure 12) while the percent of the carcasses grading Select went up. The net result of all of this is that the market is demanding more choice cattle and producers are producing more select cattle.

This is further demonstrated by looking at Kansas State University’s Choice/Select Price Spread Index (Figure 13). A large index suggest a larger Choice/Select price spread. The Choice/Select price spread has followed a distinct pattern. The Choice/Select prices index is low during the first four months of the year. By May, the index gets large and stays large the
rest of the year peaking in November. The price spread tends to be widest in the fall months.

This Kansas research suggests that during 8 out of the 12 months the premium for Choice cattle is large. Once again, the market is signaling that it wants Choice cattle. The Choice-Select price spread averaged $15.09 per hundredweight in October 1999. This Choice/Select price spread is the fundamental source of premiums paid for value-based beef.

D. National Beef Quality Audit

The 1995 National Beef Quality Audit (NBQA) suggested that current USDA quality grading system segregates carcasses into: 1 percent Prime, 47 percent Choice (11 percent upper 2/3 Choice and 36 percent Low Choice), 47 percent Select, and 5 percent Standard. Slaughter quality in the 1995 Audit quality actually decreased from the earlier 1991 NQBA. Based on USDA 1974 data, the percent cattle grading prime and choice decreased 36 percent from 1975 to 1995. Decreasing demand since 1975 has paralleled this beef quality decrease since 1975.

The 2000 National Beef Quality Audit showed some improvement over the 1995 audit. The 2000 Survey showed that U.S. cattle producers have responded to the market place, delivering higher quality product to consumers then they did in the mid-1990s. The percentage of Choice and Prime carcasses went from 48 percent in 1995 to 51 percent in 2000. Prime percentages went from 1.3 percent to 2 percent in 2000. Clearly, the beef industry is moving in the right direction but progress is slow.

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20Get this footnote from ??
23Ibid.
Retailers indicate that 50 percent of the beef marketed through their stores must be Select to meet consumer demands. Exporters, on-the-other-hand, say they need 30 percent prime, 42 percent upper 2/3 Choice and 28 percent low Choice with no Select to satisfy their customers. Food service representatives need another product mix different yet from retailers and exporters.

To adequately meet the needs of all customers, the U.S. beef industry should produce cattle grading 7 percent prime, 21 percent upper 2/3 Choice, 34 percent low Choice, and 38 percent Select carcasses. Ranchers will increase market segmentation and targeting will be necessary to efficiently match production resources to consumer demand specifications.

E. Increased Demand For Value-Based Beef

Increased demand for quality graded beef at the retail level has resulted in beef packers offering cattle producers premiums and discounts based upon the quality and yield grades of their cattle. With the current flurry of marketing alliances, it behooves alliance participants to understand how the market’s increasing demand for Choice beef is in direct conflict with the past genetic trend in the beef industry. This all suggests that, as the quantity of Choice slaughter cattle goes down, price premiums for Choice cattle will go upward. In the mean time, meeting consumer demand for Choice beef necessitates the importation of Choice beef and cattle from Canada.

5. The Good News Is That Demand May Have Changed Upward

The most exciting news impacting the beef industry in years is the recent change in beef demand. Kansas State University researchers have documented 1) the magnitude in the drop in demand during the 1990s and 2) the apparent turn around in demand towards the end of the decade.

Figure 14: Demand Turned Around in 1999.

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Figure 14 illustrates the decrease in demand during the 1990s where 1990 was set as the base of 100. By 1997, retail beef price was down to 83 percent of what it would have been if demand had stayed at the 1990 level. This represents a 13 percent drop in demand over the 7-year 1990 to 1997 period.

Beef cutout demand went down 30 percent over this same 7-year period and live slaughter steer demand also went down 30 percent over this same 7-year period. All three demand values went down even more in 1998.

The apparent turnaround in demand is illustrated in the 1999 data and preliminary year 2000 data as both years generated increases in all three values (again see Figure 15). By June 2000, the retail beef index went up to 91, beef cutout was up to 83 and the live steer price index went up to 76. While two years do not make a trend, this apparent increase in demand is the best news that the beef industry has received in many, many years. Increasing demand changes the dynamics of marketing beef.

6. Ranchers Are Now Marketing Beef Cattle On An Up Market

Figure 16 presents the opening slide that I have used over the past year in my beef producer presentations.

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Source: Jim Mintert’s Kansas State University Monthly Beef Newsletter.
conferences and meetings. Note the champagne bottle on the slide. Also, note the fist-of-money on the other slide of Figure 16. Why would I begin my beef presentations with a bottle of champagne and a fist-full of money? After showing the bottle of champagne and the fist-of-money to last year’s audiences, I have asked the question: “ARE YOU READY TO MAKE SOME MONEY??”

As this point in my introduction, I then draw the conference participants’ attention to the relative profitability of beef by asking: “What other commodity group could I stand in front of in year 2001 and ask if they are ready to make some money?”

It is interesting to see the response that this discussion gets from beef producers. Ten to twenty percent respond by vigorously shaking their head yes and immediately echoing “You bet we are ready to make some money!” The rest are either in shock that I would ask such a question or in complete disbelief of the whole situation.

I certainly would not do this in front of wheat producers. I assure you that I would not do it with corn producers. I would not do it with swine producers nor dairy producers. My whole point with all of this is that the beef cow industry is currently positioned in the cattle cycle to have several very favorable years. Let me summarize all of this by stating that the beef business goes in 10-year cycles and we are in the upward phase of the current beef price cycle.

Figure 17 presents my current planning prices for North Dakota beef cow producers. These are October’s average monthly prices for 500-600 pound steer calves marketed in Western North Dakota. The left-hand side presents historical prices from 1990 through year 2000. The right-hand side presents my projected planning prices for years 2001 through 2009. These projections suggest that we will see steer calf prices trend upward for the next 2-plus years with the projected price peak in year 2003.

Let’s take a more in-depth look at short-run feeder calf planning prices.
Economics Section, Department of Agribusiness and Applied Economics, North Dakota State University, posts weekly my Futures based planning prices generated from the weight/price spreads of last week’s feeder cattle auction sales and the Futures market. Figure 18, prepared from May 23, 2001 Western North Dakota salebarn prices and May 30, 2001 feeder cattle Futures prices, compares October 2001 projections with historical prices for three previous Octobers. Prices are presented for steer calves weights ranging from 400 to 925 pound feeders.

Two price trends are evident in Figure 18. First, feeder steer prices for all feeder weights have trended upward from 1998 through 2000 and are projected to continue this trend into the Fall 2001. Second, cheap feed grains, and the resulting low-cost gains, are driving the price of light-weight feeder calves up relatively more than the price for heavier-weight feeders. This is evident by the clock-wise rotation of the price lines in Figure 18.

In summary, this section has highlighted one more change for ranchers. Ranchers are now marketing beef cattle on an up market.

Summary

Change is now a common everyday word in beef marketing and change is the central theme of this paper. Today’s beef industry is also caught up in the U.S. economy’s overall drive for efficiency. Consumers are demanding value in everything they purchase and beef purchases are no exception. Changes in beef marketing are in the works.

The beef industry is changing into two distinctly different marketing systems based on two distinct production systems – one production system for commodity beef and one production system for value-based beef. By definition, commodity beef is a homogenous product with little or no product differentiation. Without product differentiation, commodity beef producers

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26: The web page is www.ag.ndsu.nodak.edu/cow under the “weekly prices” hot button.
compete by being the lowest cost producer.

In order to increase economic efficiency, reduce production costs and increase overall beef cow profits, the beef industry has developed and implemented the Integrated Resource Management (IRM) and the Standardized Performance Analysis (SPA) Systems. The key focus of IRM is on integrating financial management and production management into a single management information system that sends integrated management signals for enhancing beef cow profits. Today’s leading IRM cooperators are generating profits of over $200 per cow producing commodity beef.

Value-based beef is the newer beef marketing system and is being marketed and priced based on selected quality factors targeted toward consumers’ expressed wants and desires. Value-based beef producers are recognizing that consumers have specific quality specifications for what they consume and consumers are willing to pay a premium price for that quality product.

Consumers demand for year around supply necessitates value-based producers banding together to meet this year around demand. Certified Angus Beef is the best known example of value-based beef alliance. Today, there are many difference beef alliances and new ones are forming each year. The logical next step in value-based marketing will be branded beef.

There are six fundamental factors underpinning the change in the current beef marketing system. These six factors are:

1. Cattle cycle and its resulting beef price cycles
2. Economic hurt in the mid-1980s
3. Increasing production per cow
4. Decreasing demand for beef
5. The good news is that consumer demand has turned up
6. Ranchers are marketing on an up-market

The single most important factor impacting beef marketing is the cattle cycle and it resulting beef price cycle. Beef prices go in 10-year cycles that correspond to the decades. Market prices are typically high in the beginning and ending years of the decade. Produces can expect the cycle low in beef prices to occur in the mid-part of each decade. Farm Business Management data also suggests that beef cow profit margins are getting smaller and smaller with each progressing cattle cycle.
Change is again impacting feeder cattle marketings. As beef cow producers now decide to divert heifers from feeding to breeding, the supply of feeder cattle will decrease. This reduction in feeder cattle supply over the next 2 years will put beef cow producers in the drivers seat with respect to feeder cattle sales.

Over the past 30 years, beef cow numbers have trended downward and total beef production has trended upward. Beef production per cow has increased over the years due to increased carcass weights, increased feeder cattle imports, and reduced veal calf slaughter. Beef production per cow has been increasing at such a rapid pace that lagging beef demand has led to reduced beef cow numbers.

While the amount of beef per cow is rising at a rate of 1.8 percent per year, domestic and foreign demand is only increasing at about 1.3 percent per year. This means that the production increases per cow will continue to decrease brood cow numbers over time.

Long-term decreasing demand for beef led to a long-term decrease in the real price of beef. While nominal steer prices trended upward since the early 1960s, inflation has driven the real (inflation adjusted price) ever downward. By 1995, the real steer price was only one-half of the real steer price in 1979.

To remain competitive during times of decreasing demand, beef producers have had to increase production efficiency. This was the only way that they could even begin to maintain the family living draw from the ranch in times of reducing real market prices. Over the last 25 years, ranch after ranch has been forced out business by decreasing demand. This pressure for generating family living led to the general consolidation of smaller ranches into larger, more efficient ranches as a way of reducing family living draw per cow.

Producers feeling continued pressures to increase production efficiency, looked to the exotic breeds for significant increases in size and cutability as another means of increasing production efficiency. This industry wide focus on increasing weaning weights lead to the rise in the production of USDA Select grade beef. At the same time, meat retailers turned to increased the use of USDA beef quality grading systems in response to the heightened consumer demand for quality information and segregation at the retail level.

It appears that today’s beef industry is currently living with its focus on weaning weights
in the 1970s and 1980s. During the 1990s, the percent of the carcasses grading Choice went down while the percent of the carcasses grading Select went up. The net result of all of this is that the market is demanding more Choice cattle and producers are producing more Select cattle. Quality price premiums are now being established in the market.

Increased demand for quality beef at the retail level has resulted in beef packers offering value-based cattle producers premiums based upon the quality and yield grades of their cattle. Today, meeting the demand for Choice cattle includes importing Choice cattle from Canada.

Change spells out “Cattlemen Have A New Great Encore” and the most exciting encore is that beef demand may have turned upward for the first time in 25 years. This is the best news that the beef industry has received in many, many years. Increasing demand changes the dynamics of beef marketing.

Ranchers are once again marketing in an up-market. Part of this up-market is due to the cattle cycle and part of this up-market is due to increased demand. Yes, change is here -- “Cattlemen should Have A New Great Encore.”
Preweaning survival in swine

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ABSTRACT: A limited ability to cope with environmental stressors (cold, disease, limited nutrition), particularly over the first 2 to 3 d of life, predisposes the piglet to relatively high rates of neonatal morbidity and mortality. Due to the serious economic impact, numerous surveys of preweaning losses have been conducted over the last century. Although losses are still significant, the existing literature indicates a significant improvement in piglet survival over time, as determined by reports of 35% preweaning mortality in 1924 and 13 to 15% in 2000. Major sources of mortality have been categorized as overlying by the sow, insufficient energy intake, and disease. Causes of mortality may be more closely linked with one another than previously believed. Interactions exist between disease, thermoregulation, and nutrition. Piglets with disease and nutritional problems experience hypothermia and express altered behaviors that increase the likelihood of their being laid on by the sow. High probabilities of neonatal losses are associated with low birth weights, cold ambient temperatures, and scours. An understanding of the interactions between environmental stressors and the biology of the piglet forms the basis for strategies and recommendations for improving preweaning survival.

Key Words: Mortality, Piglets, Preweaning Period, Survival

Introduction

A survey of 712 swine farms, representative of 95% of U.S. producers, was conducted for the first time by the National Animal Health Monitoring System, USDA-APHIS-VS in the year 1990 (NAHMS, 1991) and again in 1995 (representing 90% of producers, NAHMS, 1995). These surveys estimated a national average of 9.9 piglets born alive per litter and 8.4 piglets weaned per litter, representing a 15% preweaning mortality for the year 1990, and they estimated a national average of 9.5 piglets born alive per litter and 8.6 piglets weaned per litter, representing a 9% preweaning mortality rate for the year 1995. According to survey results, piglets born alive per litter has decreased during the 5 yr between surveys but piglets weaned has increased, effectively decreasing preweaning mortality. The percentage of farms using total confinement during farrowing did not change, remaining constant at 81%.

Within the United States, of the preweaning losses 48.1% are due to the sow’s lying on the piglets, 15.3% are due to starvation, and 13.3% are due to scours (NAHMS, 1995). Other reviews of preweaning mortality are in general agreement with regard to major categories of crushing, starvation, and disease (Svendsen et al., 1986; Varley, 1995). Reflecting the economic importance of neonatal survival, numerous surveys of piglet losses have been conducted over the last century (Zavoral, 1924; Hutchinson et al., 1954; Koketsu, 2000). In 1928, average preweaning mortality was reported at 35% of all liveborn piglets (Zavoral, 1924). Losses in excess of 30% are still reported in some less-developed countries (Chabo et al., 2000). These numbers should be viewed carefully, though, because many factors affect what is reported.

Overview

Economic Impact

The value of saving additional piglets can be dramatic. The National Swine Improvement Federation estimates that each additional piglet born has a value of $13.50 (NSIF, 1997). The value of saving piglets could be calculated using this value assuming there is no added value prior to weaning. Until recently there was not a market for weaned piglets, and little effort was
placed on determining the value of a weaned piglet. With the move to segregated-early-weaning, however, it has become necessary to determine the value of piglets at less than 21 d of age. Dhuyvetter (1996) has estimated that a weaned piglet has a value of $33.00. Some of the substandard piglets that typically die are not this valuable, even though they cost that much to produce. Therefore, estimating the value of saving additional piglets using this figure may be overinflated.

According to USDA statistics (USDA, 2000) there were 11,462,000 litters farrowed in the United States in 2000. The average litter size weaned was 8.84 piglets. An assumed 9% preweaning mortality suggests an average of 9.71 liveborn piglets, and a loss of 0.87 piglets per litter. The total value of preweaning loss in 2000 can then be calculated either conservatively or liberally as follows:

\[
\text{Value} = 11,462,000 \text{ litters} \times 0.87 \text{ piglets per litter} \times \$13.50 \text{ per piglet} = \$329,074,020
\]

Accepting these values as lower and upper limits suggests that the annual cost of preweaning mortality to the U.S. swine industry is between $130 and $330 million.

Many of the underlying causes of neonatal mortality are interlinked. For example, neonatal losses due to cold stress are rarely recorded, although the resulting hypothermia may lead to starvation, crushing, and(or) disease (Curtis, 1974; Kelley, 1985; English, 1993). Weaker piglets that are not able to effectively compete for colostrum and milk become hypothermic (Svendsen et al., 1986). As hypothermia and lack of nutrition further weaken the piglet, problems with orientation and locomotion occur (DeRoth and Downie, 1976; Svendsen et al., 1986), which increase the probability of crushing. Preweaning mortality is influenced by birth weight, litter size, duration of farrowing, dystocia, birth order, thermal environment, nutritional status, disease, sow and piglet behavior, sex, and genetics.

**Piglet Size and the Birth Process**

The low-birth-weight piglet is particularly at risk for preweaning morbidity and mortality. Piglets weighing less than 0.8 kg (1.8 lb) at birth have a 32% survival rate, compared with 97% for piglets weighing 2 kg (4.4 lb) or more (Gardner et al., 1989). The low-birth-weight piglet is physiologically compromised in terms of energy stores and susceptibility to cold and is at a disadvantage in competing with larger littermates at the udder. Within-litter variability in piglet weights is known to be associated with higher preweaning losses (English et al., 1982; Marchant et al., 2000). In some instances, cross-fostering to create more uniformity in piglet weights has been shown to reduce mortality by 40% (English et al., 1982). Cross-fostering should be utilized during the early postnatal period, because continuous cross-fostering later in the preweaning period can decrease overall growth (Straw et al., 1998).

Dystocia, and the resulting oxygen deprivation, has long been associated with stillbirths (Jackson, 1975). Hypoxia during farrowing is an important contributing factor to the 70 to 90% of stillbirths when death occurs during the farrowing process (English and Morrison, 1984). Some decrease in blood flow to the fetus is common during normal uterine contractions at farrowing. However, more serious reductions can occur through damage or occlusion of the umbilicus, or placental detachment. The resulting hypoxia can result in stillbirths and reduced postnatal viability. Piglets born in the latter part of the birth order experience a greater degree of hypoxia. Hypoxia increases the amount of time between birth and first suckling and is associated with hypothermia, reduced postnatal growth, and higher neonatal mortality (Herpin et al., 1996). Minor direct effects of hypoxia on thermoregulatory ability may exist (Herpin et al., 1999); however, the major detrimental effects are likely related to depressed colostrum intake and carbohydrate metabolism (Herpin et al., 1996).

Large litters result in a longer farrowing duration and thus may be critical to survival for piglets born toward the end of farrowing. Litter size can also influence piglet survival after birth; research has shown that piglet losses are greater in large litters (Fahmy and Bernard, 1971; Dyck and Swierstra, 1987; Marchant et al., 2000). These losses are largely attributed to the within-litter variation in piglet body weight (Marchant et al., 2000). Pigs born to and reared in large litters have lower preweaning survival rates and depressed preweaning gain and are older at 105 kg than counterparts born to and reared in smaller litters (Stewart and Diekman, 1989).

**Prolonged Farrowing**

Dystocia, or difficult farrowing, in sows is generally the result of uterine and maternal exhaustion. Primary uterine inertia associated with a deficiency in the contractile potential of the myometrium is uncommon in the sow (Britt et al., 1999). Secondary uterine inertia is not a cause of the dystocia, but rather is a result of the dystocia associated with fetal malpresentation or maternal obstruction (Britt et al., 1999).

Pigs born after an extended labor are more likely to experience a higher death loss associated with hypoxia (Randle, 1971). In the early 1970s it was reported that an 11.8% perinatal mortality rate was observed in litters farrowed in less than 6 h, compared to a 21.3% perinatal mortality rate in those litters farrowed over more than 6 h (Bille et al., 1974a,b). Housing conditions during gestation, litter size, season, and disturbances from stockpersons influence overall duration of the expulsion phase of parturition in sows (Naaktgeboren, 1979; Svendsen and Bengtsson, 1983).


**Thermal Environment**

Cold stress is a critical factor affecting piglet survival over the first several days of life (Curtis, 1970, 1974; Kelley, 1985). Cold exposure begins at birth with a rapid 15 to 20°C transition from the uterine environment to ambient temperature conditions. The newborn piglet has a relatively high thermoneutral zone (TNZ), which is defined by upper critical and lower critical temperatures (UCT and LCT, respectively). Ambient temperatures higher than the UCT and lower than the LCT activate the animal's thermoregulatory mechanisms in order to maintain core body temperature within normal limits. Due to the high UCT, heat stress is rarely a problem for the newborn piglet; however, a LCT of 34.6°C highlights the concern raised by cooler temperatures. However, the piglet's ability to tolerate cooler temperatures increases rapidly with age. Between 24 and 48 h of age, the LCT decreases from 33.3 to 30.1°C (Berthon et al., 1993), and by 1 wk the LCT of the piglet has rapidly declined to approximately 25°C (Svendsen et al., 1986).

In addition to thermal environment, physiological factors also play an important role in the thermoregulatory ability of the neonate. Brown fat, for example, is an important source of metabolic heat production in many neonates (Benito, 1985). An important peculiarity in the thermoregulatory ability of the piglet relative to other species stems from the absence of brown fat (Trayhurn et al., 1989). Uncoupled oxidative metabolism of brown fat mitochondria can generate a sustained thermogenic response that can constitute one-third of the overall metabolic rate in neonatal animals (Foster, 1984). The newborn piglet, however, is able to mount other thermoregulatory responses (Stombaugh et al., 1973). Exposure to cold elicits piloerection, although the piglet’s hair coat limits the effectiveness of this heat-conserving mechanism. Other physiological factors such as reduced blood flow to the periphery, shivering, and increasing metabolic rate also aid in heat production. Shivering is an important heat-generating mechanism in the neonatal piglet (Noblet et al., 1997). Although not highly efficient thermogenically, shivering in piglets is associated with increased body temperature and metabolic rate (Herpin and Le Dividich, 1995; Berthon et al., 1996; Lossec et al., 1998).

The newborn piglet increases its metabolic rate linearly as environmental temperatures decrease from approximately 34 to 18°C. At 18°C, metabolic rate reaches an upper limit (summit metabolic rate). Summit metabolic rates in piglets of 36.6, 43.3, and 46.8 kJ/hr/kg have been reported at 2, 24, and 48 h of age, respectively (Berthon et al., 1993). At these higher metabolic rates, the importance of adequate intake becomes critical. Body heat production is linearly related to colostrum intake (Le Dividich and Noblet, 1983). At the summit metabolic rate, the newborn piglet utilizes its energy stores in 11 to 12 h without nutritional intake (Herpin and Le Dividich, 1995). In contrast to older animals, the early neonatal piglet does not increase its intake in response to cold temperature. Colostrum intake actually decreases during cold exposure, exacerbating the likelihood of starvation (Le Dividich and Noblet, 1981).

Behavioral adaptations also play an important role in maintaining body temperature. Neonatal piglets are able to choose microenvironments that reduce exposure to cold temperatures. Such behavior has been demonstrated in laboratory settings (Balsbaugh et al., 1986); however, piglets still prefer to huddle close to the sow and littermates during the first 3 d of life regardless of thermal environment or the presence of supplemental heat (Hrupka et al., 1998). Proximity to the sow is a concern with regard to increasing the risk of piglet crushing (Wechsler and Hegglin, 1997); therefore, the design of microenvironments that provide warmth and keep the piglets at a safer distance is of considerable interest. It is important to keep in mind that this strategy must be balanced with keeping the piglets by the dam’s side during the first 24 h to ensure that they ingest enough colostrum to maintain their health. Interestingly, neonatal piglets show a significant reduction in huddling behavior during the acute-phase response to an immunological challenge (Matteri et al., 1999). Consistently, piglets with scours prefer cooler ambient temperatures when allowed to choose locations within an experimental thermocline (Balsbaugh et al., 1986).

Piglet size is also an important factor associated with thermoregulation in the newborn. The low-birth-weight piglet is particularly at risk for hypothermia, with a greater body surface-to-volume ratio and reduced energy stores (English and Morrison, 1984). The rate of body temperature loss during cold exposure is inversely related to piglet weight; however, Meishan piglets are better able to maintain body temperature than Large Whites on a body-weight basis (Le Dividich et al., 1991). The increased cold resistance of the Meishan piglet is not related to fat stores; the well-known difference in body fat composition between Meishan and European breeds develops after the neonatal period. The colostrum of the Meishan sow, however, has a high fat content that can provide her piglets with the energy needed to maintain body temperature (Le Dividich et al., 1991).

Sow feed intake is likely a greater concern at high ambient temperatures for piglet survival. Increasing ambient temperature has been shown to decrease intake in lactating sows, with a suppression of piglet growth, but not survival, at temperatures above 25°C (Quiniou and Noblet, 1999). In fact, a slight increase in piglet survival was observed at 27°C. The ambient temperatures used to produce heat stress in the sows were closer to the TNZ of the piglets, which would be expected to decrease hypothermia and metabolic energy requirements, allowing the piglets to perform well at the expense of their dam.

**Nutritional Status**

The piglet is born with relative physiological deficiencies that predispose it to mortality and morbidity.
The newborn piglet has a low energy reserve, approximately half of that of lambs and calves (Mellor and Cockburn, 1986; Herpin and Le Dividich, 1995). Adequate ingestion of colostrum is crucial for neonatal survival (Noblet et al., 1997). Accordingly, factors related to limited intake and(or) increased energy expenditure have a serious impact on survival (NAHMS, 1991). Body fat is only 1 to 2% of body weight at birth, with most lipids existing in cell membrane structure (Mersmann, 1974; Svendsen et al., 1986). The ability of the newborn piglet to oxidize fatty acids is extremely low (Mersmann and Phinney, 1973). Accordingly, the early neonatal piglet relies heavily on carbohydrate stores, with glycogen levels in liver and muscle of approximately 200 and 120 mg/g tissue weight, respectively (Mersmann, 1974). Liver and muscle glycogen stores reach minimum levels at 12 to 18 and 36 to 48 h of age, respectively. The piglets’ respiratory quotient usually decreases by 12 h, reflecting an increased utilization of dietary fat (Mersmann, 1974).

Increasing levels of colostral fat have a positive linear effect on the piglet’s energy intake and fat deposition, although total colostral intake is somewhat reduced (Le Dividich et al., 1991). Increasing dietary fat for the sow in late gestation and lactation can significantly increase the fat content of colostrum and improve survival of low-birth-weight piglets (Pettigrew, 1981; England, 1986). This becomes especially important in induced farrowings when parturition occurs 1 to 2 d prior to natural farrowing (Jackson et al., 1995). The use of long- and medium-chain triglycerides (LCT and MCT, respectively) in sow feeds is also of interest, because the conversion of these compounds into ketones has a glucose-sparing effect that may be passed on to nursing piglets. In particular, the MCT are readily metabolized. Consistent with earlier findings (Pettigrew, 1981), Azain (1993) found that the survival of low-birth-weight piglets (< 900 g) was significantly improved by feeding triglycerides to sows. Survival rates of these small piglets in control, LCT, and MCT treatment groups were 32, 53, and 68%, respectively. Based on such findings, earlier authors have concluded that feeding sows high-triglyceride diets could be beneficial in herds with a history of high preweaning losses (Pluske et al., 1995).

Considering the importance of piglet nutrition for neonatal survival, maintaining the lactational performance of the sow is a high priority. Sow feed intake during lactation has a recognized influence on milk yield and the associated nutritional status of piglets as well as rebreeding performance (Verstegen et al., 1985; Britt, 1986; England, 1986; Koketsu et al., 1996). Providing a healthy and a minimally stressful environment for the lactating sow is an important management goal, because environmental and disease stressors all can contribute to depressed intake (Matterti et al., 2000).

Disease

As indicated above, causes of neonatal mortality are tightly interlinked. Major death losses due to crushing and starvation likely reflect a variety of etiologies. Piglet losses tend to be the result of noninfectious causes and are strongly associated with management practices. However, epidemics of certain neonatal diseases can occur and may result in extremely high levels of mortality for limited periods of time (Vaillancourt et al., 1994). Accordingly, the immunological development of the neonatal piglet has been extensively studied. In all cases it is important to maintain high levels of sanitation and biosecurity (see Amass and Clark for review, 1999).

The piglet is immunologically immature at birth and depends on early postnatal transfer of maternal antibodies from colostrum for immune protection. Colostrum is a rich source of immunoglobulin-G (IgG), which provides the piglet with circulating immunity against disease organisms. Immunoglobulins are maximally absorbed from the jejunum into lymphatic vessels within the first 12 h of life. The ability of the immunoglobulins to pass through the gut declines thereafter. By 48 h of age, no further transfer occurs (gut closure). However, IgG have a relatively long half-life of 14 d, which provides some immunological overlap with the onset of endogenous antibody production at approximately 10 d of age (Wilson, 1974; Gaskins and Kelley, 1995). Antigen-stimulated lymphocyte proliferation increases and T-cell differentiation markers appear and increase during the first weeks of life (Becker and Misfeldt, 1993). As colostrum production ends and milk production begins, the primary antibody transferred to the piglet is IgA (60% of the immunoglobulin content of milk). Rather than being absorbed, as is the IgG, sow-derived IgA coats the gut mucosal surfaces, forming a barrier against enteric diseases. Fangman et al. (1996a) have speculated that scurfing in weaned piglets resulting from transmissible gastro-enteritis virus (TGE) exposure could be related to the withdrawal, associated with early weaning, of maternal IgA as the piglet switches from a diet of sow’s milk to a solid feed.

Neonatal mortality has been associated with low concentrations of serum IgG (Klobasa et al., 1981). Obviously, factors that decrease colostrum/milk ingestion reduce energy intake and protection against disease. For instance, the decrease in suckling induced by cold stress reduces the acquisition of maternal antibodies (Kelley, 1985). Although birth order may have less influence on total colostrum intake than once believed (Fraser et al., 1995), it may still influence the total amount of colostral IgG ingested by the piglet. Colostral IgG levels drop by 50% within 6 h of the first nursing; thus, late-born piglets may receive significantly lower levels of passive immunity than littermates born earlier in the farrowing order (Gaskins and Kelley, 1995). Elevated environmental temperatures may also be a concern, because stress during late gestation is associated with elevated circulating cortisol concentrations in sows and their newborn piglets, increased cortisol concentrations in colostrum, and lower serum IgG concen-
trations in piglets at 24 h of age (Machado-Neto et al., 1987).

The thermal environment can also significantly influence disease susceptibility and subsequent survival (Kelley, 1985). The ability to maintain body temperature is lower in the diarrheic piglet (Balsbaugh et al., 1986). Pigs that die of cold and chilling have lower gamma globulin concentrations on d 1 than those that survive (Blecha and Kelley, 1981). The interaction between thermal environment and disease status in the neonatal piglet is multifaceted. Whereas a loss of body temperature in newborn piglets can be caused by disease (Matteri et al., 1998), exposure to a cold environment increases the neonatal piglet’s susceptibility to immunological challenges (Carroll et al., 2000), thus increasing the risk of hypothermia. This work indicates that the pathogenic environment may be an important factor with regard to chilling of newborn piglets. Interestingly, hypothermia resulting from an endotoxin challenge can be blocked by ensuring a warm ambient temperature (Carroll et al., 2000) or by preventative treatment with aspirin-related compounds (Matteri et al., 1999). Hypothermia, whether induced by thermal environment or disease challenge, increases the thermotaxic response of neonatal piglets, which often seek warmth from the sow. Additionally, piglets experiencing hypothermia due to disease challenge are typically more lethargic and less active than healthy piglets, and thus the risk of being crushed by the sow becomes compounded by piglet behavior under these circumstances.

The endemic pathogen status of the sow herd can also influence the disease status of the newborn piglet. Increased deaths due to infectious causes including Streptococcus sp., Escherichia coli, and Clostridium perfringens and viruses such as rotavirus (Rota), coronavirus (Corona), and TGE are more likely in litters of sows affected with these postparturient diseases (Fangman et al., 1996b). There has been a considerable shift in the prevalence of agents causing neonatal diarrhea in swine. Enterotoxigenic E. coli and TGE were once the most common pathogens identified. Now these organisms are detected in only a small percentage (15%) of neonates with scours. However, Rota continues to be a significant problem and has been joined by Clostridium difficile and Porcine Reproductive and Respiratory Syndrome virus as the most common pathogens identified in neonates with diarrhea (Yaeger, 2000).

Sow and Piglet Behavior

The initial move to decrease piglet crushing consisted of confining the sow to a smaller pen than was traditional. The incidence of crushing and related piglet mortality has significantly decreased since the popular adoption of the farrowing crate in the 1950s (Arey, 1993). Indeed, most studies have found that housing sows in a small pen, or farrowing crate (0.6 × 1.7 m), does decrease piglet mortality (e.g., Friend et al., 1988; McGlone et al., 1994). This management practice gained momentum in the 1960s (Blackshaw et al., 1994) as more economic pressures were applied to the swine industry. Unfortunately, piglet crushing remains a problem for swine producers. Data from NAHMS indicate that the rate of piglet crushing has remained at a high, stable rate from 1991 to 1995 (NAHMS, 1991, 1995). The incidence of preweaning mortality continues to average approximately 15% (NAHMS, 1991; Kosetsu, 2000), representing a significant source of economic loss to the swine industry. Interestingly, approximately 50% of these preweaning death losses occur during the first 3 d of life (Bauman et al., 1966; English and Smith, 1975; Cieslak, 1983; NAHMS, 1991). More specifically, it is during the first 48 h after farrowing that the majority of crushing deaths occur (Rudd and Marchant, 1995). Unfortunately, the incidence of crushing can be attributed to many factors such as low birth weights, environmental temperature, facilities, and disease, which contributes to the complexity of solving this problem. The implications of crushing on piglet well-being are obvious, but crating sows has raised concerns for the well-being of the sow, which must remain in an environment in which she may not perform typical maternal behaviors and in which her mobility is restricted to such a point that she may not turn around. However, production parameters such as feed consumption and return to estrus remain high for the sow, which suggests that the sow’s well-being is adequate in these systems.

Many experiments have been conducted to investigate the effect of the design of the sow’s housing during farrowing in reducing preweaning mortality (Curtis et al., 1989; Blackshaw et al., 1994; Morris and Hurnik, 1995). The typical farrowing crate of approximately 0.6 × 2.2 m is the prevalent form of housing today, but animal well-being continues to stimulate interest in the farrowing pen. Most studies indicate that fewer pigs die in crates than in pens. For instance, Blackshaw et al. (1994) reported mortality in farrowing crates of 14% and in farrowing pens of 32%. Bäckström (1973) reported crushing of 3.4% in crates and 5.9% in pens. Also, crate design has been found to influence piglet mortality; Curtis et al. (1989) found more crushing in wide crates (64 cm wide) than in narrow crates (55 cm wide). Unfortunately, relatively little work has been conducted to determine the effect of gestation housing on subsequent piglet survival. One study (Cronin et al., 1996) in which sows were housed in a gestation crate or pen and then farrowed in a pen or crate found that gestation environment did not affect the number of piglets born or weaned, although the authors believed there was a trend for the crate-housed sows to give birth to fewer piglets. In contrast, Marchant et al. (1994) found that litter size was greater for sows that gestated in crates; however, mortality rate was also greater compared to that of piglets from sows that gestated in groups. He suggests that the differences in
mortality rate are likely due to the sow’s having a larger litter. This research also found that sows that were group-housed during gestation produced more pigs if they farrowed in a crate rather than in a pen. More research in this area will help to build complementary gestation and farrowing accommodations.

Several researchers have evaluated alternate methods of confinement to determine whether sows could be confined in more space but still maintain a low incidence of crushing (Friend et al., 1988; McGlone and Morrow-Tesch, 1990; Cronin et al., 1996). McGlone and Morrow-Tesch (1990) noted a reduced piglet mortality when sows farrowed in pens with a slope (approximately 8%), whereas Grissom et al. (1990) found no effect on piglet mortality when sows were housed in similar accommodations. Environmental factors such as types of flooring also have been found to influence the rate of piglet crushing (Walker and Knox, 1996). These researchers found that although some floor types and crate configurations may save more piglets initially, all systems tested produced the same number of weaned piglets. This was thought to be due to a system’s saving small piglets early on, which altered death loss prior to weaning. Cronin and van Amerongen (1991) found that sows housed in crates but given access to straw and covered with a hessian cover during farrowing were more responsive to the distress vocalizations of their piglets, and piglet mortality was decreased. Sows farrowing in pens have been found to have shorter birth intervals, wean the same number, but heavier, piglets (Biensen et al., 1996), and have an increased expression of maternal behavior (Cronin et al., 1996). Unfortunately this increase in the expression of maternal behavior was not associated with an increase in piglet survival. A great deal of variation exists in the current literature as to whether farrowing crates decrease piglet mortality. Several studies (McGlone and Blecha, 1987; Arey and Sanchez, 1996; McGlone and Hicks, 2000) have found no difference in piglet mortality when comparing a crate and pen (or outdoor) system.

One major reason changes in pen sizes and shapes may not have been successful in decreasing crushing is because piglets are attracted to their dam’s udder immediately upon birth and prefer to lie there the majority of time during the first 3 d after birth. After this initial 3 d, piglets are often seen using the heat lamp instead of the sow’s udder. This change of preference for lying area may help the piglets avoid death due to crushing. Although the sow’s housing environment has been shown to have a profound effect on piglet crushing, the physical constraints of the sow and the behavior of both the sow and piglet should not be overlooked.

Physical Constraints. The physical attributes of the sow may be one important factor in piglet crushing. For instance, the larger the sow, the less physical control she may have over her body in the given space. The percentage of piglets crushed has been found to be positively correlated with sow body length (Rudd and Marchant, 1995). During the previous 10 yr, sows have been selected to produce piglets that grow quickly and produce a large amount of lean mass. This selection pressure has caused not only large piglets, but large sows as well. Unfortunately, as the sows have become larger, the gestation crate and farrowing crate have not changed in size. This mismatch between sow size and crate size is of important concern for both sow well-being and productivity. Data collected by the NAHMS (1995) indicate that 40.7% of sows are culled due to “age or size.” Sows kept in gestation crates also receive less exercise than sows kept in gestation pens or outside, resulting in reduced cardiovascular and muscular fitness (Marchant et al., 2000). All these factors may increase the crated sow’s difficulty in lying down carefully. Rudd and Marchant (1995) proposed that crates compensate for careless lying behavior, but they inhibit careful lying behavior.

Activity level of the sow has also been found to affect piglet mortality. Svendsen et al. (1986) found that most traumas to piglets occur when the sow changes position; standing up, lying down, walking, and so on. This suggests that a sow that spends more time lying quietly is less prone to crushing her piglets than a sow that is more active. Sows housed in farrowing pens spend approximately 90% of the time lying during the 3 d following farrowing (Hohenshell et al., 1996; Minnick et al., 1997). Compounding the chances of getting crushed is the finding that sows housed in crates performed twice as many position changes between lie:sit and sit:lie compared to sows housed in pens, although pen-housed sows performed more rolls (Weary et al., 1996a). In addition, Haussmann et al. (1999) noted that some sows possessed pressure point sores on their shoulders and limb joints and that this may increase the number of position changes a sow makes; therefore, they administered a potent analgesic to sows (butorphanol tartrate) and found that butorphanol administration to sows within 4 h after farrowing decreased the total number of body position changes that a sow makes during the 3 d after farrowing. These data indicate that research on improving farrowing crate flooring may improve sow well-being and piglet survival.

Maternal Behavior. In conjunction with research on different housing methods for sows to address the problem of piglet crushing, several researchers have examined the sow’s behavior to determine exactly how piglets become crushed (e.g., Svendsen et al., 1986; Rohde Parfet et al., 1989; Weary et al., 1996a). These researchers found that piglets are crushed when the sow changes position, essentially moving between lying and standing and vice versa. However, Weary et al. (1996a) found that pen-housed sows also crushed a significant number of piglets while changing lying positions and that most crushings occurred during the 1st d of life. Interestingly, evidence exists to suggest that early experience affects maternal ability, and sows reared in group-housing systems have been found to exhibit a lower piglet mortality rate (Wechsler, 1996).
Sows are capable of exhibiting beneficial maternal behavior, and confinement has been shown to prevent their natural “anti-piglet-crushing” behavioral repertoire (Blackshaw and Hagelsø, 1990; Algers, 1992), thus suggesting a reason for the variable success of crates. Feral sows perform pre-lying behavior that is designed to remove piglets from the lying area (Rudd and Marchant, 1995). This pre-lying behavior, consisting of rooting through the bedding and vocalizing to the piglets, may decrease piglet mortality. Blackshaw and Hagelsø (1990) reported that 79% of sows rooted before lying down on the day after farrowing when housed in pens. Marchant et al. (2001) found that sows housed in a group farrowing system were much more likely to perform dangerous lying behavior and increase the risk of crushing piglets when they did not perform piglet-directed behaviors prior to lying. Interestingly, these authors found that sows performed the greatest amount of piglet-directed behaviors during the 1st d after farrowing, the precise time that piglets are the most vulnerable to becoming crushed. Sows confined to crates, in which they cannot turn, are hindered from performing pre-lying behavior repertoires.

An outstanding anomaly in the piglet mortality problem is that the majority of sows do not respond to the distress vocalizations of their piglets when they are being crushed. However, sows that are responsive to piglet distress calls are better able to release trapped piglets prior to crushing (Wechsler and Hegglin, 1997). One theory to explain the nonresponsiveness is that sows in farrowing crates are subjected to the distress vocalizations of neighboring piglets, and regardless of their responses they cannot make the neighboring piglet stop vocalizing and thus they learn to be nonresponsive when piglets vocalize. Housing methods to reduce crushing may have met with variable success largely because research efforts have concentrated on controlling and/or altering the behavior of the sow and have largely ignored the piglets’ role in crushing mortalities. Weary et al. (1998) found that it was a combination of increased sow parity, small piglet size, and large litters that increased piglet crushing, although one factor alone could not be implicated as being most important because they are confounded.

Another anomaly in preweaning piglet deaths is due to savaging of piglets by the sow. Savaging behavior is characterized by a sow that is overtly aggressive to her piglets and may result in injury and death to a portion of the litter. Savaging behavior has been noted in captive wild boars. Harris et al. (2001a) found that 8.3% of wild boar sows used in their study killed piglets and that one genetic line in particular was characterized by more aggression and a longer duration of parturition. English and Morrison (1984) examined the incidence of savaging attempts (any attempt by the sow to bite her piglet) of 31 farrowings and found that 89% of the gilts attempted to savage their piglets, and this percentage decreased to approximately 20% for subsequent farrowings. Because these sows were not culled if they savaged, the decrease in savaging across parities could not be attributed to culling for the later parities. In a more comprehensive survey of commercial sows, Harris et al. (2001b) evaluated the incidence of savaging and some factors that are correlated with this deleterious behavior. They collected data from seven farms, representing 8,800 gilts and 5,232 sows. Their data revealed that 5.3% of gilts expressed piglet directed aggression and 2.9% of these gilts fatally savaged at least one of their piglets. Aggressive behavior of gilts toward their offspring resulted in a 0.6% death loss and 0.14% of piglets were injured. Interestingly, these authors found that if the lights were left on in the farrowing house, a reduction in the incidence of savaging was realized. Additionally, animals that savaged piglets as gilts were more likely to savage during their second parity. The behavioral differences at parturition in wild boar sows that savage may be indicative of problems in commercial sows. Appleyard et al. (2000) found that savaging sows were more active prior to farrowing, showing more ventral lying and shifting between positions. Similarly, Marchant et al. (2001) found that savaging sows are more fearful of humans and that sows that readily interacted with humans were not savaging and were more protective of their litters. Fear of the piglets (Harris et al., 2001a), lack of experience during adolescence (Knap and Merks, 1987), and the pain associated with parturition (Hansen and Curtis, 1981) have all been implicated in savaging behavior; however, the definitive cause(s) of savaging remains elusive.

**Piglet Behavior.** Piglet behavior during the early postnatal period (d 1 to 3) is another area that has received considerable attention with regard to trying to reduce neonatal mortality. Similar to newborn mice, gerbils, guinea-pigs, and rabbits (Dawes and Mestyan, 1963; Eddy and Ogilvie, 1970), the newborn piglet huddles with littermates against the dam, presumably to conserve heat and metabolic fuel (Mount, 1959). This innate behavior ultimately increases the neonatal piglet’s likelihood of being crushed by the sow when it is lying down or rolling over (Wechsler and Hegglin, 1997). Weary et al. (1996) found that low-weight piglets spent more time by the sow’s udder, actively massaging her udder, and therefore were in greater danger of becoming crushed. Intuitively, if piglets are huddling with littermates and the sow to conserve heat, then providing an alternative heat source to attract piglets away from the sow should decrease the incidence of piglet crushing. In support of this idea are prior studies that demonstrated a thermotaxic response of newborn piglets when exposed to a thermocline (Balshaugh et al., 1986). Thus, initial research efforts focused on exploiting the neonatal piglet’s innate thermotaxic response as a method for drawing the piglet away from the sow by evaluating the location of various heat sources (conventional heat lamps, heaters, and hovers) in farrowing crates.

Early studies by McGinnis et al. (1981) and Saldierna et al. (1987) suggested that the use of supplemental
heat sources can be used to reduce the incidence of diarrhea, and thus supplemental heat may be more advantageous to the young piglet’s overall health during periods of pathogenic exposure. Although providing supplemental heat to newborn piglets during the first 2 d of life has been shown to increase survival rates (Adams et al., 1980; McGinnis et al., 1981; Saldierna et al., 1987), the addition of more supplemental heat sources, the type of heat sources (i.e., conventional heat lamps, heaters, and hovers), and the location of supplemental heat sources in the farrowing crate (rear, front, or lateral) do not result in further improvement in survival rates (Ogunbameru et al., 1991; Hrupka et al., 1998). Hrupka et al. (1998) reported that during the first 3 d of life the neonatal piglet tends to lie in close proximity to the sow regardless of the heat source location or the environmental temperature. Additionally, 1-d-old piglets spend the majority of their time (60 to 75%) suckling the sow or huddling near the sow (Titterington and Fraser, 1975; Lewis and Hurnik, 1985). Of the time spent in close proximity to the sow during the 1st d of life, only about 40% of this time is associated with suckling (Lewis and Hurnik, 1985). Therefore, the newborn piglet spends 20 to 35% of its time in close proximity to the sow without suckling, increasing the risk of death by crushing for no apparent reason. Thus, in order to make significant progress in reducing preweaning mortality losses, an understanding of environmental factors other than temperature that modulate the behavior of the newborn piglet must be addressed.

It is intuitive that piglets should have a high attraction to their dam’s udder and its associated warmth, nutrition, and comfort. Several studies have examined the auditory, olfactory, visual and tactile cues in order to identify those factors that drive the neonatal piglet to huddle with littermates and the sow (Welch and Baxter, 1986; Rohde Parfet and Gonyou, 1991; Hrupka et al., 2000a,b). Welch and Baxter (1986) reported that piglets are attracted to the physical and thermal properties of the sow’s udder, and Rohde Parfet and Gonyou (1991) reported that the attraction to the sow’s udder is associated with the odor of the sow’s milk. Rhode Parfet and Gonyou (1991) noted that piglets have a tendency to move in the direction of the dam’s orientation, thus directing them toward the udder. Upon birth, piglets have a highly developed sense of smell and are attracted toward the dam’s udder. Morrow-Tesch and McGlone (1990) found that piglets were highly attracted to the odor of their dam’s feces and teat washings and that they learned this attraction within the first 12 h of life. Similarly, Horrell and Hodgson (1992) noted that piglets were able to distinguish odors associated with their dam (urine, feces, udder) compared to an unfamiliar dam and that they were particularly attracted to the wood shavings that had been previously associated with their dam’s udder. Rhode-Parfet and Gonyou (1991) found that piglets were attracted to the odor of the sow’s milk. However, they were also attracted to the odor of birth fluids and sow vocalizations (two paths that would lead them away from the udder). The piglets’ attraction to the udder is most likely dependent on odor. When a sow farrows, the majority of the piglets move directly toward the udder, and very few venture the long way around the back. This indicates that the piglets have a drive to move toward the udder, despite their known lack of significant vision at this time. Several factors are likely responsible for orientation.

It is this attraction of the piglet, due to warmth, odor, and tactile stimuli, to the sow’s udder that puts the piglet into a position to become crushed. In fact, Weary et al. (1996) have shown that it is more probable to find the smaller, weaker piglets near the udder, thus increasing their chance of becoming crushed. These authors hypothesized that these smaller piglets were hungry and thus maintained contact with the sow’s udder in order to gain access to her warmth and milk.

Following up on these earlier studies, Lay et al. (1999) explored the possibility that newborn piglets are attracted to the odor, as well as the warmth and tactile properties, of the sow’s udder. They demonstrated that the presence of a simulated udder, possessing olfactory, tactile, and thermal characteristics of the sow, in the farrowing crate could attract piglets away from the sow more effectively than heat lamps alone. Further work by Hrupka et al. (2000a,b) examining the thermal, visual, and physical cues that may act as attractants to neonatal piglets demonstrated that piglets choose physical contact with an anesthetized littermate in a cold environment (24°C) as opposed to a warm environment (45°C) without the presence of a littermate. Additionally, they demonstrated that visual recognition does not influence huddling; piglets demonstrated no preference in huddling activity between littersmates and nonlittersmates. Collectively, these data suggest that tactile and olfactory cues are the primary innate stimuli that increase the risk of piglet crushing from birth to 3 d of age. It should be mentioned, however, that although supplemental heat may not be considered a primary attractant, its positive role in the prevention of hypothermia and illness in the newborn piglet is without question. Until we can develop sows with good maternal behavior, future studies that perfect simulated udder designs such as that used by Lay et al. (1999) may prove to be the most effective means to reduce neonatal mortality caused by crushing in the newborn piglet. In the meantime, the presence of a trained attendant may be highly beneficial in reducing piglet loss due to crushing (Holyoake et al., 1995).

Facility design was shown to be an important influence on sow behavior, and the same may be true for the piglet. Rohde Parfet et al. (1989) have shown that crate design affects important behaviors of the piglet. In fact, Blackshaw et al. (1994) found that piglets would spend twice the amount of time at their dam’s udder if they were housed in a crate compared to a pen. If a sow’s piglets would move to the heat lamps or pads provided to them, they would certainly decrease their
chances of becoming crushed. Svendsen et al. (1986) noted that it took piglets up to 48 h to start using these heat sources, and Blackshaw and Hagelsø (1990) noted that 94% of piglets would stay under their heat source by d 8 after parturition. Obviously, no matter how careful and attentive a sow may be, if her piglets will not move when she lies, she has little choice but to crush them.

Sex

Although slightly more males than females are born in a litter, females have a greater survival advantage than males (Bereskin et al., 1973; Svendsen et al., 1986; Becker, 1995). In addition, a larger litter was found to be more detrimental to survival for male than for female piglets. Males are more susceptible to stillbirth, weakness/starvation, and crushing (Svendsen et al., 1986). McGlone et al. (1993) reported that castration of male piglets at any age leads to less time spent nursing and standing and more time spent lying, which may lead to more clinical and subclinical disease, resulting in greater mortality compared to females. More recently, Becker (1995) reported that the greater mortality in males was due to more males being crushed and chilled.

Although the underlying mechanism(s) responsible for this sexual dimorphism in preweaning mortality rates has not been elucidated, there are some unique sex differences that may account for these observations. For instance, the higher basal concentration of cortisol observed in the male piglet as compared to the female piglet (Ruis et al., 1997) may cause male piglets to be more susceptible to the deleterious effects of stress and therefore succumb to subsequent disease challenges. One possible factor that may account for a greater rate of crushing in male piglets is their potential for an increased sensitivity to pheromones. In a study by Dorries et al. (1995), male piglets were reported to have a fivefold increase in their sensitivity to androstenone compared to female piglets. Although the focus of this study was on sensitivity of adult piglets to a sex pheromone, it is plausible that a more highly developed vomeronasal sensitivity in the neonatal male piglet could result in an increased amount of time spent near the sow due to pheromones associated with the sow’s udder, thus increasing its risk of being crushed.

Genetics

The sow is apparently the only mammal that produces large litters and lies on a significant portion of them within days of parturition. Because of the risk associated with parturition and the repartitioning of nutrients associated with producing young, piglet crushing by the dam is not consistent with current evolutionary theory. Likely, the modern sow has been altered through genetic selection, resulting in its being a “poor” mother. Algers (1992) suggests that farrowing crates have reduced the selection pressure for beneficial maternal characteristics in sows. Interestingly, it was probably the introduction of farrowing crates into the swine industry that allowed producers to put less emphasis on maternal behaviors and more emphasis on other reproductive traits, thus inadvertently implementing a selection program for nonmaternal behaviors that contribute to piglet crushing. In support of this theory are the maternal characteristics of the Meishan sow from China. These sows are known to produce large litters, and Meishan piglets have been found to have a 5% advantage in piglet survival rate over Large White piglets (Bidanel et al., 1990). Meunier-Salaun et al. (1991) reported that Meishan sows had 13.6 piglets born alive and weaned 12.4 piglets, whereas Large White sows farrowed 8.6 live piglets and weaned 7.4. The superior production of the Meishan has been attributed to behavioral characteristics and a greater number of teats. Hohenshell et al. (1996) studied the behavior of Meishan sows to determine how their behavior immediately after parturition differed from that of our modern production sow. Their preliminary research on these sows indicates that the Meishan sow may be more vigilant and aware of her piglets’ location and then she quickly lies down without crushing them. Common breeds used in U.S. pork production may also vary in their rate of crushing piglets. Curtis et al. (1989) found that Duroc-sired sows crushed fewer piglets than Landrace- or Hampshire-sired sows. Unfortunately, modern genetic selection of breeding stock has emphasized piglet growth characteristics, number of piglets born alive, and number of piglets weaned, not sow maternal behavior. Therefore, maternal behavior varies widely among sows.

The increase in neonatal mortality typically seen with increasing litter size differs significantly among swine breeds. With 10 liveborn piglets, preweaning mortalities in Large White and Pietran swine have been reported at approximately 12 and 20%, respectively (Blasco et al., 1995). A positive effect of heterosis on piglet survival is known to exist, and an improvement of 5 to 6% in survival can be expected in litters of crossbred, compared with purebred, piglets (Blasco et al., 1995). An additional concern is raised by rapid changes in genetics related to lean growth. Selective breeding could result in metabolic and compositional changes that affect the newborn piglet’s ability to adapt to the postnatal environment. Relative to Meishan and European white breeds, crossbred piglets selected for enhanced lean tissue growth have been shown to possess lower body fat stores and a reduced ability to metabolize triglycerides (Herpin et al., 1993). The genetic correlation between backfat thickness and daily feed intake is 0.55 (Stewart and Schinckel, 1991), thus selection for decreased fatness results in decreased feed intake. This could result in sows that are unable to consume adequate feed to meet the milk production needs of a large litter.
Sow and Piglet Well-Being

The use of gestation and farrowing crates is certainly one of the major targets of growing international concerns for swine well-being. Sows housed under restricted housing conditions, such as the gestation and farrowing crate, and restricted feed conditions during gestation are known to perform stereotypic behaviors such as bar biting and excessive rooting. In addition, a large percentage of sows have limb abrasions, lameness, stomach ulcers, and a high group mortality rate (Deen and Xue, 1999; Geiger et al., 1999) indicating that their well-being is not adequate. However, sows housed in less-restrictive environments, as groups, must contend with competition from penmates and are often subjected to aggression from which they cannot escape. Obviously, this raises a different set of well-being concerns for group-housed sows. A gestation system such as that developed by Hurnik and Morris (Morris and Hurnik, 1995) may well improve the well-being of group-housed sows; these researchers found that sows in the Hurnik-Morris system performed fewer stereotyped behaviors and produced more piglets. Although more scientific data are needed, the popular concept is that sow well-being is improved in systems that provide more natural physical and social environments (Wechsler, 1996). Mortality and morbidity in the piglets, however, appear to be compromised in a large portion of such alternative production environments (Arey, 1993; Wechsler, 1996; Marchant et al., 2000).

Implications

It is apparent that neonatal, preweaning mortality in many cases is an unnecessary production loss and an animal well-being concern. Most losses due to stillbirths, crushing, chilling, and starvation should be preventable given good management, genetics, facilities, and health. However, our understanding of the underlying mechanisms that allow these losses to occur needs further development in order to be implemented in a production situation. Currently, we do not understand the implications that gestation housing, farrowing environment, and sow stress has on neonatal piglet mortality. We work to control factors known to be detrimental to piglet survival, such as disease, unequal competition between littermates, thermal stress to the piglet, and inadequate nutrition.

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Control of ovulation rate in swine

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ABSTRACT: Follicular recruitment and atresia are important processes associated with ovulation rate in swine. Follicle-stimulating hormone regulates granulosa cell division, differentiation, and steroidogenic function, and, as such, significantly influences follicular growth and development. Follicle-stimulating hormone is an inducer of follicular recruitment in swine and an inhibitor of granulosa cell apoptosis, and it seems to be a major regulator of ovulation rate in swine. Although local factors, such as growth factors and steroid hormones, might regulate follicular development by controlling the expression of gonadotropin receptors or by modulating other related processes, the dominant role of FSH cannot be ignored. Recent results indicate that androgens might be among the local factors regulating ovulation rate in swine. Administration of testosterone or the nonaromatizable androgen dihydrotestosterone increased the number of ovulations in gilts in a dose-dependent manner. Furthermore, administration of dihydrotestosterone increased the amounts of FSH receptor mRNA in pig preovulatory follicles. Steady-state amounts of FSH receptor mRNA are relatively high during the early follicular phase but decrease significantly as follicles grow and approach ovulation, suggesting that major changes in amounts of FSH receptor mRNA occur during late follicular development in pigs. Local ovarian factors that regulate follicular responsiveness to gonadotropins seem to be important components of the mechanisms that control ovulation rate in pigs.

Key Words: Ovarian Development, Ovulation Rate, Pigs

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Introduction

A fundamental function of the ovary is to support development of oocytes. Oogenesis begins during fetal life and is highly influenced, later during the reproductive period, by follicular development. Beginning at puberty, about 10 to 25 follicles develop to the ovulatory stage and release oocytes every estrous period. The total number of ovulations is called the ovulation rate and it is an important parameter of swine reproductive efficiency. It should be noted that although ovulation rate is a limiting factor in determining the number of offspring born, numerous additional factors act upon the uterus and conceptuses throughout gestation and contribute to the number of healthy fetuses that develop to term.

Factors that alter ovulation rate might function by modulating, directly or indirectly, how many follicles grow or how many follicles die (atresia). Follicular growth or atresia will be the main focus of the present review. Initially this review will describe follicular development and then will partition factors that affect recruitment from atresia. This overview will continue by reviewing some recent observations from our laboratory that suggest a novel role of androgens in regulating follicular development. Finally, a brief description of how some other factors might regulate recruitment or atresia will be discussed.

Folliculogenesis

Primordial follicles form the stock from which all follicles emerge (Peters, 1978). Approximately 500,000 primordial follicles are present in both ovaries by 10 d after birth in swine (Black and Erickson, 1968). Primordial ovarian follicles in this population are not stimulated to grow at the same time, and only a small number begin their development while the rest remain quiescent. In mammals, this characteristic increases the possibilities of having progeny throughout a rather long reproductive life.

Initiation of growth of primary follicles involves endocrine actions and regulatory effects of local factors from the somatic cells of the follicle (Hirshfield, 1991) and probably from the growing oocyte (reviewed by Picton...
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et al., 1998). Early follicular growth is characterized by an increase in the number and layers of granulosa cells, which subsequently separate from each other resulting in formation of the antrum, a fluid-filled cavity (Zamponi, 1974). Initial studies using hypophysectomy techniques, and more recent experiments using knockout mice lacking a functional FSH receptor (FSHR) gene (Dierich et al., 1998), indicated that FSH seems to be absolutely necessary for antrum formation and postantral follicular development. Therefore, development of responsiveness to FSH might be a key factor controlling follicular differentiation and function.

Growth rates of antral follicles of pigs and other species follow an exponential curve because of a dramatic increase in proliferation of granulosa cells and an increase in size of the antrum (Clark et al., 1975; Grant et al., 1989). Activated primary follicles of pigs require approximately 84 d for growing to the antral stage and an additional 19 d to grow to the preovulatory size of 10 mm (Morbeck et al., 1992). The rate of growth of porcine follicles from 3 to 10 mm in diameter has been estimated to be 1.14 mm/d (Dailey et al., 1976). During final maturation, cells of the theca and granulosa layers synthesize and secrete significant amounts of steroids, peptide hormones, prostaglandins, and other substances. These hormones are important because they participate locally in follicular development, and some of them convey signals that coordinate the functions of the hypothalamic-hypophyseal-ovarian axis.

Follicular recruitment refers to the formation of a pool of antral follicles from which the oculatory follicle(s) is subsequently selected (Fortune et al., 1991). Follicular recruitment in pigs occurs between d 14 and 16 of the estrous cycle (Clark et al., 1982; Foxcroft and Hunter, 1985) or shortly after weaning. On d 16, approximately 40 to 50 follicles, 2 to 6 mm in diameter, are present in both ovaries (Grant et al., 1989). A number of these follicles are growing and represent the population of recruited follicles. Most follicles, and the oocytes they contain, degenerate and disappear from the ovaries through the process of atresia. Although atresia may occur any time during development of antral follicles, most follicles, for a given species, are lost during the transition from the small to large size (Fortune, 1994). Therefore, only a small proportion of recruited follicles (about 30 to 40%) are selected to complete final maturation and ovulate while the remaining become atretic, most of them before reaching 6 mm in diameter (Grant et al., 1989; Dailey et al., 1976). Ovulatory follicles are not readily identifiable until d 20 (Grant et al., 1989), which suggests that the process of selection is not completed until near ovulation. Therefore, the final number of ovulatory follicles is determined by how many follicles are recruited and by the ability of recruited follicles to continue to grow and avoid atresia. Because follicles might become atretic, even close to the time of ovulation, the process of selection probably takes place continuously, over the entire follicular phase (from luteolysis at approximately d 13 to 14 to ovulation; Foxcroft et al., 1987). Follicular dominance, which occurs in cattle (Ko et al., 1991) and primates (Zelegnik and Kubik, 1986), has not been demonstrated in pigs.

Within each mammalian species, ovulation rate is regulated within a relatively narrow range. Changes in rates of follicular recruitment or atresia could alter the number of follicles that ovulate. This notion has been supported in recent studies. For instance, Meishan sows have a higher ovulation rate than Large White hybrids (27.7 vs 17.6 CL, respectively) and, probably related, Meishan sows have more follicles ≥2 mm on d 16 than Large White sows. Also, in Large White sows the number of follicles decreased from d 16 to 19, but this decrease does not occur in Meishan sows (Miller et al., 1998). Collectively, these observations suggest that the greater ovulation rates in the Meishan breed than in Large White hybrids is related to differences in both recruitment and atresia. Alternatively, the possibility that ovulation rate can be altered by manipulating the incidence of atresia alone has been shown in mice that exhibit increased ovulation rate and litter size following overexpression of the antiapoptotic factor bcl-2 (Hsu et al., 1996).

Follicle-Stimulating Hormone is an Effective Inducer of Follicular Recruitment

The number of follicles that are recruited might depend on concentrations of FSH or other regulatory factors, or on the number of follicles responsive to FSH present at the time of recruitment. Whether the latter is related to some endocrinological event occurring before recruitment, or what other factors might influence it, is not known. Several relationships support a regulatory role of FSH on follicular recruitment in swine, and some have been known for many years. Treatment with FSH or PMSG on d 15 and 16 of the estrous cycle increases the number of ovulations in gilts, but the effect significantly diminishes when given after d 16 (Hunter, 1979). Administration of FSH or PMSG increases ovulation rate in estrus-synchronized sows (Guthrie et al., 1997) and induces follicular recruitment in prepuberal gilts (Paterson, 1982) or during the luteal phase in postpuberal gilts in a manner that is dose-dependent (Hunter, 1979). Partial suppression of FSH by administration of porcine follicular fluid to gilts during the early follicular phase reduced the subsequent number of small, medium, and large follicles, possibly due to inhibin present in follicular fluid (Guthrie et al., 1987). In another experiment, the numbers of medium-sized follicles were partially restored when FSH was given following treatment with porcine follicular fluid (Guthrie et al., 1988; Knox and Zimmerman, 1993). Active immunization against inhibin increased concentrations of FSH (area under the curve) by 27% and number of ovulations by 39% in gilts (King et al., 1993). A similar increase of 35% in ovulation rate was reported by other investigators in gilts immunized against inhibin (Brown et al., 1990). However, diminishing the
decrease in FSH that occurs after weaning in sows by passive immunization against inhibin did not alter numbers of piglets born (ovulation rate was not evaluated; Wheaton et al., 1998).

Despite the effects of exogenous FSH on ovulation rate, which indicate that it is a major inducer of follicular recruitment in pigs, a clear increase in FSH concentrations coincident with the period of follicular recruitment has not been detected in gilts (Flowers et al., 1989; Guthrie and Bolt, 1990) or sows (Shaw and Foxcroft, 1985; Foxcroft et al., 1987). A small increase in plasma FSH concentrations occurs around estrus in postpubertal gilts, coincident with the preovulatory LH surge, which is followed by a second increase approximately 72 h later. No significant changes in concentrations of FSH occur during the luteal phase until the time of luteolysis, when FSH concentrations decrease gradually through the period of estrus (Brinkley, 1981; Van de Wiel et al., 1981; Guthrie and Bolt, 1990; Guthrie et al., 1993). Likewise, during the follicular phase, FSH binding and FSH-stimulated adenylate cyclase activity by granulosa cells decrease as follicle size increases (Nakano et al., 1977; Lindsey and Channing, 1979). Moreover, amounts of FSHR mRNA determined using in situ hybridization (ISH) decrease from the time of recruitment to undetectable levels at estrus (Liu et al., 1998). In another study, FSHR mRNA became undetectable by ISH procedures when follicles reached 4 mm in diameter in sows after weaning (Liu et al., 2000). Experiments using reverse-transcription polymerase chain reaction (RT-PCR), a very sensitive technique, indicated that FSHR mRNA in surface walls of the largest follicles present from d 13, 15, and 17 of the estrous cycle were not different but decreased by d 19 (about fivefold relative to d 13, Cárdenas and Pope, unpublished data). This significant down-regulation of FSHR around estrus is only present in late-developing follicles, because small antral follicles permanently exhibit high amounts of FSHR throughout the estrous cycle (Yuan et al., 1996; Liu et al., 1998).

The decrease in plasma FSH concentrations and amounts of FSHR mRNA in late-developing follicles suggests a diminished influence of FSH on porcine follicles as they advance to the preovulatory stage. This does not necessarily mean that FSH is not needed for recruitment. The relatively greater concentrations of FSH before recruitment, and the concentrations present during recruitment, although decreasing, are probably enough to support follicular growth and function. For example, synthesis of estradiol, a process partially regulated by FSH, is still increasing even though FSH and FSHR mRNA are decreasing. The significance of the FSH decrease is not apparent. Perhaps, lesser concentrations of FSH would inhibit incorporation of more follicles into the cohort of recruited follicles, thus decreasing follicular heterogeneity. Reduced diversity among follicles is important to ensure uniform response to ovulation or decrease diversity in oocyte or embryonic development (Pope et al., 1990). Furthermore, decreased FSH stimulation might allow only those follicles that have reached certain developmental conditions to continue to grow, to avoid atresia, and to ovulate. Although this concept seems attractive as a mechanism of follicular selection in pigs, it will need to be examined further. As FSH stimulation becomes attenuated, additional support for follicular development could come from growth factors, LH, and steroid hormones.

Unlike FSH, LH remains almost unchanged during the follicular phase, except near the onset of estrus when the preovulatory LH surge occurs (Brinkley, 1981; Van de Wiel et al., 1981; Guthrie and Bolt, 1990). Luteinizing hormone binding in theca and granulosa cells increase as follicles become larger during the follicular phase (Nakano et al., 1977; Foxcroft and Hunter, 1985), increasing the ability of late-developing follicles to respond to LH. Amounts of LH receptor mRNA in granulosa and theca interna cells increases as follicles grow from 2 to 6 mm in diameter and then decrease in 8-mm preovulatory follicles (Liu et al., 2000), indicating that the LH receptor gene is down-regulated as follicles approach ovulation.

Specifically, what FSH does to stimulate follicular recruitment in swine is an important question. In vitro experiments conducted in swine or other species indicate that FSH might influence granulosa cell division by stimulating mitogen-activated protein kinases (Babu et al., 2000) or cell cycle regulators such as cyclin D2 (Siciński et al., 1996). Also, FSH significantly stimulates estradiol synthesis by several mechanisms including regulation of expression of the CYP 19 gene that encodes for aromatase cytochrome P450 enzyme (Hickey et al., 1988), synthesis of progesterone (Ford and Howard, 1997), and expression of LH receptors, an important factor in the availability of aromatizable androgens. Inhibin secreted by maturing follicles is a potent enhancer of LH-stimulated androgen synthesis by theca cells (Hillier et al., 1994). Estradiol, in turn, stimulates granulosa cell proliferation, enhances the actions of FSH and LH on steroidogenesis (Daniel and Armstrong, 1980; Richards, 1980), and appears to be absolutely necessary for follicular growth and maturation (reviewed by Drummond and Findlay, 1999). Differences in litter size not necessarily related to ovulation rate have been associated to the chromosomal locus where the estrogen receptor alpha gene is located (reviewed by Rothschild et al., 1997).

Although FSH seems to be important in the control of follicular recruitment, a relationship between ovulation rate and peripheral concentrations of FSH has not been clearly demonstrated. For instance, lines of pigs differing in ovulation rate did not exhibit differences in LH, FSH, progesterone or estradiol during the estrous cycle (Mariscal et al., 1998). Similarly, no associations were found between plasma concentrations of FSH and ovulation rate in other species such as sheep (Gibbons et al., 1999). However, differences in the ability of follicles to respond to FSH through the influence of other
factors such as the number of FSHR might exist and could help to explain the differences in ovulation rate.

Cell signaling by FSH is mediated by a plasma membrane receptor, which is present exclusively in granulosa cells in females and is associated with the cAMP-protein kinase A and probably calcium second messenger systems (Flores et al., 1992; Simoni et al., 1997; Touyz et al., 2000). Factors that regulate expression of the FSHR gene have been investigated in different species. In cultured rat granulosa cells, amounts of FSHR mRNA were increased by treatment with FSH (Tilly et al., 1992b). The effect of FSH on FSHR mRNA was enhanced by IGF-I, which apparently occurred due to an increase in mRNA stability (Minigeshi et al., 2000). In cultured granulosa cells of swine, small amounts of FSH increased FSHR mRNA (Sites et al., 1994); however, more recent results demonstrated that FSH, and other ligands that signal through cAMP, decreased steady state amounts of FSHR mRNA (Murphy and Dobias, 1999). Activin increases the number of FSH receptors in preantral follicles and prevents premature luteinization of large antral follicles (Findlay, 1993; Minigeshi et al., 2000). Findlay (1993) speculated that the effect of activin on FSHR could be of particular importance for initiation of follicular development. In primates, testosterone administration increased FSHR mRNA in granulosa cells of primary follicles but did not alter FSHR mRNA in more advanced follicles (Weil et al., 1999). We have determined the effects of androgens on amounts of FSHR mRNA in porcine follicles and the results are discussed below.

**Follicle-stimulating Hormone is an Inhibitor of Atresia in Granulosa Cells**

Follicular atresia in swine (Tilly et al., 1991; Guthrie et al., 1995), and probably most mammals (Kaipia and Hsueh, 1997), is primarily induced by programmed cell death or apoptosis of granulosa and theca cells. Apoptosis is characterized by internucleosomal DNA fragmentation, cell shrinkage, plasma membrane blebbing, and formation of apoptic bodies (Hsu and Hsueh, 2000). Although considerable progress has been made in understanding the mechanisms of cell death by apoptosis, the description of the apoptotic pathway in granulosa cells is not complete. Some results indicate that, as in other cell types, caspases are the final inducers of granulosa cell degradation (Hsu and Hsueh, 1998). The members of the bcl-2 family of apoptotic and antiapoptotic factors are upstream in this pathway and some of them have been shown to be functional in granulosa cells (Hsu and Hsueh, 1998).

The specific factors that induce atresia in porcine follicles have been difficult to identify. Initially, attempts to answer this question were made by determining hormonal changes in follicles undergoing atresia relative to healthy follicles. For example, atretic follicles had lower concentrations of estradiol and contained similar or greater concentrations of progesterone and androgens in the follicular compared to nonatretic follicles (Maxson et al., 1985; Guthrie et al., 1993; Cárdenas and Pope, 1994). Atresia of pig follicles was also associated with a decrease in expression of mRNA for aromatase and gonadotropin receptors (Tilly et al., 1992a) and with a loss of aromatase activity (Maxson et al., 1985). Although these findings did not demonstrate cause-effect relationships, they seemed to indicate a role for estrogens and gonadotropins as inhibitors of atresia. This notion was supported by other experiments in which estrogen treatment decreased apoptosis in granulosa cells of rats while testosterone antagonized the effects of estrogens (Billing et al., 1993). More recently, Meishan sows that exhibited lesser rates of atresia than Large White hybrids during the follicular phase were observed to have greater concentrations of estradiol in follicular fluid (Miller et al., 1998).

Follicle-stimulating hormone decreased apoptotic DNA fragmentation by 60% and was regarded as a major suppressor of apoptosis in cultured rat granulosa cells or follicles (Chun et al., 1994, 1996). Likewise, FSH, as well as IGF-I, decreased DNA fragmentation in porcine granulosa cells in culture (Guthrie et al., 1998). Kaipia and Hsueh (1997) proposed that FSH could directly regulate apoptotic factors or influence other inhibitors of granulosa cell death or growth promoters. Recently, mcl-1, a new member of the bcl-2 family, inhibited apoptosis in rat granulosa cells, and amounts of its message were enhanced by gonadotropin treatment (Leo et al., 1999).

**The Role of Androgens in Follicular Development and Ovulation Rate**

Follicular theca and granulosa cells undergo steroidogenesis in a cooperative manner (Short, 1962). Aromatizable androgens (testosterone and androstenedione) are synthesized by thecal cells upon stimulation by LH, which then diffuse to granulosa cells for subsequent conversion into estradiol (pigs, Evans et al., 1981). In pigs, synthesis by theca cells and follicular fluid concentrations of androstenedione during the mid- and late-follicular phase are severalfold greater than those of testosterone (Evans et al., 1981; Tsang et al., 1985). The conversion of androgens into estradiol requires stimulation by FSH (Dorrington et al., 1975; Moon et al., 1975). Androstenedione can be converted into testosterone in a reversible reaction catalyzed by 17β-hydroxysteroid dehydrogenase or aromatized to estrone, which then can be converted to estradiol-17β. Testosterone is directly aromatized into estradiol-17β (Peters and McNatty, 1980).

Evidence has accumulated to indicate that androgens play regulatory functions in follicular development. Androgens enhanced FSH-stimulated progesterone production and aromatase activity in rat and primate granulosa cells in vitro (Armstrong and Dorrington, 1976; Daniel and Armstrong, 1980; Harlow et al., 1986). Similarly, androgens stimulated [3H]thymidine incorpora-
testosterone treatment increased (induced to ovulate by a single injection of hCG, 72 h testosterone treatment using PMSG, and follicles were cycle. Follicular recruitment was induced the 1st d of (gilts were administered daily injections of vehicle or 1 related to or influenced by the physiological conditions (Vendola et al., 1998, 1999). Moreover, we demonstrated for the first time that administration of androgens during the follicular phase increased ovulation rate in postpubertal gilts. A summary of results using small doses of androgens is presented in Table 1. In one experiment, testosterone administration on d 17 and 18 of the estrous cycle increased ovulation rate in gilts, apparently by decreasing the incidence of atresia (Cárdenas and Pope, 1994). In another experiment, a longer period of testosterone administration, from d 13 to estrus, not only increased ovulation rate, but also increased the percentage of blastocysts surviving to d 11 of gestation (Cárdenas and Pope, 1997). The total number of blastocysts was therefore increased by the combined effects of testosterone on ovulation rate and survivability of conceptuses. It is possible that factors that enhance follicular development, such as testosterone, could optimize oocyte growth, resulting in conceptuses with greater ability to survive.

The effect of testosterone on ovulation rate was also observed when follicular recruitment and ovulation were artificially induced during the luteal phase, indicating that this effect of testosterone is not necessarily related to or influenced by the physiological conditions present during the follicular phase. In this experiment, gilts were administered daily injections of vehicle or 1 mg of testosterone on d 11 to 16 or 4 to 9 of the estrous cycle. Follicular recruitment was induced the 1st d of testosterone treatment using PMSG, and follicles were induced to ovulate by a single injection of hCG, 72 h later. Testosterone treatment increased ($P < 0.05$) the number of induced corpora lutea when treatment began on d 4, but the effect ($P = 0.09$) was not clear when testosterone treatment began on d 11 (Table 2). Superimposing testosterone treatment on ovulation induction using PG600 in prepubertal gilts did not alter ovulation rate but had a significant effect on increasing embryonic survival (Table 3). An important practical question has been whether the increase in ovulation rate and embryonic survival produced by treatment with testosterone would be translated into more piglets born. Results (unpublished) of a field trial indicated that treatment of multiestrous gilts with vehicle (85 gilts treated and mated) or 1 mg of testosterone (84 gilts treated and mated) on d 17 and 18 of the estrous cycle increased litter size by approximately one pig (9.6 in vehicle- vs 10.7 in testosterone-treated gilts, $P = 0.03$). Farrowing rates (gilts farrowing/gilts treated and mated) were 80 and 76.2% in vehicle- and testosterone-treated gilts, respectively.

It is possible that the effects of testosterone on ovulation rate described above could have been mediated by estradiol. Alternatively, it might be possible that testosterone, independent of estradiol, acting via the androgen receptor (AR), enhanced transcription of certain genes involved in follicular development. In addition, androgens have been shown to induce rapid changes in intracellular Ca$^{2+}$ in luteinizing granulosa cells (Machelon et al., 1998). Effects of this nature are so-called nongenomic and apparently do not involve the AR; however, participation of membrane receptors has been proposed for nongenomic actions produced by other steroids (reviewed by Wehling, 1997). Nongenomic actions of androgens have not been demonstrated in vivo, and it is not clear whether they could be involved in the effects of testosterone observed in our experiments.

Kreider et al. (2001) recently reported that active immunization against androstenedione increased ovulation with induction of ovulation using PMSG (750 IU) and hCG (750 IU) during the luteal phase of the estrous cycle.

### Table 1. Effects of low amounts of androgens on numbers of corpora lutea and conceptuses or offspring in pigs

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Corpora lutea</th>
<th>Conceptuses or offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Androgen</td>
</tr>
<tr>
<td>Testosterone (d 17 and 18, 1 mg/d)</td>
<td>14.4</td>
<td>16.7*</td>
</tr>
<tr>
<td>Testosterone (d 13 to estrus, 1 mg/d)</td>
<td>14.8</td>
<td>16.2*</td>
</tr>
<tr>
<td>Androstenedione (d 13 to estrus, 1 mg/d)</td>
<td>13.3</td>
<td>14.9*</td>
</tr>
<tr>
<td>DHT (d 13 to estrus, 6 μg/[kg BW-d])</td>
<td>17.4</td>
<td>20.3*</td>
</tr>
<tr>
<td>DHT (d 13 to estrus, 60 μg/[kg BW-d])</td>
<td>19.5</td>
<td>26.6*</td>
</tr>
</tbody>
</table>

*Different from control ($P < 0.05$).

### Table 2. Numbers of induced corpora lutea (CL) in gilts treated with vehicle or testosterone coincident with induction of ovulation using PMSG (750 IU) and hCG (750 IU) during the luteal phase of the estrous cycle

<table>
<thead>
<tr>
<th>Beginning of treatment</th>
<th>Vehicle</th>
<th>Testosterone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 11&lt;sup&gt;a&lt;/sup&gt;</td>
<td>15.7 ± 2.4</td>
<td>22.4 ± 2.6</td>
</tr>
<tr>
<td>Day 4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5.9 ± 1.1&lt;sup&gt;c&lt;/sup&gt;</td>
<td>11.9 ± 2.5&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Experiment 1. Gilts ($n = 10$ per treatment) received PMSG on d 11, hCG on d 14, and daily doses of 1 mg of testosterone on d 11 to 16. Induced CL were counted on d 23.

<sup>b</sup>Experiment 2. Gilts ($n = 18$ per treatment) received PMSG on d 4, hCG on d 7, and daily doses of 1 mg of testosterone on d 4 to 9. Induced CL were counted on d 12.

<sup>c</sup><sup>d</sup>Means within a row with different superscripts differ ($P < 0.05$).
rate in gilts by approximately three corpora lutea (ovulations). It is not clear how immunization against androstenedione, a weak androgen that can be converted into testosterone and estrogens in ovarian follicles, would increase ovulation rate in pigs. In a previous experiment, active immunization against androstenedione increased ovulation rate in gilts, did not affect concentrations of FSH and LH, but increased concentrations of androstenedione in follicular fluid (McKinnie et al., 1988). Perhaps it can be speculated that an increase in androstenedione would increase testosterone and estradiol in the follicular fluid, which in turn would stimulate follicular development.

The AR and receptors for other steroid hormones, thyroid hormones, retinoids, and vitamin D are structurally related proteins that regulate gene transcription (Tsai and O'Malley, 1994). A long (A, 110 kDa) and a short (B, 87 kDa) form of AR, having similar functional activities, are present in different organs and are derived from differences in translation initiation of the AR mRNA (Gao and McPhaul, 1998). Similar to that in rats and primates (Tetsuka et al., 1995; Hillier et al., 1997), the AR protein in swine ovaries was localized mainly in granulosa cells of small and medium-sized follicles during the 1st wk following ovulation (Garret and Guthrie, 1996). We determined the relative amounts of the AR protein and mRNA in ovarian follicles of swine from d 13 to 19 of the estrous cycle using immunohistochemistry and RT-PCR. These preliminary results (Cárdenas and Pope, unpublished data) suggested that AR protein and mRNA are 1) present in maturing follicles during the follicular phase and 2) their relative amounts do not seem to change during follicular growth from recruitment to the preovulatory stage.

To examine the involvement of the AR in ovulation rate in pigs, we administered daily injections of 0, 6, 60, or 600 µg/kg BW of dihydrotestosterone (DHT) from d 13 to estrus. Dihydrotestosterone binds and activates the AR, but unlike testosterone it cannot be aromatized due to 5α-reduction of the A ring (Wilson, 1975). Ovulation rate significantly increased by approximately 3, 10, and 17 with each additional dose of DHT. However, the number of d-11 blastocysts drastically decreased as dose of DHT increased and no blastocysts were recovered in gilts that received the highest dose of DHT (Cárdenas et al., 2002). Low recovery rates of blastocysts were associated with opaque uterine flushings, indicating that uterine function could be altered by overexposure to DHT. In a subsequent experiment, it was determined whether the effects of DHT on ovulation rate were associated with specific periods of the follicular phase. Gilts received daily i.m. injections of vehicle from d 13 to estrus or they received 60 µg/kg of DHT from d 13 to estrus (entire follicular phase), d 13 to 16 (follicular recruitment), or d 17 to estrus (postrecruitment). Results demonstrated that all three periods of DHT administration increased ovulation rate and that numbers of embryos in gilts treated from d 13 to estrus were not different compared with controls but increased in gilts treated from d 13 to 16 or d 17 to estrus (Cárdenas et al., 2002).

In another trial, gilts received daily injections of vehicle or 6 µg/kg BW of testosterone or DHT from d 13 to estrus. Tissue from the largest follicles was collected the 1st d of estrus and processed for determination of AR and FSHR mRNA by RT-PCR. Amounts of AR mRNA were not altered by androgen treatment. However, a significant increase (about onefold) in amounts of FSHR mRNA occurred in gilts treated with DHT compared with those that received vehicle (Cárdenas et al., 2002).

These results using DHT demonstrate that stimulation of AR, probably at the ovary, is capable of altering late follicular development, resulting in increased ovulation rate. The effects of DHT were more pronounced relative to those of testosterone, which might be explained by the greater androgenic activity of DHT compared with testosterone in other cell types. This effect of DHT is unique, and based on present knowledge only treatment with FSH, eCG or, in the recent study, DHT has increased ovulation rate at this magnitude in pigs. Although the mechanisms involved in this effect of DHT are probably numerous, the up-regulation of FSHR mRNA might be one of the mechanisms in place. An effect of this kind would increase the ability of follicles to respond to the stimulatory effects of FSH during recruitment or to continue growing and be selected into the ovulatory pool, when otherwise they could become atretic. These effects could also increase the estrogenic activity of growing follicles due to the effects of FSH on aromatase. The relationships just described might be helpful in understanding the control of ovulation rate in pigs and are summarized and integrated with previous knowledge in Figure 1.

### Table 3. Corpora lutea (CL) and d-11 blastocysts in prepubertal gilts induced to ovulate with PG600 and treated daily with 1 mg of testosterone from day of PG600 administration to mating

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of CL</th>
<th>Number of blastocysts</th>
<th>Blastocyst survival, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle (n = 19)</td>
<td>16.1 ± 1.3</td>
<td>11.4 ± 1.3</td>
<td>71.3 ± 6.1a</td>
</tr>
<tr>
<td>Testosterone (n = 19)</td>
<td>16.7 ± 1.6</td>
<td>14.5 ± 1.6</td>
<td>85.6 ± 3.2b</td>
</tr>
</tbody>
</table>

*Means within a column with different superscripts differ (*P < 0.05).*

**Other Factors That Alter Ovulation Rate May Modulate the Actions of Major Regulators of Follicular Growth or Atresia**

It is well recognized that nutritional conditions may affect reproductive performance of domestic mammals.
Figure 1. Follicle-stimulating hormone (FSH) is a major factor that stimulates follicular growth and induces follicular recruitment during the early follicular phase (d 14 to 16 of the estrous cycle) in swine. Recruited follicles continue their phase of rapid growth and most of them (60 to 70%) become atretic before d 17. The number of recruited follicles and incidence of atresia are key determinants of the number of follicles that ovulate. Follicular growth following recruitment might continue to be supported by FSH; however, other factors such as luteinizing hormone (LH), estradiol, and growth factors possibly become increasingly important due to decreasing concentrations of FSH and amounts of FSH receptor (FSHR). Up-regulation of FSHR (dotted line) might be a way to increase responsiveness to FSH, resulting in enhanced follicular growth and decreased atresia.

including swine, and that maintaining normal levels of nutrition is important for optimal ovarian function. Under certain conditions, particularly related to animal age, follicular development becomes responsive to changes in feed intake. For instance, increasing feed intake (flushing) in pubertal gilts increased ovulation rate, but the treatment was less effective in postpubertal gilts (Rhodes et al., 1991). In the review by Prunier and Quesnel (2000), it was concluded that in postpubertal gilts, nutrition restriction consistently decreased ovulation rate when applied during the luteal and follicular phases; however, in most experiments with sows, nutrition restriction did not alter ovulation rate when imposed during lactation or after weaning. Recent experiments partially support these conclusions. For instance, in gilts that were fed a high plane of nutrition during the entire estrous cycle or were restricted during d 1 to 7 or 8 to 15, ovulation rate was not altered but embryonic survival by d 28 was lower in gilts restricted from d 8 to 15 than in the other groups (Almeida et al., 2000). In another experiment, 50% restriction or 125% overfeeding during lactation in primiparous sows did not alter ovulation rate or embryonic survival (Zak et al., 1997, 1998). Likewise, administration of GnRH every 6 h during feed restriction from d 22 to 28 of lactation failed to affect ovulation rate, embryonic survival, or plasma concentrations of progesterone in primiparous sows (Mao et al., 1999).

The effects of nutrition on ovulation rate might be mediated by changes in secretion of growth factors, metabolic hormones, and gonadotropins (Flowers et al., 1989; reviewed by Cox, 1997) and/or their interactions. Components of the IGF system have been identified in ovarian follicles of swine and have been shown to be associated with follicular growth (Mondschein et al., 1991; Yuan et al., 1996, Liu et al., 2000) and partial inhibition of follicular atresia (Guthrie et al., 1998). Transforming growth factor β has also been shown to influence granulosa cells (Gangrade and May, 1990; Chang et al., 1993). Interestingly, although there have been some indications that administration of insulin increases ovulation rate, the results have not been consistent (reviewed by Cox, 1997). Administration of insulin to primiparous sows after weaning tended to in-
crease the number of follicles on d 5 but reduced concentrations of estradiol, IGF-I, and IGF-I mRNA in large follicles (Whitley et al., 1998b). In a recent study (van den Brand et al., 2000a), changes in plasma insulin concentrations were induced by feeding sows a high- or low-energy diet (with fat or starch as energy source) during a 21-d lactation period. Postprandial plasma glucose and insulin were greater and ovulation rate tended to be greater in sows fed the starch diet than in sows fed the fat diet, and there was no association between glucose or insulin and LH concentrations. In a follow-up experiment (van den Brand et al., 2000b) ovulation rate tended to be greater in sows fed the high-energy than in those fed the low-energy diet. These results indicate that increasing dietary energy, and the consequent increase in insulin, did not clearly affect ovulation rate. Similarly, ovulation rate was not altered when insulin was administered for 4 d to primiparous sows beginning the day after weaning (Whitley et al., 1998a) or when feed-restricted primiparous sows received insulin for 5 d during the weaning period (Quesnel and Prunier, 1998). Although altering nutrition has not been able to consistently change ovulation rate in sows, some follicular characteristics were altered, and it is not clear whether these changes could perhaps affect oocyte development.

Differences in ovulation rate between breeds, or lines within breeds, have been demonstrated. Ovulation rate can respond to selection and lines of pigs with greater ovulation rate than others have been developed (Johnson et al., 1999). Selection for FSH concentrations to increase ovulation rate was estimated to be effective and more practical than direct selection on ovulation rate (Cassady et al., 2000). This supports the importance of FSH actions on follicular development and ovulation rate.

Implications

Increasing ovulation rate has the potential to increase swine reproductive efficiency. Identification of important regulators of ovulation rate will help us to design systems for hormonal supplementation, nutritional manipulation, or genetic selection directed to improve the quantity and quality of oocytes released during the ovulatory process. Although our knowledge of ovulation rate in swine is far from complete, experimental results indicate that FSH and ovarian factors that regulate its actions (hormone receptors, growth factors and their receptors, steroid hormones, and enzyme activities) seem to be critical in determining the number of follicles that ovulate. Investigative efforts need to continue to focus on understanding FSH secretion and its action on target cells of the ovarian follicle to better control follicular development and ovulation rate.

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Early embryonic survival in the pig: Can it be improved?1

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ABSTRACT: A major limitation for increasing litter size in swine is embryonic loss that occurs during the 2nd to 3rd wk of gestation. High ovulation rates of modern sows have more than supplied the potential number of embryos necessary to improve litter size. The current challenge is determining how early conceptus development affects the ability to maintain the viability through the remaining 90 d of gestation to maximize farrowing house production. To achieve this, it is necessary to identify and understand the possible causes of embryonic death. Because fertilization rates are generally high in swine, early embryonic loss during the first 20 d of gestation is considered to critically effect potential litter size. There are three periods during which early embryonic loss can occur: 1) pre-elongation development, 2) trophoblastic elongation, and 3) placental attachment. The first two periods are related to time of fertilization and subsequent developmental rate for each individual embryo within the litter. Asynchrony in embryonic development relative to uterine development can result in loss of embryos before d 10 of gestation. Competitive acquisition of adequate uterine space between littermate embryos, essential for blood flow delivery of nutrients needed for survival to term, is established during conceptus elongation on d 12 of gestation. Progressive changes in the uterine microenvironment between d 10 and 16 of gestation play a major role in embryonic survival following trophoblast elongation and placental attachment. In current production systems, there can still be sufficient numbers of embryos present after d 30 of gestation to provide improvement in average litter size at farrowing. However, producers are still faced with the challenge of maximizing fetal survival to term. Therefore, fully understanding the biological controls of follicle ovulation rate, synchrony of ovulation, embryonic developmental rate, uniformity of conceptus elongation, uterine horn capacity, uterine glandular and vascular development, and placental vascularization could provide possible clues to improving embryo quality.

Key Words: Embryo, Pigs, Pregnancy, Uterus

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Introduction

Improving litter size would have a substantial impact on the efficiency of swine production; Tomes and Nelson (1982) and Rothschild (1996) have indicated that overall profitability increased as the number of pigs per sow per year increased. Although it has long been recognized that increasing litter size would increase the efficiency of production, significant improvements have not been achieved. There is potential for average litter sizes of 14 or more pigs if all ovulated ova develop into live pigs, but the average number of pigs born per litter in the United States is only 10.5 (USDA, 2001); approximately 30 to 50% of the ova released from the ovary do not survive through gestation (Pope, 1994). Fertilization of ovulated swine ova is generally greater than 95%; therefore, the loss of potential piglets is predominately the result of early embryonic (d 10 to 30) and fetal (d 31 to 70) deaths. A previous review by Pope (1994) indicated that although ovulation rate establishes potential piglet number, an increase in ovulation rate by itself would not result in a marked improvement in litter size. Ovulation rate responds to direct selection in swine, but the returns for improving litter size have been minimal (Cunningham et al., 1979; Lamberson et al., 1991). Eleven generations of selection for uterine capacity using the unilateral-hysterectomy-ovariectomy (UHOX) model has also failed to significantly improve overall litter size of gilts (Christenson and Leymaster, 2000). However, index selection for ovulation rate and embryonic survival, designed to maximize response in litter size, has been effective in increasing litter size after 14 generations of selection (Johnson et al., 1999). Therefore, future improvements in litter size may be realized if we gain a clearer understanding.

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of the balance of follicular maturation and timing of ovulation, as well as embryonic, uterine, and placental factors associated with conceptus development and survival.

Day 10 to 30 Is a Critical Stage in Conceptus Development

Establishment and maintenance of pregnancy involves a number of closely integrated signals between the ovary, uterus, and conceptus in most mammalian species (Bazer et al., 1982; Roberts et al., 1993). Alterations in the synchronous development of the uterine environment with the growing and differentiating conceptus during early pregnancy can result in a failure to establish pregnancy (Geisert and Yelich, 1997). In monotocous domestic species, failure of the embryo to develop and survive results in termination of the pregnancy, but in the polytocous pig, failure of individual embryo survival within the uterus is a norm that does not necessarily affect continuation of the pregnancy. However, total loss of conceptuses early in development would result in a failure to maintain functional corpora lutea beyond d 15 of gestation (Bazer et al., 1984).

The majority of embryonic mortality usually occurs prior to d 20 to 30 of gestation (Pope, 1994). Data for the gilt, excluding females in which total fertilization failure occurs, have indicated that little embryonic loss takes place before 7 d after the onset of estrus (Polge, 1982). Estimates suggesting that the majority of embryonic mortality occurs between d 10 and 30 of gestation are not surprising given the critical events that occur during this period. The reasons for which early embryonic mortality occurs can be quite extensive and complex (see Dzuik, 1987). Improper timing of conceptus and uterine development, which involves synthesis of nutrients and attachment factors, failure of conceptus signaling, competition of embryos (uterine crowding), and genetic factors all contribute to early conceptus loss. The following review will attempt to bring together the current information available on factors that are proposed to be involved with conceptus development, factors leading to embryonic mortality, and the many approaches taken to improve embryonic survival in the pig.

Conceptus Development

To understand the cause for loss of apparently healthy embryos during the first third of pregnancy, one first needs to understand how pig conceptuses interact with the uterine environment to modulate endometrial function and placental attachment for nutrient exchange from the mother (reviewed by Stroband and Van der Lende, 1990). In the pig, conceptus development and release of estrogen on d 11 to 12 and 15 to 20 of gestation provides the signal to maintain luteal production of progesterone throughout gestation (Geisert et al., 1990). In order to deliver estrogen throughout the majority of the uterine surface, the perimplantation embryos migrate and space themselves throughout both uterine horns between d 8 to 11 of gestation (Pope et al., 1982a; Dzuik, 1985). Following migration within and between the uterine horns, conceptuses undergo a rapid differentiation and expansion of their trophoblastic membranes between d 11 and 12 of gestation (Anderson, 1978; Geisert et al., 1982a,b). Conceptuses change in diameter and morphology as they develop from a 1- to 2-mm sphere to a 3- to 8-mm ovoid and a 9- to 20-mm tubular shape on d 10 to 11 (Geisert et al., 1982b). Once reaching approximately 10 mm in diameter, conceptuses rapidly elongate (2 to 3 h) to a thin, filamentous (> 100 mm) form and initiate attachment to the uterine surface epithelium (Dantzer, 1985; Blair et al., 1991; Burghardt et al., 1997). Rapid expansion of the trophoblast, which is linked to an increase in estrogen synthesis and release, is followed by a continuation of placental growth (Ka et al., 2001), and the trophoblast can exceed 1 m in length by d 16 of gestation (Perry and Rowlands, 1962). Expansion of the conceptus throughout the uterus of the pig is essential, because early pregnancy is not maintained if a substantial portion of each horn is not occupied by conceptuses (see Dzuik, 1987; Geisert et al., 1990). The morphological change in the elongating conceptus is not the result of cellular hyperplasia, but rather of cellular remodeling (Geisert et al., 1982a; Mattson et al., 1990; Pusateri et al., 1990).

Rapid transition in conceptus morphology followed by initiation of placental attachment to the uterine surface represents one of the periods of greatest embryonic loss in the pig (Pope and First, 1985). Conceptus secretion of estrogen and development from a spherical to filamentous morphology occur concurrently with the period of pregnancy establishment in the gilt (see Geisert et al., 1990) and are temporally related to changes in endometrial estrogen (Geisert et al., 1993) and progesterone (Geisert et al., 1994) receptors. The decline in uterine epithelial progesterone receptors on d 12 of pregnancy and the presence of epithelial estrogen receptors in the uterine endometrium during d 10 to 18 relates to the effects of estrogen on the uterine epithelial glycocalyx, conceptus attachment, and alterations in endometrial secretory products (Dantzer, 1985; Blair et al., 1993; Geisert and Yelich, 1997; Ka et al., 2000). Following conceptus elongation and the initiation of estrogen release, trophoblastic attachment to the epithelial lining of the endometrium occurs between d 13 and 18 of gestation (King et al., 1982; Burghardt et al., 1997). The embryo develops from the inner cell mass and the allantoic membrane expands to form the placental vascular network for transport of nutrients and fluid into the allantoic cavity (Bazer et al., 1981; King et al., 1982). Physiological events during early pregnancy are controlled by ovarian progesterone secretion, conceptus estrogen synthesis, and the cellular localization of endometrial steroid receptors (see Geisert and Yelich, 1997; Burghardt et al., 1997).
It is evident that three events, rapid trophoblastic elongation, conceptus estrogen synthesis, and placentome attachment to the uterine epithelial surface, are critical for early porcine embryonic survival. Early trophoblast expansion most likely regulates and limits the final size of each embryo's placental surface area throughout gestation. The synthesis and release of growth factors and cytokines by the developing conceptus during the preimplantation period of embryonic development are considered to play potentially critical roles in cellular growth, differentiation, and remodeling of the embryo and extraembryonic tissues. Both embryonic and endometrial production of various growth factors, as well as interactions between the maternal endometrium and developing conceptus, are essential for providing the synergistic environment for endocrinological and immunological signals for establishment of pregnancy (see review by Geisert and Yelich, 1997; Ka et al., 2000). Developmental events that influence embryonic differentiation and growth are most likely regulated through the programmed expression of growth factors and their specific receptors. Both the conceptuses and endometrium must actively participate in balancing the presence of many proteolytic enzymes and their inhibitors to mediate the epitheliocorial type of placental attachment and growth in the pig (see Geisert and Yelich, 1997).

The previous information provides a base to understand the many temporal interactions that occur between the conceptuses and the uterine environment during establishment of pregnancy and placental attachment. The following sections will now try to provide some insight into the cause(s) of early conceptus loss and attempts to alleviate mortality.

**Litter Embryonic Diversity**

One of the easiest times to observe embryonic developmental diversity within individual litters is to recover embryos from the uterus between d 11 and 12 of pregnancy. Perry and Rowlands (1962) and Anderson (1978) demonstrated the size and morphological differences that can occur within a litter prior to and during the period of trophoblastic elongation. Geisert et al. (1982b) indicated that the conceptuses initiate elongation upon reaching an approximate spherical diameter of 10 mm on d 11 to 12. However, although these conceptuses can elongate, littersmates that are 7 to 8 mm or smaller may not elongate for at least another 4 to 8 h. This transitional lapse in development can obviously create a problem in gaining appropriate uterine territory for survival of the less-developed embryos to term if uterine space is limiting. The classic studies of William Pope clearly illustrated that competition between embryos can occur within the uterus. Through embryo transfer, it was demonstrated that asynchrony in development of healthy porcine conceptuses leads to a competitive advantage of the more developmentally advanced littersmates (Pope et al., 1982b, 1986b). Wilde et al. (1988) also confirmed that less-developed embryos within a litter are just as capable of surviving when not placed in competition with more-developed littersmates.

Possible reasons for the diversity of conceptus development within a litter have been suggested. Considerable information has indicated that the Ped (preimplantation embryo development) gene influences the time to cleavage and thus the rate of early development in mice (Warner et al., 1998; Wu et al., 1999). The Ped gene product is the major histocompatibility complex (MHC) class Ib, Qa-2 protein that is expressed on the cell surface, and it seems to function through a crosslinking mechanism to influence rate of cleavage in early mouse embryo development (McElhinney and Warner, 2000; McElhinney et al., 2000). The lack of inbred lines to discern the presence of a similar relationship in the swine leucocyte antigen (SLA) MHC has limited our knowledge of the Ped gene in pigs. There has been some indication for haplotype differences in ovulation rate and number of embryos in inbred miniature pigs (Conley et al., 1988), but its effect on embryo development has not been established. A search for the human homologue to the Ped gene is currently underway (Warner et al., 1998); if it is identified this may assist in locating the Ped gene in swine.

Although the data for pigs are extremely limited, we must also not overlook the possible paternal contributions to early conceptus development (Dzuik, 1987). The fertilizing sperm can influence variation in fertility; Eid et al. (1994) indicated that the rate and time of entry of the oocyte into the S-phase of the cell cycle is different with sperm from high- vs low-fertility bulls. The transition from maternal to embryonic genome regulation of cell function occurs at the four-cell stage of development in the pig (Prather, 1993). The classic experiments of Surani et al. (1986) first demonstrated the critical function of both the maternal and paternal genome in modulating normal embryonic and placental growth in mice. Genomic imprinting (see John and Surani, 2000) has been demonstrated to have major effects on placentation and fetal survival in mice (Georgiades et al., 2001). Insulin-like growth factor-2 and insulin-like growth factor-2 receptor are two of the genes proposed to be imprinted during early embryonic development (see Moore and Reik, 1996). The presence of insulin-like growth factors in the porcine uterine lumen and insulin-like growth factor receptors in the developing conceptus (Geisert and Yelich, 1997) certainly suggest that if imprinting occurs similarly to that in the mouse, the paternal genome could contribute to the rate of conceptus growth and differentiation in the pig.

Asynchronous oocyte maturation and variation in time of ovulation for a cohort of developing antral follicles have been linked to the diversity of embryos within a litter (Pope et al., 1990; Pope, 1994). Utilizing transrectal ultrasonography to evaluate time of ovulation in pigs, Soede et al. (1992) determined that ovulation of follicles occurred within 1 to 4 h and was not related to embryo diversity. However, a number of stud-
ies have reported that the duration of ovulation can vary from 1 to 9 h between individual animals (see Pope, 1994). Although the majority of follicles ovulate over a short period of time, a few (one to four) ovulate over a more protracted period. Pope et al. (1988) demonstrated that elimination of the late-ovulating follicles on d 1 of the estrous cycle removed the diversity in embryo development at d 11 of gestation. Furthermore, Xie et al. (1990a,b) demonstrated that the later-ovulating follicles become the less-developed embryos in the litter. These later-ovulating oocytes clearly contribute to the pool of embryos that are less-developed on d 11 of gestation and, therefore, maybe the first to be eliminated from the litter when uterine space is limited. Whether it is time of fertilization or genes that control cleavage rate of the embryos, some major and minor differences in embryo development within a litter do exist.

How Can Embryonic Diversity Determine Survival?

It is clear that embryonic diversity can affect survival of littermate embryos (Wilmut et al., 1985; Pope, 1994). When does selection of embryos begin? There are two periods of uterine selectivity during early embryonic development in the pig. The first period of embryonic loss (d 5 to 10) is not related to competition between embryos but to individual embryo asynchrony with its uterine environment. A portion of early selection could be attributed to meiotically immature or genetically abnormal ovulated oocytes that fail to develop at all or at a normal rate in pace with uterine development. Indeed, Hunter (2000) recently reviewed the factors involved in oocyte maturation and follicle heterogeneity, which if suboptimal could compromise subsequent embryo development. Koenig and Stormshak (1993) indicated that immature and chromosomally abnormal ova may represent as many as 30 to 40% of the oocytes ovulated in gilts, and this could account for the lower embryo survival in gilts bred on first vs third estrus. These data suggest that the quality of the oocytes ovulated may play an important role in subsequent development and survival. Asynchronous embryo transfer studies have indicated that porcine embryos become highly sensitive to the changing uterine environment during the blastocyst stage of development. The uterine environment seems to support various stages of development up to d 6 to 7 of gestation. However, Polge (1982) demonstrated that pregnancy rates decrease with transfer of embryos 24 h behind in development with the recipient uterus and decrease to nearly zero if they are 48 h behind. Rapid embryo deterioration within 24 h occurred in d-6 embryos transferred to a d-8 uterine environment (Geisert et al., 1991). Thus, if embryos are greatly behind in development, the uterine environment established through corpus luteum progesterone stimulation can have a negative influence on survival.

The second period of uterine selectivity of embryonic survival occurs with conceptus elongation and estrogen synthesis on d 11 to 12 of pregnancy. Vallet et al. (1998) documented that changes in uterine secretion on d 11 to 12 of pregnancy are related to progressive alterations in protein secretion induced by progesterone rather than being an event completely triggered by the conceptus. Precise timing for the changes in uterine secretion most likely occurs with progesterone-induced down-regulation of uterine epithelial progesterone receptors on d 10 of the estrous cycle and pregnancy (Geisert et al., 1994). Loss of progesterone receptor is specific to the endometrial surface and glandular epithelium, because receptor levels are maintained in the stroma. The elegant study of Cunha et al. (1983) first demonstrated the interactions between developing epithelium and mesenchyme. It is clear that epithelial-mesenchyme interactions are involved with hormonal responsiveness of the uterus (Cooke et al., 1998; Kurita et al., 1998). Many effects of progesterone on uterine epithelial function can be attributed to progesterone activation of stromal progesterone receptors and the stimulated release of progestamedins such as keratinocyte growth factor (KGF) (Ka et al., 2000). A switch from epithelial progesterone regulation to stromal control would not only allow an alteration in uterine protein and enzyme release into the uterine lumen, but also induce changes in epithelial apical glyocalyx permissive to placental attachment (Dantzer, 1985; Burghardt et al., 1997; Geisert and Yelich, 1997). Uterine release of tissue kallikrein, a serine protease, on d 12 of the estrous cycle in the pig may function to alter the uterine epithelial glyocalyx for attachment (Vonnahme et al., 1999) and activate many growth factors for conceptus growth (Geisert et al., 2001). These studies indicate that the uterus dictates the period of rapid conceptus growth and attachment following hatching from the zona pellucida. However, there are also select changes in uterine release of ions, growth factors, and enzymes that are stimulated by the elongating conceptus (Geisert and Yelich, 1997; Ka et al., 2000). Several studies have indicated that estrogen from the tubular and elongating conceptuses can alter the uterine environment, which may influence the ability of lesser-developed littermates to either elongate or obtain sufficient uterine space to survive (Pope et al., 1990; Xie et al., 1990b; Geisert et al., 1991). Estrogen release from elongating conceptuses may induce a uterine secretory environment that is not conducive to later elongation of less-developed littermates, resulting in their degeneration, as has been proposed by Pope et al. (1990). Certainly, the uterine environment is changed with the synthesis of estrogen and elongation of the conceptuses throughout the uterine horn (see Geisert and Yelich, 1997). Although this seems to be a very plausible hypothesis, a degree of caution must be taken because data have indicated that administration of estrogen to pregnant gilts prior to conceptus elongation does not interfere with development on d 11 and 12 of pregnancy (Morgan...
et al., 1987a,b; Geisert et al., 1991; Cardenas et al., 1997). However, administration of estrogen prior to conceptus elongation does act as an endocrine disruptor and affects subsequent survival of embryos after d 16 of pregnancy (Long and Diekman, 1986; Pope et al., 1986b; Morgan et al., 1987a). The loss of embryos seems to be an effect of estrogen on the uterine environment and epithelial glyocalyx rather than a direct effect on the conceptus (Blair et al., 1991); estrogen treatment on d 12 of pregnancy does not interfere with embryo survival (Geisert et al., 1991).

Although uniformity in embryonic development is an attractive model, it does not seem to be the sole basis for increased prolificacy of the Chinese Meishan pig (Wilmut et al., 1992; Ford, 1997). The advantage of the Meishan embryos in litter size seems to be achieved through modulating placental length that can be generated following the initial elongation of the conceptuses coupled with an increase in placental vascularity (see Ford, 1997; Biensen et al., 1999). Meishan embryos have similar numbers of inner cell mass cells but contain fewer trophectoderm cells and produce smaller amounts of estrogen compared to contemporary Yorkshire embryos (Anderson et al., 1993; Rivera et al., 1996; Kaminski et al., 1997). These two key factors would effectively restrict the surface area occupied by each conceptus following expansion of the trophoblast and reduce the effects of estrogen on neighboring littersates. The high concentrations of estrogen from the developing Yorkshire gilts is not necessary to support development; a 57% reduction in conceptus estrogen synthesis with aromatase inhibitors did not affect early conceptus development (O'Neill et al., 1991). So, does the lower estrogen synthesis by the developing conceptuses lead to greater survival? Although exogenous estrogen seems to have an obvious effect on embryo survival, there is a question as to whether even the higher amounts of estrogen produced by Yorkshire conceptuses can have more than a local effect on the uterine microenvironment that it contacts.

The inability of the sow to maintain a unilateral pregnancy early in pregnancy (Anderson, 1966) and the need for at least two embryos in each uterine horn to establish pregnancy in the pig (Polge et al., 1966) suggests that estrogen does not diffuse throughout the uterine horn easily. The presence of sulphotransferase in the porcine endometrium effectively conjugates and inactivates estrogens moving through the endometrium (Pack and Brooks, 1974). Thus, although effects of estrogen cannot be discounted, the Meishan embryos’ slowed rate of development (Youngs et al., 1993) and uterine inhibitory effect on embryonic development (Youngs et al., 1994) have provided possible clues for survival through restriction of conceptus elongation and development of a more vascular placenta, as proposed by Ford (1997). Determination of how the decrease in trophectoderm cell number is regulated either in the conceptus or through uterine secretion needs to be evaluated. On d 10 to 12 of gestation, the pig uterus is a rich source for growth factors such as insulin-like growth factor (IGF)-I and -II, epidermal growth factor, leukemia inhibitory factor, KGF, and connective tissue growth factor (see Geisert and Yelich, 1997; Ball et al., 1998; Ka et al., 2000), most of for which their ligand receptor is expressed in the developing pig conceptus (Geisert and Yelich, 1997; Ka et al., 2001). The reported decrease in uterine protein secretion in Meishan compared to commercial pigs (Youngs et al., 1994; Vallet et al., 1998) would support a uterine role in modulating conceptus growth. However, the reciprocal conceptus transfer study of Youngs et al. (1994) indicated that, in addition to the uterine environment, genotype of the conceptus is also involved with preimplantation growth, which links back to the previous conceptus Ped gene discussion. Increasing our understanding of the factors modulating conceptus trophoblast elongation and placental angiogenesis following placental attachment to the uterine surface will become increasingly important for future attempts to improve competition among embryos within the pig uterus.

Progress has been made in determining changes in gene expression during the process of conceptus elongation (Yelich et al., 1997a,b; Wilson et al., 2000); however, the key(s) to triggering the process or understanding the pathway is far from established at this time. Recent studies have suggested the presence of a positive feedback loop for conceptus growth (Green et al., 1995); the conceptus seems to stimulate endometrial release of IGF and KGF into the uterine lumen during the developmental period preceding conceptus elongation (Geisert et al., 2001; Ka et al., 2001). Treatment of gilts with estrogen near the time of trophoblast elongation increases uterine protein and can advance the initiation of the cellular remodeling process (Cardenas et al., 1997). Ka et al. (2001) have demonstrated that conceptus estrogen release during pregnancy increases uterine epithelial KGF expression, which in turn stimulates proliferation and differentiation of conceptus trophoderm. The known role of KGF in stimulating epithelial proliferation, migration, and cellular differentiation (Rubin et al., 1995) makes the interactions between IGF, estrogen, and KGF an attractive model for conceptus growth and remodeling. Interrelationships between these factors can explain conceptus growth regulation by the uterus and the conceptus itself, as previously discussed. These data would also lead to the suggestion that the more developmentally advanced, estrogenic conceptuses gain an even more competitive advantage in enhancing trophoderm growth.

Is Embryonic Uniformity the Model for Improving Litter Size?

Given all the information on conceptus growth and development, one must ask whether conceptus uniformity is an important factor contributing to litter size in commercial swine herds. Theoretically, in the perfect pregnancy, embryo uniformity would be the most desir-
able situation for the pig. This would require that the number of ova
culated were at the same maturity and viability, fertilized synchronously, and had the same
genetic potential for rate of development, and equidistant uterine spacing occurred. Asynchrony with the
uterine environment would not be a problem because the
time of ovulation regulates when the initial increase
in luteal progesterone secretion occurs to stimulate the
uterine secretory program for conceptus development.
In this paradigm, ovulation rate should not exceed uter-
ine capacity because this could in theory lead to uterine
crowding and loss of the entire litter if no mechanism
for having a competitive advantage between embryos
existed. It is difficult enough to control any one of the
aforementioned factors, which explains our inability to
rapidly improve litter size. With this thought in mind,
it would be remiss not to acknowledge the thoughtful
and insightful paper Dzuik (1987) published 14 yr ago
addressing the same question. Dzuik (1987) champi-
oned that asynchrony in conceptus development is actu-
ally a survival advantage in the pig and that we may
pay too much attention to embryonic loss rather than
focusing attention on why some embryos survive. A
limited amount and degree of nonuniformity between
groups of developing porcine embryos is actually an
attractive model. When ovulation rate does not exceed uter-
ine capacity, the majority of embryos that are devel-
velopmentally competent to survive through d 8 will elon-
gate despite some variation in development rate. Even
if these embryos are somewhat variable in develop-
ment, they should have less difficulty in acquiring suf-
ficient uterine space for placental development. The
number of conceptuses present on d 12, not conceptus
uniformity, directly affects litter size in this female. If
ovulation rate exceeds uterine capacity in a female, then there will be a number of possible scenarios for the
potential outcome in litter size. There could be greater
early (before d 8) loss of embryos through ovulation of
immature and(or) defective oocytes and late-ovulating
follicles that places a number of developing embryos in
jeopardy of being asynchronous with the uterine envi-
ronment. Loss of these early embryos could normalize the
space available for the surviving conceptuses depend-
ing on the number developing to d 12 and set in
motion the competition related to rate of growth and
elongation. This female would be limited by both uter-
ine capacity and the number of conceptuses initiating
elongation, which makes for a variable range in possible
outcomes with litter size. For example, if 18 viable emb-
ryos were present on d 12 and they all elongated at the
same time, crowding would cause fetal survival
problems after d 30 of gestation, depending on the indi-
vidual placental surface area providing nutrients for
each fetus. If 10 to 12 embryos elongated first, they
would have space available to develop but could restrict
lesser-developed littermates from either elongating or
having sufficient placental space to develop to term. If
a ligation is placed 15 cm from the tip of the uterine
horns following fertilization, the restricted conceptuses
reach the tubular stage of development but become de-
formed and do not elongate (J. P. Harney and F. W.
Bazer, personnel communication). Thus, during the
process of trophoblast elongation, some conceptuses
that are lodged between two elongated embryos most
likely will not undergo elongation and subsequently
become deformed in development. Wu et al. (1988) indi-
cated that an embryo requires more than 20 cm of uter-
ine horn length to survive after the 7th wk of gestation.
Therefore, although there will be viable embryos that
develop to d 30 of gestation, they may not have sufficient
placental surface area to survive to term.
So how are consistent large litter sizes achieved? Be-
cause some embryonic loss is inevitable, the ovulation
rate needs to be high enough to overcome the loss of
early defective embryos but provide a developing cohort of
15 to 16 embryos that can elongate relatively synchro-
nously. Total synchrony of ovulation is not important
as long as cohorts of 15 to 16 quality oocytes are present
at fertilization (see Pope et al., 1990). The majority of
the three to four lesser-developed embryos would either
be eliminated (fail to elongate) or, depending on individ-
ual positioning of embryos within the horn, fill in space
if available. Positioning of conceptuses in relation to
one another within the uterus is still an important issue
to survival (Dzuik, 1987). Embryo survival in this fe-
male would depend on the ovulation rate, number and
quality of embryos developing in the uniform cohort,
and the uterine capacity of the dam, which leads back
to the traits of Meishan embryos. What are the traits
of the embryos from more contemporary sows developed
with the index selection for ovulation rate and embry-
onic survival (Johnson et al., 1999) that have increased
litter size? Is there balance in ovulation of a cohort of
quality embryos and/or increase in placental effi-
ciency? Although a larger, more complete study is
needed, Wilson et al. (1999) suggested that selection
based on placental size and efficiency could improve
litter size at term. If placental size and vascularity
are the important modulators of improved efficiency,
research is needed to determine how to effectively de-
tect sows with increased placental efficiency or deter-
mine methods to regulate conceptus and uterine devel-
opment in pigs.

Attempts to Improve Embryonic Survival

The multitude of studies attempting to improve litter
size through selective time of breeding, regulation of
ovulation, feed intake, steroid therapy, and nutritional
supplementation have been previously reviewed (Chris-
tenson, 1986; Dzuik, 1987; Ashworth, 1994; Pope, 1994;
Foxcroft, 1997). For the most part, studies evaluating
nutritional supplementation have suffered from the
lack of sufficient animal numbers and have failed to
either clearly demonstrate improved fertility or have
had no effect (Foxcroft, 1997). Certainly the presence
and important role of uterine factors such as riboflavin,
It should seem obvious that if we want more uterine space, we need to select for pigs with longer horns. Uterine length seems to be a limiting factor to litter size when ovulation rate increases (Wu et al., 1987). However, although variation in uterine horn length exists, a difference between commercial breeds and Meishan pigs is not apparent (see Ford, 1997). Gama and Johnson (1993) also indicated that there was no significant change in uterine dimensions of cyclic gilts following eight generations of selection for litter size. If the data do not indicate variation in length of the uterine horns as a major factor in embryo survival, what uterine parameter(s) would affect placental surface area necessary for embryo survival? The level of endometrial folding, number of uterine glands, and uterine capillary bed density within the endometrium are likely candidates that cannot be easily evaluated in the live animal. Porcine endometrium is not a flat, smooth surface but contains many macroscopic folds that branch off into numerous primary and secondary ridges to increase surface for the placenta (Bjorkman et al., 1981; Danzter, 1984, 1985; Keys and King, 1990). Density of endometrial folding cannot be accounted for by only measuring horn length because this folding, along with uterine growth, provides for the expansion of the uterus after d 18 of gestation (Wu et al., 1988). A key component for uterine survival in all species, especially true for epitheliochorial-type placentation in the pig, is nutrient passage to the placenta established through capillary blood flow within the endometrium (Ford, 1995). Alteration of blood flow to the uterus is evident at the time of conceptus elongation and during expansion of the allantois to fill the uterine horn between d 15 and 30 of gestation (Ford, 1995). The conceptus induces an inflammatory response to enhance nutrient flow into the uterine lumen (Keys and King, 1988, 1995). The presence of kinin β2 receptors in the endometrium and the conceptus-induced release of kinins (Allen et al., 2002), potent regulators of blood pressure, indicates the active participation of the conceptus in modulating maternal blood flow to the porcine placenta. Although from a different species and type of placentation, vascular casts of the uterus and maternal cotyledons (Figure 1) in Florida native ewes compared to the more prolific Blackfaced ewes (two to three lambs) illustrates the alteration in vascular density that can be developed to support multiple fetuses in the prolific breed of sheep (F. W. Bazer, F. F. Bartol, and D. H. Barron, unpublished data). The vascular networks of the maternal uterus and fetal placenta in the pig are complementary to one another and become more complex as gestation proceeds (Lesier and Danzter, 1988). Many angiogenic factors are involved with regulating endometrial and placental vascular growth (see Reynolds and Redmer, 1995). However, we currently do not have a clear understanding of the regulation of angiogenesis during pregnancy in the pig.

The superficial attachment and placentation of the pig dictates the critical need for endometrial generation

uterofererin, retinol-binding protein, and folate-binding protein (Malathy et al., 1990; Vallet et al., 1996, 1999) fueled the numerous nutritional supplementation trials attempting to increase embryonic survival (see Dzuik, 1987; Ashworth, 1994; Foxcroft, 1997). Given that the uterine environment of pigs on a nutritionally balanced diet is not significantly altered by additional nutrients or vitamins and that it is difficult to affect conceptus developmental rate, it is not surprising that studies have failed to demonstrate consistent, if any, beneficial effects. Indeed, embryo survival is not significantly affected in gilts subjected to inanition for the first 40 d of gestation (Anderson, 1975). Problems in growth, survival, and maintenance of pregnancy occur if the period of inanition is increased to greater than 40 d, but pregnancy is maintained if the females are supplemented with daily treatments of progesterone and estrogen.

Improvements in embryo survival have been noted when gilts are treated with retinyl-palmitate prior to the time of ovulation (Coffey and Britt, 1993; Whaley et al., 1997). An increase in embryo survival was attributed to advancing resumption of meiosis and improving embryo quality rather than to any direct effect through altering uterine function (Whaley et al., 2000). Feeding above maintenance requirement before mating also improved blastocyst cell numbers and reduced size variability within litters (Ashworth et al., 1999). Cardenas et al. (1997) indicated that treatment of gilts with testosterone from d 13 of the estrous cycle until the following estrus improved blastocyst survival, possibly through improved oocyte quality. These data are consistent with the previous report of Hunter et al. (1993), who indicated that oocytes in Meishan gilts are more mature and uniform than Large-White gilts. Thus, information points to the importance of increasing the number of developmentally mature oocytes before we even progress to the uterine environmental modulation of conceptus development.

So what can be done to improve the interaction between conceptus and uterine environment? Obviously, understanding how placental length and vascularity are modulated will help direct us to studies that may alter early development of the conceptus. Development of differential-display PCR, PCR-based cDNA subtraction, and the forthcoming production of microarrays will accelerate identification of genes involved with conceptus and uterine development. Information concerning genes involved with conceptus and uterine development may improve our search for and use of genetic markers for reproductive efficiency as the pig genome map is completed (Rothschild et al., 1997; Linville et al., 2001). Technologies in transgenesis and cloning are attractive methods to develop increased reproductive efficiency in swine but have been rather difficult to develop, and the low heritability of litter size will still not provide the rapid increase that most might expect (Haley et al., 1988).
Early embryonic survival in the pig

Figure 1. Vascular casts of the maternal cotyledons from a single-lamb-bearing Florida native ewe (B, C) and a prolific, multilamb-bearing Blackface ewe (A, D).

of uterine secretions. The importance of glandular support for the developing porcine conceptus has been made even more evident by the failure of early ovine conceptuses to elongate and attach in uterine gland knockout ewes (Gray et al., 2001a,b). Prolonged neonatal exposure of ewes to progesterone ablates uterine gland morphogenesis and absence of glands in the adult (Bartol et al., 1999). Thus, it is clear that neonatal exposure to steroids or other endocrine disruptors can alter uterine function in the adult. In the pig, uterine glands are absent at birth and uterine adenogenesis in the pig occurs from birth to 21 d postnatally (Bartol et al., 1993; Tarleton et al., 1999). Tarleton et al. (1999) demonstrated that estrogen stimulates but treatment with the estrogen antagonist ICI 182,780 inhibits adenogenesis in the neonatal uterus. Therefore, it may be possible to alter neonatal uterine glandular morphogenesis and development through steroidal and(or) lactogenic hormone administration. Spencer et al. (1999) proposed that sequential exposure of the endometrium to steroids and lactogenic and somatogenic hormones is involved in the endometrial gland remodeling and secretory function in the pregnant ewe. Uterine infusion of growth hormone and placental lactogen increases uterine glandular development and secretory function in steroid-treated, ovariectomized ewes. It is also possible to treat neonatal lambs with prolactin and increase the number of uterine glands in the adult (T. E. Spencer, personal communication). The presence of prolactin receptors in the porcine endometrium (Young et al., 1990) suggests that it may be possible to influence the number of uterine glands in the pig. With the known effects of estrogen and prolactin on uterine and glandular development in females, uterine alterations and litter capacity in pigs need to be evaluated following neonatal treatment with estrogen and prolactin.

Over the past 40 yr of probing the complexity of embryonic development and loss, we have developed more answers for why embryonic loss occurs but provided little in the solution for rapidly improving litter size in the pig. Improvements are not likely to result from any nutritional or steroid therapies aimed at changing
uterine function during gestation but could result through better control of ovulation and oocyte quality or changes in the uterine vascular and secretory capacity, as we should have already learned from the mammary gland. Can we modify uterine and conceptus function in the future? The rapid improvements in technology will certainly allow us to gain more understanding of conceptus and uterine factors involved with development. Only time will tell if we can use the information to develop methods to modulate average uterine capacity beyond the levels of production today.

Implications

The numerous biological factors involved with regulating litter size in pigs have slowed progress for rapidly increasing litter size. Our knowledge of the factors regulating conceptus and uterine development and function has increased but is far from complete. The developing technologies to investigate gene and protein expression will continue to assist in unraveling the mysteries of early embryonic survival in the pig. However, improvements in litter size will only occur when we can use the information to increase placental efficiency and(or) uterine secretory function. It is clear that the uterus in the pig can be modified to alter glandular development. Therefore, a combination of increased endometrial glandular density and placental vascularity may move litter size beyond the current plateau currently achieved in the swine industry.

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Uterine capacity in the pig reflects a combination of uterine environment and conceptus genotype effects

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ABSTRACT: Prenatal losses in U.S. pig breeds range from 30 to 50%, of which greater than 75% occurs before d 30 of gestation and is thought to result from littermate asynchrony. Numbers of embryos can be experimentally increased to d 30 using superovulation (excess ova shed) and superinduction (transfer of embryos to an already pregnant uterus); however, these females farrow the same number of pigs as untreated controls. These data demonstrate that between d 30 and parturition there are significant additional periods of conceptus loss, which has led to the conclusion that uterine capacity (i.e., the number of conceptuses a sow uterus can accommodate) is the major limitation to litter size in the pig. The special importance of uterine capacity in the pig may result from the noninvasive epitheliochorial type of placentation in this species, making the surface area of attachment between the placenta and endometrium a limiting factor. In devising selection schemes for this trait, one could logically conclude the selection for either longer uterine horns or for a reduced conceptus size should potentially increase litter size in the pig. Researchers have evaluated the impact of differences in prepubertal uterine horn length on subsequent uterine capacity using a unilateral hysterectomy-ovariectomy model but have had modest and variable success in increasing litter size at farrowing. In contrast, results from our laboratory suggest that placental size is moderately heritable and results in consistent increases in litter size of two to three pigs in the Yorkshire breed with little impact on pig birth weight or neonatal viability. This selection of pigs for smaller and relatively more efficient placentae (i.e., the number of grams of fetus that can be supported by 1 g of placenta) seems to provide a useful method for increasing litter size in the pig. A careful evaluation of the physiologic and genetic differences of conceptuses with differing placental efficiencies is necessary if we are to determine specific factors affecting litter size in the pig.

Key Words: Litter Size, Placenta

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Introduction

Uterine capacity is defined as the number of conceptuses that the pig uterus can successfully carry to term. Data suggest that limitations of uterine capacity are set early in gestation, possibly around the time of conceptus elongation on d 11 through 13 (Figure 1). It is during this time that the conceptus begins to produce and secrete significant amounts of estrogen into the uterine lumen, which results in endometrial secretion of a myriad of growth factors such as IGF-I, which could affect subsequent uterine as well as conceptus growth and development (Wilson and Ford, 1997). At this time, littermate conceptuses space evenly throughout the uterus (Dhindsa et al., 1967; Dziuk, 1968, 1985) and expand asynchronously from 1-cm spherical blastocysts to filamentous forms of variable length (Geisert et al., 1982), in association with a 20 to 30% conceptus loss in U.S. and European pig breeds (Dziuk, 1968, 1987; Pope, 1994). Uterine capacity begins to measurably affect litter size after d 30 of gestation in the pig (Fenton et al., 1972; Pope et al., '97; Huang et al., 1987), when a real competition for limited uterine space and nutrients by littermates becomes increasingly critical.

Uterine capacity can be defined in terms of the relative surface area of placental endometrial attachment required to support the nutrient requirements of an individual fetus throughout gestation. Recent evidence suggests that placental efficiency (PE; fetal wt/...
Figure 1. A time line demonstrating the time periods of conceptus loss in the pig.

placental wt) is an individual conceptus trait and is highly variable within a litter (Wilson et al., 1999). Impacts of selection for uterine length (Christenson et al., 1990), ovulation rate (Johnson et al., 1999), and placental efficiency (Wilson et al., 1999) have shown variable success in increasing litter size. In this paper, we will attempt to summarize the various approaches used to increase uterine capacity, both from the maternal and fetal sides, and the impacts they have had on litter size.

Genetic Selection

Johnson and co-workers at the University of Nebraska have used genetic selection in an attempt to increase litter size in the pig, but with limited success. Johnson et al. (1999) conducted 11 generations of selection (from a Large White and Landrace genetic base) for increased index of ovulation rate followed by three generations of selection for litter size. By the 11th generation of selection they verified a selection advantage of 7.4 ovsualations and 3.3 fetuses on d 50 but only realized an advantage of 1.1 live pigs at farrowing. The response to selection at generation 14 was an increase of 1.4 live pigs/litter; however, the number of stillborn pigs increased and pig birth weights decreased. As a result, the number of pigs weaned actually declined in the selected line compared to the control line. The authors speculated that as ovulation rate increased in the selection line uterine capacity increasingly became the limiting factor in prenatal survival after d 50 of gestation. The authors went on to speculate that selection on component traits of litter size would have been more effective if in addition to ovulation rate a measure of uterine capacity had also been included, as previously suggested by Bennett and Leymaster (1989).

Cassady et al. (2001) attempted to identify chromosomal regions harboring QTL for reproductive traits in pigs using a reference population created by Rathje et al. (1997) at the University of Nebraska. Grandparents of this population had been selected for ovulation rate and embryonic survival. While reporting evidence for QTL for a number of reproductive traits (including ovulation rate, age at puberty, number of teats, and number of fully formed pigs) he concluded that few, if any, major genes for reproductive traits were segregating in the population. He went on to conclude that little evidence exists to encourage marker-assisted selection at the present time.

This conclusion is consistent with results recently reported by Linville et al. (2001), who used the candidate gene approach to determine whether specific loci explain the observed differences in litter size. They found no associations between six polymorphic markers in two lines of pigs, again originating from the selected and control lines described by Johnson et al. (1999). In fact, for several of these markers, the estimated effect of purported favorable alleles was negative. They reported that these selection lines exceeded the control line by 20 to 50% in both ovulation rate and litter size. The authors went on to explain the rationale for the selection of the six specific markers chosen, on an individual basis, but, as Cassady et al. (2001) concluded for this same population, selection for ovulation rate, embryonic survival, and litter size seems to have acted on multiple loci, each of which exerts only a modest effect (i.e., these are polygenic traits). Although there are many possible reasons for this lack of association reported by Linville et al. (2001) between selected markers and litter size, a failure to understand what specific physiologic differences were selected for in this population suggests that little progress should be expected using only this approach.

In the next section, we will discuss the findings of several researchers who are attempting to understand the necessary interactions between the conceptus and the uterus that promote optimal conceptus survival through alteration of uterine capacity.

Conceptus-Uterine Interaction

Evidence suggesting that uterine capacity is limiting to litter size after d 30 of gestation is based largely on studies using superovulation (excess number of ova shed), superinduction (transfer of embryos to an already pregnant uterus), and unilateral hyster-
ectomy-ovariectomy (UHO) models. Superovulation and superinduction increase the number of conceptuses surviving to d 30 (percentage of embryo survival is similar); however, these females do not farrow litters larger than controls (Fenton et al., 1972; Monk and Erb, 1974; Webel and Dziki, 1974). Females subjected to UHO ovulate normal numbers of ova, but only farrow approximately one-half the number of pigs of intact controls (Christenson et al., 1987). The UHO model has been used to estimate uterine capacity per uterine horn in the absence of any possible limitation in ovulation rate (Christenson et al., 1987). In these studies, it was concluded that UHO gilts that had the largest litters (> 1/2 of control gilts) at farrowing may provide the most optimal uterine environment (i.e., increased uterine capacity. Following this rationale, Gama and Johnson (1993) used UHO in lines of gilts at the University of Nebraska that had been selected for differences in ovulation rate, embryo survival to d 50, and litter size. Pregnant gilts were slaughtered on d 93 through 100 of gestation and ovulation rate, number of fully formed pigs, and number of mummified pigs were determined. As previously reported by Christenson et al. (1987), uterine capacity was estimated as twice the number of fully formed fetuses in the remaining horn. When this was accomplished, the estimated difference between individuals selected for increased litter size and the randomly selected controls was $0.66 \pm 1.28$ pig. Although this increase was not significant, the authors suggested that these data indicate that additive genetic variance for uterine capacity does exist in swine.

In the pig, uterine capacity may specifically relate to epitheliochorial and diffuse placentation, whereby the chorionic epithelium is in direct contact with the uterine luminal epithelium (Grosser, 1933; Benirchke, 1983; MacDonald and Bosma, 1985). This placental type, which is appositional rather than invasive and relies largely on simple diffusion, requires an adequate surface area for nutrient exchange from the maternal to fetal blood streams. Between d 20 and 30 of gestation, there is a rapid increase in placental length that slows asymptotically, reaching a plateau around d 70 before increasing again after d 100 (Pomeroy, 1960; Knight et al., 1977). From d 30 to 40, the placenta progresses from a very simply organized structure, consisting of a thin membrane, hyaluronic acid gel, and a rapidly proliferating system of blood vessels to a more complex structure (Perry, 1981; Bazer, 1989). Also between d 30 and 35 of gestation, the yolk sac rapidly regresses, and the responsibility for the absorption of oxygen and nutrients and the removal of carbon dioxide and waste is shifted to the highly vascularized chorioallantoic membrane (Björkman, 1973; Tiedemann and Minuth, 1980; Dantzer, 1985).

Placental capillaries ramify throughout the entire surface of the placenta in close contact with the chorionic epithelium, except for the ends, which are nonvascular and are referred to as necrotic tips (Patten, 1948). From d 35 to 70 of gestation, the surface area of the chorioallantoic membrane increases rapidly (Knight et al., 1977). This results from the prolific folding of the placental surface into permanent folds in the endometrium, followed by the development of an interlocking network of placental and endometrial microvilli, which function to further expand the placental:endometrial surface area of exchange (Friess et al., 1980; Björkman and Dantzer, 1987). From d 70 through approximately d 90 there is little noticeable change in placental surface area (Knight et al., 1977), but from d 90 of gestation through term as much as a doubling of placental surface area is seen (Wigmore and Strickland, 1985; Biensen et al., 1998).

As previously stated, the limitations of uterine capacity begin to affect conceptus survival after d 30 and are associated on d 35 to 40 with a marked and abrupt increase in the surface area of placental exchange due to the development of microscopic interdigitations between the placenta and uterine luminal surface referred to as primary rugae (Björkman and Dantzer, 1987; Leiser and Dantzer, 1988; Leiser and Dantzer, 1994). During the last third of gestation, when another period of observed fetal loss occurs (Christenson et al., 1987; Johnson et al., 1999), the functional surface area for nutrient and waste product exchange is again accelerated in association with rapid fetal growth by the development of secondary rugae, an additional tier of interdigitation along the primary rugae (Friess et al., 1980; Björkman and Dantzer, 1987).

In addition to the progressive increases in the functional placental:endometrial surface area allowing fetal-maternal exchange, the vascularity of placental and adjacent endometrial tissues also changes with the advancement of gestation, in conjunction with a progressive decrease in the diffusion distance between the placental and fetal capillaries. Vonnahme et al. (2001) demonstrated that in the white composite breeds, density of placental blood vessels per unit surface area tissue (vascular density) actually decreased during the first rapid expansion of the placenta from d 25 through 44, then increased progressively from d 44 through 90 before reaching a plateau until term (Figure 2). Of interest is the fact that vascular density did not increase during either the early or late periods of increased fetal death. Further, Vallet et al. (1996) and Pearson et al. (1998) have suggested that fetal erythropoiesis is negatively affected by intrauterine crowding and may play a role in fetal loss. Vonnahme et al. (2001) also reported that placental vascular endothelial growth factor (VEGF), a potent angiogenic and permeability-enhancing factor, followed the same pattern as that of placental vascular density throughout gestation and was positively correlated with both placental ($r = 0.34; P < 0.05$) and adjacent endometrial ($r = 0.34; P < 0.05$) vascular density changes of individual placetae (see Vonnahme et al., 2001 for technical details). Increased permeability at the placental:endometrial interface with advancing gestation was sug-
Figure 2. (a) Changes in vascular endothelial growth factor mRNA and (b) the relative number of blood vessels per unit area of placental tissue throughout gestation in the pig. Means and SEM with different superscripts within a measurement differ ($P < 0.05$) (reproduced with permission from Vonnahme et al., 2001).

Given by Freiss et al. (1980, 1982), who demonstrated that the functional maternal:fetal intercapillary distance decreased from 15 to 20 μm to approximately 2 μm with the advancement of gestation.

In the pig, placental transfer of freely diffusible nutrients seems to rely on a vascular anatomy that is either concurrent or possibly crosscurrent (Friess et al., 1982). Transported solutes such as glucose, amino acids, ions such as sodium, potassium, calcium, and protons require transporter protein-mediated transfer (Sibley et al., 1997). In the pig, this transporter-mediated transfer seems to be concentrated in the troughs of the chorionic folds, which are adjacent to the ridges of endometrial folds, and is generally not tied directly to the rate of blood flow (Friess et al., 1980; Poston, 1997; Sibley et al., 1997). In addition to the transfer that occurs across the uterine luminal epithelial-chorionic epithelial interface, there is also transfer of large macromolecules such as uteroferrin, which are produced by the uterine glands and then absorbed intact by the placental areolae (Perry, 1981; Freiss et al., 1982; Roberts et al., 1986; Leiser and Dantzer, 1994). All of these transfer mechanisms are, however, dependent on an adequate surface area of functional contact between the placenta and uterine wall if the fetus is to exhibit optimal growth and development.

**Placental Efficiency**

To avoid the confounding effects of differences in ovulation rate and uterine length, both of which have been reported to have impacts on litter size, we chose to compare and contrast the reproductive physiology of the prolific Chinese Meishan gilt (two to five postpubertal estrous cycles) with Yorkshire gilts of similar reproductive age. Although Meishan and Yorkshire gilts at this reproductive age exhibit similar ovulation rates (16.5 ± 5 and 16.3 ± 0.4, respectively) and uterine lengths, the litter size of Meishan gilts was markedly greater (12.3 ± 0.4 vs 8.9 ± 0.4 live pigs/litter; Ford, 1997). Further, the Meishan and Yorkshire gilts in our herds ovulated at the same time after the initiation of estrous activity, as evidenced by the recovery of embryos at similar stages 48 to 54 h after estrus onset (one to eight-cell embryos). From d 5 to 12 of gestation, however, Meishan conceptuses are smaller than Yorkshire conceptuses due to a selective reduction in the number of trophoderm cells, the cell type containing the rate-limiting enzyme for conceptus estrogen synthesis (Youngs et al., 1993; Rivera et al., 1996; Wilson and Ford, 1997). Further, we observed that although both Meishan and Yorkshire conceptuses initiated estrogen secretion and elongated on the same days of gestation (d 11 to 12), Meishan conceptuses secreted less estrogen into uterine luminal fluid and were smaller (Anderson et al., 1993). The decreased uterine luminal estrogen concentrations in Meishan vs Yorkshire females on d 11 to 12 was associated with reduced levels of total protein, calcium, oxytocin, and IGF-I in the same fluid (Ford and Youngs, 1993; Wilson and Ford, 1997; Vallet et al., 1998). This is consistent with the role of IGF-I in increasing trophoderm mitotic rate in pig conceptuses (Lewis et al., 1992). As a result, Meishan filamentous conceptuses were shorter and contained fewer cells than Yorkshire conceptuses on d 14 (Wilson et al., 1995). Further, Meishan conceptuses exhibit markedly smaller placentae on d 30, 50, 70, 90, and 110 and at term (Hunter et al., 1994; Biensen et al., 1998; Wilson et al., 1998) than do conceptuses of a variety of less-prolific pig breeds. This reduced placental size of the Meishan regardless of the number of conceptuses present seems to be a direct result of a reduced preimplantation uterine exposure to estrogen. Injections of estrogen into pregnant Meishan females around the time of conceptus elongation was found to markedly increase placental size at term (Wilson and Ford, 2000).

The real breakthrough in our understanding of how the Meishan fetus survived on such a tiny placenta came when both Meishan and Yorkshire embryos were placed in the uterus of a Yorkshire recipient female on d 2 and allowed to compete for survival (Wilson et
al., 1998). At farrowing, the umbilical cord of each pig was double-ligated and tagged so that all pigs could be matched with their placenta when they were expelled en masse after all pigs were farrowed. To our surprise, Meishan (n = 7) and Yorkshire (n = 7) pigs exhibited similar birth weights compared to those farrowed normally by straightbred Meishan females, which averaged 800 to 900 g (Figure 3). Further, all Meishan pigs were gestated on very small and highly vascular placenta, and all their Yorkshire littermates were gestated on much larger and less-vascular placenta (209 ± 17 and 472 ± 46 g, respectively). At this point we began employing PE as describing the grams of fetus that could be supported by a gram of placenta, as previously used by others (Molton et al., 1978; Kurz et al., 1999). Placental efficiency of Meishan pigs in the litter averaged 6.25, and the PE of their Yorkshire littermates averaged 3.36. These PE differences result from a 56% difference in placental weights and a 17% difference in pig weight. These data confirm that the PE is an individual conceptus trait independent of uterine environmental control. In subsequent studies, we determined that changes in PE were a result of changes in placental weight, not pig weight. Further, there was much less variation in the weights and vascularity of the Meishan placenta within a litter than exhibited by their littermate Yorkshire placenta (S. P. Ford, unpublished observations). Thus, we speculated that during the domestication of the Meishan breed, which encompassed as many as 7,000 yr (Yun, 1988), an intense selection for litter size may have resulted in an indirect selection for small, highly vascular, and relatively uniform placenta. If this was indeed the case, then we felt that there might be significant variation in this trait in our Yorkshire population.

In a subsequent study (Wilson et al., 1999) using our Yorkshire population, pigs were matched to their placenta as described above, and we found that there was significant (threelfold) variation in placental weights across females, with as much as twofold differences exhibited within a single litter. From these litters we then selected boars and gilts with birth weights ≥ 1,250 g that had higher than average PE and those that had lower than average PE. Although pig birth weights of the high-PE group were similar to those of the low-PE group, their placentae were markedly smaller and more vascular. We then allowed these pigs to reach puberty and at the second estrus we bred gilts of each group (high PE or low PE) to boars of the same group and collected farrowing data from parities 1 and 2. In both parities, the high-PE females farrowed more (P < 0.05) live pigs than the low-PE group (12.5 ± 0.7 vs 9.6 ± 0.5). Although the high-PE group farrowed pigs that were about 20% lighter than the low-PE group (1.2 ± 0.1 vs 1.5 ± 0.1 kg, P < 0.05), their placentae were 40% lighter (250 ± 10 vs 347 ± 15 g, P < 0.01), resulting in an increased PE for pigs farrowed in the high-PE group. Interestingly, Vonnahme and Ford (2001) recently reported that selection of Yorkshire pigs for high PE markedly increased placental VEGF mRNA compared to unselected controls. Also of interest was the fact that numbers of stillborn pigs and postfarrowing death losses were low and similar for both groups, suggesting no negative impact on pig viability. Further, when the association between a pig’s PE at birth was compared to subsequent production traits in a commercial herd of Yorkshire and Landrace females, no effect of PE was seen on 21-d weight, days to 105 kg, backfat depth, or loin muscle area (Biensen et al., 1999). These data suggest that the selection for PE might be a valuable tool for increasing litter size in commercially relevant pig breeds without decreasing periparturient pig viability.

Validation of the Impacts of Ovulation Rate, Uterine Size, and PE in a Commercial Swine Herd

In a recent study (Wilson et al., 2000), we used a very large, highly productive (average litter size 10.4 pigs/litter), and healthy herd in Iowa (Dayton Pork, Dayton, Iowa; a portion of Swine Graphics Enterprises, Inc., Webster City, IA) to gain insight into the factors that limit litter size in commercial swine production. For too long, researchers have used a few university herds for their studies on litter size without comparing physiological differences in reproductive function (i.e., ovulation rate, uterine length, placental size, etc.) of their herds to those used by the swine industry, or for that matter other university herds. Thus, many of the conclusions drawn from these studies may have limited relevance to today’s swine industry. In our attempt to understand the factors limiting litter size, researchers have focused on three main

Figure 3. Similar-sized Meishan and Yorkshire littermates farrowed by a Yorkshire sow.
traits: 1) ovulation rate, 2) uterine size, and, more recently, 3) placental efficiency. Although all three seem moderately heritable, selection for increases in ovulation rate and uterine length have resulted in very limited and highly variable increases in litter size, whereas recent and limited studies using selection for placental efficiency have shown a much greater effect.

For this study (Wilson et al., 2000), a total of 190 Camborough line 6-02 (PIC) sows representing parities 1 to 14 were slaughtered on d 25 (n = 63), 36 (n = 60), or 44 (n = 67) of gestation, and the gravid uteri and associated ovaries were recovered. Uterine length and the number of ovulations were not different among the three groups, averaging 434 cm and 26.6, respectively. Further, there was no correlation between uterine length or ovulation rate and the parity of the sow. Viable conceptus number decreased from 15.8 on d 25 (before the limitations of uterine capacity) to 12.9 on d 36 (after the impact of uterine capacity), then remained relatively constant through d 44 (12.1 fetuses). This reduction in the number of viable conceptuses under the limitation of uterine capacity was reflected by a marked decrease in conceptus survival (number of conceptuses/number of corpora lutea), which decreased from 60.2% on d 25 to 50.1% on d 36.

Although ovulation rate was highly and positively correlated (P < 0.01) with the numbers of conceptuses present on d 25 (r = + 0.50) before the limitations of uterine capacity were seen, by d 36 this association was lost (r = + 0.02; P > 0.10). In contrast, length of uterine horns was not associated with the numbers of conceptuses found on d 25 (r = −0.03; P > 0.10), but these traits were positively correlated (P < 0.01) thereafter (d 36, r = + 0.36; d 44, r = + 0.40). Interestingly, although fetal weight was not associated with conceptus number on any of the days examined, placental weight was negatively correlated (r = −0.32; P < 0.01) with the number of viable conceptuses on all 3 d examined. We have previously shown (Biensen et al., 1998) that placental weight is highly correlated (r = + 0.82; P < 0.001) with placental surface area, regardless of breed, sex, or day of gestation, and therefore is a good indicator of placental size.

These data suggest that larger litters on d 25, 36, and 44 are composed of conceptuses exhibiting fetuses of similar size, but with smaller placenta and thus exhibiting an increased PE. Further, the ovulation rate of sows from this commercial herd was extremely high compared to that reported by investigators for their research herds (Christenson, 1993; Ford, 1997; Johnson et al., 1999) but was similar to that reported by Foxcroft (1997) for another line of commercial sows. Additionally, although conceptus number was positively related to ovulation rate on d 25, by d 36 the limitations of uterine size began to reduce conceptus number regardless of ovulation rate. These data suggest that ovulation rate was not a limiting factor for litter size in this large group of commercial sows.

Based on the data reported here for this highly productive commercial herd, it is imperative that we define the reproductive phenotypes of our research herds to make sure that the conclusions we draw are relevant to the industry. This is especially critical in the use of the candidate gene approach, which is being increasingly promoted for the determination of whether specific loci contribute to an increased litter size.

Implications

Data presented in this review suggest that more than adequate numbers of viable embryos enter the uterus on d 2 or 3 of gestation, but due to an asynchrony of development, 20 to 30% of conceptuses are lost by d 18. Additional periods of conceptus loss occur between d 30 and 40 (15 to 20% loss) and during the last third of gestation (5 to 10%) as the competition for limited uterine space becomes critical (i.e., uterine capacity). Uterine capacity seems to be increased by increasing uterine size (maternal effect), or alternatively by decreasing placental size, with a corresponding increase in placental efficiency (individual conceptus effect). If an optimal litter size is to be achieved, future research must concentrate on the selection for reproductive phenotypes that is based on a thorough understanding of the physiological factors mediating successful conceptus-uterine interactions during these three critical periods of conceptus loss.

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Increasing fertilization rate of boars: Influence of number and quality of spermatozoa inseminated

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ABSTRACT: The influence of the number and quality of spermatozoa inseminated on litter size in swine is examined in this paper. There is evidence to support the following observations. Litter size varies among boars when insemination doses contain the same numbers of spermatozoa. Increasing the number of sperm inseminated generally has a positive effect on the number of pigs born alive, especially between the range of 1 to 3 x 10⁹ cells. The manner in which litter size responds to increasing the number of spermatozoa inseminated varies among boars. These relationships between the number of sperm inseminated and the resulting litter size provide credence to the idea that boars exhibit unique fertility patterns. These divergent fertility patterns probably reflect variability in the ability of spermatozoa from different boars to fertilize ova. A number of semen quality tests have been developed to estimate the fertility of semen. Several of these have documented that increases in estimates in sperm quality are associated with increases in litter size. However, the relative effectiveness of each of these for determining the optimal number of spermatozoa that should be included in insemination doses remains to be elucidated. In summary, increasing the fertilization rate of boars should be possible by improving semen quality, increasing the number of spermatozoa inseminated, and adjusting using estimates of sperm quality to adjust number of sperm inseminated. However, the magnitude of changes in litter size resulting from these strategies is likely to vary considerably among boars.

Key Words: Boars, Litter Size, Spermatozoa

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Introduction

A spermatozoon that ultimately results in the birth of a live piglet is transported from the cervix through the uterus and enters the uterotubal junction (Hunter, 1990). At this point it attaches to an oviductal cell until it is released and, eventually, encounters an ovum after ovulation (Sirard et al., 1993). During interaction with the ovum, a spermatozoon must bind to and then move through the zona pellucida (Miller, 2000). This allows it to enter the perivitelline space and fuse with the plasma membrane, which eventually leads to the union of its genetic information with that of the ovum.

Presumably, a boar associated with a high farrowing rate and large litters consistently produces inseminations that contain sufficient numbers of spermatozoa capable of completing all of these tasks. Therefore, it is physiologically reasonable to assume that there are two basic characteristics that are directly responsible for a boar’s influence on litter size: the number of spermatozoa inseminated and the proportion of these that can successfully engage ova. The latter of these is often referred to as the quality of spermatozoa and can be estimated in a variety of different ways, including the monitoring of several physical and biochemical traits that allow spermatozoa to fertilize ova.

Whether or not increases in the number of spermatozoa can compensate for decreases in sperm quality is a question that is often posed but has yet to be resolved. This is due to the fact that most studies have examined the effect of these variables on litter size independently or have used a limited range of sperm numbers or quality ratings (Flowers, 1997; Xu et al., 1998). As a result, information about the effect of their interactions on litter size is limited. The purpose of this paper is to discuss recent information examining the relative importance of the number and quality of spermatozoa inseminated in terms of the manner in which they affect the ability of boars to produce live pigs.

Litter Size Based on Numbers of Spermatozoa Inseminated

Salisbury and Vandermark (1961) proposed a theoretical relationship between male fertility and semen
characteristics that resembles a positive, asymptotic equation. Initially, when the number of spermatozoa is low, male fertility is poor. Increasing the number of sperm in the insemination dose results in a positive increase in fertility. The magnitude of this response gradually diminishes as the number of sperm cells inseminated is increased until a plateau is reached. At this point, insemination of additional numbers of spermatozoa does not affect male fertility. Salisbury and Vandermark (1961) referred to this relationship as the male fertility pattern or curve.

The physiological rationale for male fertility patterns is based on the concept that a finite number of competent spermatozoa must be present in the oviduct to successfully fertilize ova. Improvements in fertility are observed until this threshold level is achieved. After this point, there is not a concomitant increase in fertility when the number of sperm cells inseminated is increased because the population of spermatozoa in the oviduct needed to optimize fertilization has already been achieved.

It has been difficult to demonstrate the existence of fertility patterns for boars. Some of the problems encountered are physiological in nature, whereas others are associated with constraints inherent to the normal management systems in which boar fertility is assessed. Physiological limitations include the inability to store boar semen for long periods without significant reductions in its fertilizing capacity (Johnson et al., 2000) and the need to use large numbers of sperm cells in insemination doses compared with other livestock species (Flowers, 1998a). Both of these effectively limit the number of sows that can be inseminated from a single ejaculate. This, in turn, presents challenges in separating the effect of the boar on litter size from those of the sow, the production environment, and their interaction. Constraints associated with management systems include the high replacement rate for boars and the diverse nature of mating regimens used (Flowers, 1998b). These also make estimation of boar fertility difficult for reasons similar to those mentioned previously.

Nevertheless, there is evidence to support the concepts that boars exhibit fertility patterns based on the number of spermatozoa inseminated and that these differ among individuals. Two assumptions central to the existence of fertility patterns are that males differ in their fertility when the same number of sperm are inseminated and that increasing the number of spermatozoa inseminated increases fertility within some portion of the fertility curve. Johnson et al. (1981, 1982) conducted two comprehensive studies that clearly demonstrated that the fertility of boars is different when insemination doses contain equal numbers of sperm. In both of these studies, insemination doses of $3 \times 10^9$ spermatozoa were used to inseminate sows once between 12 and 24 h after estrus. Collectively, there were 3,300 sows used on at least 36 different farms. The range in mean litter sizes among the 24 boars evaluated was between 8.8 and 12.2 pigs. These data provide evidence that boar fertility, as measured by litter size, can differ considerably among individuals when identical numbers of spermatozoa are inseminated. It is interesting to note that estimates used to evaluate sperm quality in these studies were high. The percentages of sperm cells that exhibited progressive forward motility and had normal morphology were greater than 71 and 91%, respectively. Consequently, it is unlikely that the observed differences in litter size were due to individual variations in these characteristics.

In contrast, Xu et al. (1998) failed to observe differences among boars but did show a positive effect of the number of spermatozoa inseminated on litter size. In their study, insemination doses of $2$ or $3 \times 10^9$ spermatozoa were produced from ejaculates collected from six boars and used to inseminate sows three times during a 2-d estrus. A total of 444 sows housed on a single farm were used. The range in mean litter size was between 10.2 and 11.5 pigs when the insemination dose contained $3 \times 10^9$ spermatozoa and between 9.1 and 10.1 pigs when $2 \times 10^9$ sperm cells were used. There was a main effect of insemination dose on litter size, but no interaction between insemination dose and boar. Collectively, these studies provide evidence that several of the assumptions involving relationships between the number of sperm inseminated and litter size central to the fertility pattern concept of Salisbury and Vandermark (1961) are fulfilled.

However, what is lacking is the demonstration that the manner in which litter size changes in response to increasing sperm numbers differs among boars. Results from a study conducted with boars in a commercial stud provide evidence for this (Flowers, 2002). In this study, 40 to 45 ejaculates were collected from 200 crossbred boars (Duroc × Pietran × Large White, 2 to 4 yr of age) over a period of 2 yr. The sperm-rich fraction of each ejaculate was used to make insemination doses consisting of 1, 3, 5, 7, or $9 \times 10^9$ total spermatozoa in 80 mL of Androhep (Minitube of America, Verona, WI) semen extender. Only ejaculates with greater than 70% motility were extended and processed for delivery to farms. At least two crossbred sows (Landrace × Large White × Yorkshire) were bred with each insemination dose from each ejaculate. This resulted in a minimum of 75 sows bred with each insemination dose from each boar. Insemination doses were stored between 16 and 18°C and used within 48 h of collection during the study.

Sows received one insemination each day of estrus. It is important to note that sows used in the study were housed on four different farms that were located within a 40-km radius of one another. Each farm consisted of two, 4,000-sow units under the same management. As a result, sows on a single farm were inseminated with semen from only 40 of the 200 boars during individual collection periods. Insemination doses were allocated to farms in a manner such that boars were used on the same farm and in combination with one another an equal number of times during the duration of the experi-
Boar effects on litter size

Each farm had similar standard operating procedures, farrowing rates (84.7 ± 5.1%), and number of pigs born alive (11.2 ± 0.6) before and during the study. Due to the experimental design of this study, boar and farm effects on litter size were partially confounded during any individual collection period. However, due to the allocation process used for boars, it was possible to estimate the effects of boars and farms. This was done with a repeated measures analysis within an incomplete block design using mixed model methodologies (Cochran and Cox, 1957; Littell et al., 1996). The incomplete block in the model consisted of the combinations of boars and farms that occurred during the study due to the allocation procedures. The statistical model included block, farm, boar, number of sperm inseminated, week, and appropriate interactions. When significant interactions between boar and number of sperm inseminated were present, differences among the number of sperm inseminated within boars were determined.

Analyses of litter size data from this study revealed several different fertility patterns as the numbers of sperm inseminated were increased from 1 to 9 × 10⁹. One pattern was similar to the asymptotic relationship proposed by Salisbury and Vandermark (1961) in which there was an increase in litter size initially before a plateau was reached. This type of relationship was present in 133 of 200 boars. In contrast, a second fertility pattern was linear. This type of pattern occurred in 32 of 200 boars. It is possible that the linear pattern observed for some boars was simply a function of the experimental design. Their fertility pattern may have actually reached a plateau if more than 9 × 10⁹ spermatozoa were inseminated. If this speculation is correct, then the range from 1 to 9 × 10⁹ sperm cells may represent the portion of their fertility curve in which litter size increases as the number of sperm inseminated increases. Finally, there were 35 boars for which a significant farm × boar interaction was observed for the relationship between litter size and number of spermatozoa inseminated. The interaction occurred because the fertility pattern for these boars reached a plateau on some farms but remained linear on others. Because the farms on which this occurred differed among boars, explanations for this interaction were not apparent.

In addition, there were distinct differences among boars in the shape of their individual fertility patterns. For those that reached a plateau, individual boar variations occurred in both the insemination dose at which the plateau occurred and the mean litter size that resulted. Similarly, the slope of the linear responses differed among boars. Selected examples of the variation in the relationship between litter size and number of spermatozoa inseminated are illustrated in Figure 1.

In summary, based on the results from these four studies, three general conclusions concerning the relationships among litter size, individual boars, and the number of sperm inseminated seem warranted. First, litter size can differ among boars when equal numbers of spermatozoa are inseminated. Second, increasing the number of sperm cells in the insemination dose results in an increase in litter size for some boars. Finally, the magnitude of the response in litter size to an increase in sperm numbers is not the same for all boars. From a practical perspective, these observations provide some important opportunities for improving litter size via boar management on commercial swine operations. Due to the variation observed among boars, it is reasonable to speculate that development of practical and cost-effective methods for determining the optimal number of spermatozoa for insemination doses would have a positive effect on litter size. For example, it would be interesting to know whether spermatozoa from boars that exhibited a linear fertility pattern were different from those with a pattern that reached a plateau in terms of key morphological and biochemical characteristics that are related to their ability to successfully...
Table 1. Summary of selected measurements used to estimate sperm quality in boars

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Rationale</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Florescent stains</td>
<td>Some fluorescent dyes (Hoechst 33258) enter if the membrane is damaged and stain only dead cells. Others (SYBR-14) enter cells with a membrane potential and stain only live cells.</td>
<td>Johnson et al., 1996</td>
</tr>
<tr>
<td>Macropscopic morphology</td>
<td>Proportion of sperm with visual morphological defects is inversely related to ability to fertilize eggs in vitro.</td>
<td>Xu et al., 1998</td>
</tr>
<tr>
<td>Hypoosmotic swelling test</td>
<td>When exposed to hypoosmotic conditions the head of sperm with damaged membranes increase in size (begin to swell). Proportion of these sperm in an ejaculate is inversely related to fertility.</td>
<td>Vazquez et al., 1997</td>
</tr>
<tr>
<td>Computer-assisted motility analyses</td>
<td>Number and characteristics of motile sperm using computer-assisted semen analysis (CASA) are correlated with fertility.</td>
<td>Holt and Medrano, 1997</td>
</tr>
<tr>
<td>Hemizona binding assay</td>
<td>Oocytes are bisected and the number of sperm from different boars that bind to each half is correlated with their fertility.</td>
<td>Fazeli et al., 1995</td>
</tr>
<tr>
<td>Sperm plasma membrane proteins present on sperm cells is positively correlated with fertility.</td>
<td>Ash et al., 1994</td>
<td></td>
</tr>
<tr>
<td>Sperm chromatin structure</td>
<td>When exposed to acidic conditions and stained with metachromatic dyes, double-stranded DNA emit a green florescence, but single-stranded DNA (damaged) emit a red florescence. Ratio of green to red sperm is correlated to fertility of a boar.</td>
<td>Evenson et al., 1994</td>
</tr>
</tbody>
</table>

Estimates of Semen Quality and Their Relationship to Litter Size

A number of procedures have been used to assess semen quality. Selected examples of these are summarized in Table 1 along with a brief synopsis of the rationale for each one. For the purpose of understanding how these tests might be used to identify boars with superior fertility, it is useful to divide them into two categories. One category includes tests that focus on determining the proportion of spermatozoa in an ejaculate that possess certain characteristics that have been shown to be involved with a sperm cell’s ability to fertilize ova. In essence, for these tests, the assumption is made that the proportion of spermatozoa with the property being measured is either positively or negatively related, depending on the characteristic, to the number of pigs born alive when the boar is used for breeding. The majority of techniques outlined in Table 1 fit into this classification, including evaluations of normal morphology (Xu et al., 1998), sperm membrane swelling (Vazquez et al., 1997), viability (Johnson et al., 1996), binding to oocytes (Fazeli et al., 1995), and sperm chromatin structure (Evenson et al., 1994).

Two of these tests, normal morphology and sperm chromatin structure, merit additional consideration because their usefulness for determining the effect of individual boars on litter size has been examined. The proportion of spermatozoa with normal morphology explained a large part ($R^2 = 0.59$) of the variance in litter size in the study of Xu et al. (1998). As mentioned earlier, this study involved semen from six boars that was used to breed 444 sows on a single farm. What is impressive about this study is that a single measure of semen quality accounted for more than one-half of the variation in litter size in a commercial setting. Consequently, these results should be encouraging for others attempting to develop prospective methodologies for estimating boar fertility.

Studies evaluating the influence of sperm chromatin structure used heterospermic inseminations composed of equal amounts of spermatozoa from two boars (Evenson et al., 1994). One of the boars used in the mixture historically produced a high number of pigs born alive, and his counterpart routinely sired small litters. The
ratio of sperm with normal DNA to those with damaged DNA was more than 90% effective in predicting the paternity of the pigs resulting from the heterospermic inseminations. Traditionally, heterospermic inseminations have been viewed as a way to minimize the influence of the sow and the production environment on estimates of male fertility (Dziuk, 1996) because spermatozoa from different individuals literally compete with one another simultaneously during fertilization. However, it is important to acknowledge that fertility studies conducted in this way are comparative, or qualitative, in nature. Their results can be used to rank boars in terms of fertility, but it is difficult to translate the rankings into a mean value for the number of pigs born alive or other measures of fertility. As a result, additional work is necessary in order to equate the proportion of spermatozoa with normal DNA in an ejaculate with actual litter size data resulting from homospermic inseminations.

The second category for semen quality tests involves procedures that quantify the degree to which individual spermatozoa exhibit a given characteristic, which, also, is involved with fertilization. For these tests, the assumption is made that sperm cells express varying levels of the characteristic. Boars whose spermatozoa exhibit increased amounts produce larger litters compared with individuals whose sperm cells have low values. Computer-assisted motility analyses (Holt and Medrano, 1997) and the protein composition of sperm membranes (Berger et al., 1996) are examples of these types of semen quality tests. In a series of studies conducted on commercial swine farms, changes in the velocity of the motion of spermatozoa during an in vitro incubation period explained 20% of the normal variation in litter size (Holt et al., 1997). Furthermore, boars whose spermatozoa exhibited increased straight-line velocity and track linearity were associated with large litter sizes. Similarly, concentrations of three proteins isolated from the plasma membrane were positively correlated \((r = 0.38 \text{ to } 0.53)\) with the ability of sperm from individual boars to bind to egg membranes (Ash et al., 1994) and the proportion of pigs they sired when heterospermic inseminations were used (Berger et al., 1996). Consequently, both of these measures of semen quality seem to be good candidates for explaining some of the variation in fertility patterns among boars.

However, what is difficult to decipher, at the present time, is which of the characteristics outlined in Table 1 simply reflect shifts along an individual fertility pattern compared with those that are involved with changing the level at which the plateau occurs or the slope of a linear response. Shifts along a given fertility curve optimize litter size for individual boars. In contrast, increasing the litter size at which the maximal response is achieved has the potential, in theory, to improve the fertility of boars regardless of their inherent pattern.

Another question that awaits resolution is the degree of dependency inherent among the characteristics measured by each of these procedures. For example, it is reasonable to speculate that spermatozoa judged to be nonviable by fluorescent stains probably also are non-motile. In this situation, viability estimates should have a high positive correlation with motility and results from either procedure should be able to identify boars that produce small or large litters. In contrast, it is conceivable that sperm cells with excellent morphology could be deficient in the protein composition of their plasma membranes. If this were to occur, then a fertility test based on normal morphology would predict the production of large litters, whereas its counterpart using sperm binding assays would not. In order to address these possibilities, studies that examine the effectiveness of using several of these tests in sequence are needed.

**Interactions Between Number and Quality of Spermatozoa Inseminated**

As mentioned previously, whether or not changes in the number of spermatozoa inseminated can compensate for variability in sperm quality is an interesting question that has important implications for increasing litter size in pigs. If one accepts the argument that a critical number of competent spermatozoa in the oviduct are required to optimize fertility, then it seems reasonable that this critical number could be achieved via various combinations of the quality and number of spermatozoa inseminated. However, in order for this to be realistic physiologically, three things must occur: 1) increases in the number of spermatozoa inseminated should increase the number of sperm entering the oviduct, 2) entry into and retention of spermatozoa in the oviducts need to differ among boars, and 3) transport and entry of spermatozoa into the oviduct should be independent of sperm quality.

There is evidence for the existence of each of these events. First, Baker and coworkers (1968) inseminated gilts with 1, 5, or \(10 \times 10^9\) spermatozoa and determined the number remaining in the oviducts 12 to 16 h later. Even though the recovery rate was low, a positive relationship between the number of spermatozoa inseminated and the number of sperm cells recovered from the oviducts was present. Second, significant effects of boars on the number of spermatozoa recovered from the lower isthmus of the oviduct around ovulation have been observed (Mburu et al., 1996). Differences among boars varied from 461 to 1,972 spermatozoa. Finally, a series of experiments by First et al. (1968) demonstrated that dead spermatozoa are transported and enter the oviduct with efficiencies similar to those of live sperm. Consequently, based on what is known about the dynamics of spermatozoa in the oviduct, adjusting sperm numbers at insemination based on some assessment of their quality seems to be a physiologically plausible way to increase litter size for some boars.

Even though critical evaluations of this strategy involving the birth of live pigs are lacking, results from a field study conducted by Johnson et al. (1988) are
encouraging. In this study, insemination doses consisting of $3 \times 10^9$ spermatozoa were used to breed sows between 0 and 72 h after collection. In contrast, if the collection-to-insemination interval was greater than 72 h, $6 \times 10^9$ spermatozoa were inseminated. No effect of semen age on litter size was observed. Although a contemporary treatment consisting of insemination doses with $3 \times 10^9$, aged (> 72 h) spermatozoa was not included in the design, it is commonly accepted that quality estimates and fertility of fresh semen decrease significantly as storage time increases. This is particularly relevant considering that the semen extenders used in their study, BTS and MR-A, are classified as short-term extenders because fertility of semen is reduced significantly after 3 d of storage (Johnson et al., 2000). Consequently, the speculation that sperm numbers can be adjusted to compensate for reduced semen quality seems to be supported indirectly by the results from field studies.

However, there are several caveats associated with this strategy that should be considered. The best estimates of sperm quality upon which adjustments should be made are not known. Nevertheless, it is logical to speculate that tests that are categorical in nature, such as the percentage of spermatozoa with normal morphology, probably are the best candidates to study initially. Based on the studies discussed previously, insemination of additional numbers of normal sperm should result in additional normal sperm in the oviduct. However, as mentioned previously, estimates based on a sequence of several different tests probably deserve equal consideration.

In addition, it is unlikely that quality adjustments for the number of spermatozoa inseminated would have similar effects for all boars in terms of increasing litter size. For example, boars whose fertility pattern reached a plateau at $3 \times 10^9$ spermatozoa would not be expected to elicit the same response as their counterparts with linear patterns or those with patterns that reached a plateau at $7 \times 10^9$ spermatozoa. Presumably, the level at which the plateau occurs reflects differences among boars in terms of the critical number of competent spermatozoa in the oviduct needed for optimal fertilization. As a result, it is reasonable to speculate that this strategy for improving litter size is better suited for boars with high rather than low requirements.

**Implications**

The number and quality of spermatozoa inseminated determine the boar’s impact on litter size. The relationship between these traits and litter size tends to be unique for boars and is best described as a fertility pattern or curve. Increasing litter size on operations using natural service is most likely to result from improvements in the quality of spermatozoa. This is due to the fact that most boars contain sufficient spermatozoa in their ejaculate to maximize sperm numbers in the oviduct. In contrast, on operations using artificial insemination, increasing litter size probably can occur in several different ways, including improving semen quality, increasing the number of spermatozoa inseminated, and using estimates of sperm quality to adjust number of sperm inseminated. However, the magnitude of changes in litter size resulting from these strategies is likely to vary considerably among boars.

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Can farm animal welfare be understood without taking into account the issues of emotion and cognition?

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ABSTRACT: Although the concept of welfare makes reference to feelings of individual animals, the exact nature of these feelings and their relationship to emotions and cognitive abilities of the animals under consideration are never detailed. Based on the concepts of stress and coping, an extensive list of indicators of physical health, production, behavior, and physiology has been set up for the purpose of recognizing good from bad welfare. However, these indicators do not allow us to make any inference about mental states. This issue is important because welfare considerations apply to farm animals of different species and, within a given species, to animals of different ages, which are likely to have varying degrees of emotional and cognitive capacity. In the past, disagreements about exact definitions of emotion and cognition have blurred the matter and hampered research. However, this should no longer be the case; the study of emotions and feelings has emerged as a field of active research in psychology and neuroscience over the last two decades. It is now possible to go over philosophical discussions on the nature of feelings and to set up a research agenda on emotion and cognition in farm animals that should help us to understand their welfare requirements.

Key Words: Cognitive Development, Domestic Animals, Emotions, Neurology, Stress

Introduction

Statements about the nature of animal welfare make explicit or implicit reference to mental states. As a typical and influential example, Broom (1986) defines the welfare of an animal as “its state as regards its attempts to cope with its environment.” In the report of the European Scientific Veterinary Committee on the welfare of calves (European Commission, 1995), this definition sets the scene and is followed by the statement that “the state of the animal, as referred to in the definition, includes the feelings of the individual animals as its physical state. Suffering is one of the most important aspects of poor welfare and we should investigate the existence of good or bad feelings wherever possible when trying to assess welfare.” However, the problem is that what these mental states termed “feelings” exactly consist of, and how they relate to coping, is never clarified. As pointed out by Dawkins (2001), research on the psychological health of farm animals has mainly concentrated on establishing checklists of biochemical, physiological, and behavioral indicators without taking the necessary steps to relate them to the occurrence of positive and negative emotional states. There are obvious reasons for that, the main one being the reluctance of ethologists to engage in a thorough study of emotions in animals. There is still the biased prejudice that research on emotion and cognition is unscientific and should be carried out only on human beings, who can express what they feel via verbal reports. The purpose of this theoretical review paper is to show that there are ways out of this conservatory attitude and it is possible to engage in objective studies of emotions in farm animals and how they relate to cognition.

Emotion and Cognition

The most elementary component of an emotional state is its affective dimension. According to Cacioppo and Gardner (1999), affective categorization and responses have been shaped by evolution to allow differentiation between hostile and hospitable stimuli. This differentiation is so critical that organisms have rudimentary reflexes for categorizing and approaching or withdrawing from certain classes of stimuli and for providing metabolic support for these actions. An additional adaptive advantage is conferred to species whose individual members have the capacity to learn based on the unique environmental contingencies to which they are exposed, to represent and predict events in their environment, to manipulate and plan based on
representations, and to exert some control over their attentional and cognitive resources.

The affective component of an emotional state can be simply assessed by determining whether the animal approaches or avoids the eliciting situation either spontaneously or after appropriate classic or instrumental learning. An object is described as pleasurable, and the animal is assumed to experience pleasure, if this object is approached and eventually consumed or if the animal remains in close contact with it. Conversely, an object is said to be aversive, and an animal exposed to this object is assumed to experience a negative emotion, if this animal escapes it or subsequently makes every effort to avoid it. Preference tests in applied ethology make use of this basic distinction to determine what is good and what is bad for the welfare of an animal. Typically, if a pig that is given the choice among two types of floor stays longer on a given floor type (e.g., a straw-bedded floor) and hardly walks or lies down on the other floor type, (e.g., concrete slats), its state of welfare will be reputed to be good or bad depending on what type of floor it is normally exposed to. More sophisticated methods have been developed to find out how much animals value resources by measuring how high a price, in terms of time and energy, they will pay to access or avoid them (Dawkins, 1983). The rewarding nature of a single resource such as food can be estimated by the use of a progressive ratio schedule that consists of requiring an animal put into an operant conditioning chamber to press a panel once to get the reward, then twice, then four times in a row, and so on, until the reward is no longer worth the effort (the so-called breakpoint) (Dantzer, 1976). Several resources can be compared by use of closed-economy set-ups in which animals have permanent access to several resources providing they pay the appropriate cost (e.g., by pushing through weighted doors) (Mason et al., 2001).

It is possible to go one step further and qualify the specific emotional state that is experienced by an animal. Primary emotions refer to a set of six to eight basic emotional reactions (e.g., fear, joy, disgust, sadness, surprise, and anger) that are innate and found in human and non-human animals (Leventhal, 2000). The usual approach for determining experimentally whether an animal can express a given emotion is to expose this animal to an emotional stimulus that is assumed to be at the source of the emotion under consideration and to assess whether it presents the behavioral and physiological changes that are congruent with the emotional nature of the stimulus. A chicken is described as frustrated if it responds to a situation in which it is prevented from performing a motivated behavior by showing signs of behavioral agitation (e.g., wing flapping, aggression toward conspecifics, spot pecking, or pacing). In the same way, a chicken is assumed to be frightened if it responds to a potentially threatening stimulus by behavioral signs of fear that vary according to the distance from the threat and the ability to avoid it. Fear responses in chickens include flight, fighting, and tonic immobility. All these behavioral responses are usually accompanied by changes in physiology that reflect activation of the hypothalamic-pituitary-adrenal (HPA) axis and the orthosympathetic branch of the autonomic nervous system. These physiological changes do not necessarily differ according to the emotion that is experienced (Dantzer, 1989). Their relation to the subjective component of emotions is quantitative rather than qualitative, in the sense that the magnitude of the physiological arousal modulates the intensity of emotion. An emotion requires both a physiological arousal and the perception of a meaningful, contextual-environmental cognition (Schachter and Singer, 1962). There has been much debate on the relative importance of the visceral and the cognitive processes in the genesis of emotion, and the order in which they take place (i.e., does the visceral arousal precede cognition, or vice-versa?). In the present case, it is not necessary to enter the details of this controversy, and it is sufficient to state that modern theories of emotion agree on the role of the environmental context in determining the specific quality of the emotional response (Leventhal, 2000). This allows us to understand why behavioral and physiological indicators of emotion in animals are mostly used for describing emotionality and its variation according to genotype and previous experience, whereas contextual cues are used to specify which type of emotion is experienced.

Whether emotions are defined on a bidirectional axis (pleasure vs displeasure) or in terms of discrete emotional states, the assumption remains the same. Animals that display behavioral and physiological signs of emotion are assumed to experience the corresponding emotional state. Many scientists choose to stay at this level when it comes to defining emotions. A typical example is Panksepp (1988), who started his career with the description of stimulus-bound behavior in rats, i.e. behavioral responses elicited by electrical stimulation of specific brain sites. Panksepp (1982) claimed that the primary emotions animals are endowed with (expectancy, rage, fear, and panic; joy was added later) arise from the operation of hard-wired neural circuits in the visceral-limbic brain that facilitate diverse and adaptive behavioral and physiological responses to environmental challenges. The mere existence of the appropriate behavioral and physiological signs of emotion allows us to infer that the corresponding emotional state exists in the animal under consideration. Although the Panksepp (1988) description is limited to the mammalian brain, it is certainly possible to find equivalents of such circuits in the reptilian brain that birds are equipped with, especially so because Panksepp also worked with chicks.

The problem with the Panksepp (1988) description of emotional states is that it does not allow us to differentiate fixed response patterns that are hard-wired and do not necessarily require a central nervous system from more plastic, adaptive responses. As aptly pointed out by Staddon (1983), relatively simple built-in re-
sponses such as tropisms enable animals to display a large set of very well-adapted behaviors, including avoiding bad things and approaching good things. Rolls (1999) claims that such adaptive mechanisms that require little or no dependence on past history do not involve any intervening emotional state. Emotions come into play when adaptive behavior depends more and more on the animal’s past. Emotions, therefore, require the ability to establish temporal and instrumental contingencies. Learning a temporal contingency refers to the ability to relate the occurrence of one stimulus to another one when both occur in succession, and to make the first one a possible causal factor for (or a predictor of) the second one. Learning an instrumental contingency refers to the ability to assess the consequences of one’s response on the environment (e.g., to learn that a given response is followed by a set of specific consequences). In this context, emotions provide the common currency with which animals can balance conflicting demands of avoiding bad things and approaching good things and evaluate the priority to be given to one over the other.

The main problem with all of that which precedes is that it describes the way an emotional system in the brain is operating and the minimum mental operations it requires, but it says nothing about the subjective aspects of emotions, or feelings. As pointed out by Le Doux (1996), “a subjective emotional experience, like the feeling of being afraid, results when we become consciously aware that an emotion system of the brain, like the defense system, is active.” To have a defense system that gives rise to appropriate behavioral and physiological responses in the face of a threatening situation is not sufficient to feel afraid; we need to have the key elements of consciousness that allow us to be aware of the activity of this defense system. Duncan and Petherick (1991) stand on the same ground when they claim that the extent to which animals are aware of their internal state while performing behavior known to be indicative of so-called states of suffering, such as fear, frustration, and pain, will determine how much they are actually suffering. Of course, emotions have evolved as brain states and bodily responses, and not necessarily as subjective feelings conveyed linguistically; otherwise, Darwin (1872) would not have been able to study their phylogeny. However, these basic elements are not sufficient to make up a full emotion. Some elements of consciousness are still necessary. For LeDoux, there is nothing special in the conscious operations that allow us to be aware of our emotional states. The mental representation of a flower and the mental representation of a threat make use of the same building blocks. What is specific is the way the sensory input is processed to give rise to a mental representation. Emotional stimuli are given a special treatment in the sense that most of them escape the sensory cortical analyzer to be deciphered at the subcortical level, via a shortcut, a neural pathway directly connecting the sensory thalamus to the amygdala.

Damasio (1998) has added to this description the somatic marker hypothesis, which allows us to relate visceral responses to feelings. Those brain areas in which emotions are represented in the form of motor programs need to be able to process visceral information and to re-actualize this processing according to the way emotions are expressed both behaviorally and physiologically. In the brain, the mechanisms of emotions are part of a survival kit, just above the basic motivations. Feelings come into action to allow anticipation of what can happen or prediction of what is going on during the course of an emotional situation that emotional responses are already dealing with. Consciousness of an emotion is a form of a meta-knowledge because it corresponds to the knowledge of one’s ability to experience emotions (Damasio, 1998).

In more general terms, the issue of the relationship between emotion and cognition has already received a lot of attention in psychology. Contrasting theories have been put forward, some proposing that there cannot be any emotion without some form of cognition, others pointing out that emotion and cognition are distinct processes. Without getting into the details of the controversy that is mainly based on empirical work carried out in human subjects, it is important to know what is at stake here because it has significant implications for the conceptualization of emotions in animals. A few scientists, such as Zajonc (1980), claim that emotions, actually confounded with preferences, are more primitive than cognition, represented by mental operations such as object recognition, and therefore can occur in the absence of any cognitive operation. The vast majority of psychologists, however, agree that an emotion involves some form of cognition about an emotional situation. For Lazarus (1984), an emotional state requires a primary appraisal of the emotional stimulus. This primary appraisal is responsible for the setting and execution of action plans, and it is followed by a secondary appraisal of the consequences of action. Contemporary psychologists have tried to describe more precisely the exact dimensions of the eliciting situation that are evaluated and give rise to an emotion. Although their description usually tells us nothing or very little about the contribution of physiological activation to this appraisal process, the dimensions that have been identified are certainly useful for trying to describe in very objective terms the types of emotion that are accessible to different animals and the way they can differ according to age and species. A very good example of this type of contribution is that provided by Scherer (1997), with his theory of the emotion-antecedent appraisal process. In contrast to most of his colleagues working on appraisal, he chose not to rely on verbal reports to assess the way appraisal is carried out; instead, he concentrated on the objective antecedents or eliciting conditions for emotional reactions. The major criteria he listed for an emotional object are its novelty, intrinsic pleasantness, goal significance, coping potential, and relevance to external and internal standards.
A Strategy for Studying Emotion and Cognition in Farm Animals

Because applied ethology deals with a wide range of species, some standardization is obviously in order to describe the range of emotional states that are accessible to farm animals. It is necessary to overcome the previously described limitations of the behavioral approaches that have been used so far for studying emotional responses in animals. In order to incorporate in this task an appropriate evaluation of cognitive abilities of farm animals, the reference framework has to rely as far as possible on observable elements rather than on linguistic labels. The appraisal model elaborated by Scherer (1997) can be proposed for this purpose. It is relatively easy to plan similar emotional situations for different animal species based on the elementary appraisal dimensions that are delineated in the Scherer (1997) theory (novelty, pleasantness, coping potential, etc.) and to investigate the details of the appraisal process rather than debating the extent to which it is cognitive or not. Based on Leventhal’s theorizing, emotions can be seen as developing from relatively simple, reflex-like forms (wired in innate sensory-motor processes) into complex cognitive-emotional processes that result from the participation of at least two distinct levels of memory and information processing, a schematic and a conceptual level (Leventhal and Scherer, 1987) (Figure 1).

Imagine an emotional state with the following antecedents: suddenness, low familiarity, low predictability, very low intrinsic pleasantness, high goal significance, and low coping potential; in all likelihood, this emotional state corresponds to frustration. This emotional state is characterized by behavioral agitation and increased pituitary-adrenal activity, as already described in pigs that have been trained to work for a food reward by pushing a panel with their snouts in an operant conditioning cage, and which, on the test day, are put into the cage with the feeder turned off (Dantzer et al., 1980). These behavioral and physiological reactions form a basic vocabulary of primitive emotions that is suggestive, and only suggestive, of the presence of an emotional state and its associated emotional experience.

Although behavioral agitation and physiological arousal are the most visible components of the pig’s automatically elicited emotional state of frustration, they are short-lived and not necessarily accompanied by a feeling of frustration. Such a feeling is most likely to arise if the pig is able to elaborate on what has happened to it and how it has reacted to it. This is where the schematic level of processing comes in. The minimum requirement here is the ability to form what cognitivists call schemata (i.e., neural representations of the situation and the organism’s response to this situation). If a pig that is repeatedly exposed to a stimulus that signals the cessation of delivery of food learns to respond to it by emitting a response that terminates the signal so that it can now be rewarded, then there is some reason to believe that it is able to feel frustrated. Note that schemata operate automatically and are not easily controlled by conscious reasoning or voluntary effort. The fact that mammalian farm animals can learn temporal and instrumental contingencies is a good index of their ability to form schemata. A pig that has learned to avoid impending electric shocks by jumping from one side of a two-compartment cage to the other will respond to a fear signal (i.e., a tone previously associated with electric shock) by increasing its response rate (Dantzer and Mormède, 1976) (Figure 2). Conversely, it will react to a safety signal (i.e., a tone signaling the absence of electric shock) by decreasing its response rate. In other words, pigs make use of their past experience to predict what is likely to happen in the situation they are exposed to.
The synchrony between behavioral and physiological responses that is characteristic of an emotional response takes place not only at the sensory-motor level, but also at the schematic level that involves situational and response expectations. The ability to control the emotional situation by a suitable behavioral response results in physiological de-activation (Dantzer, 1989, 1993). Conversely, the inability to control the situation is a strong inducer of physiological arousal. The way animals respond to the frustrating situation is determined by their expectation of the food reward, which itself influences their blood levels of cortisol. This syn-

Figure 1. Multilevels of emotion processing (adapted from Leventhal and Scherer, 1987).

Figure 2. Behavioral responses of pigs with a continuous avoidance history to a fear signal (CS+) and to a safety signal (CS–). Pigs were trained to avoid painful electric shocks by crossing a barrier in a two-compartment cage according to a continuous avoidance procedure (shock-shock interval = 10 s, response-shock interval = 30 s). After stabilization of performance, they were presented with a 5-s tone always (CS+) or never (CS–) followed by shock, 10 times for each tone, in four conditioning sessions. On the next day following the last discriminative fear conditioning session, they were tested in the two-compartment cage in extinction conditions (i.e., without any shock), and CS+ and CS– were presented in random order nine times each. Half the pigs were pretreated with saline (n = 4) or with 1 mg/kg diazepam (n = 4) 30 min before the session. Each graph shows the mean number of responses (mean ± SEM) in 5-s successive intervals just before the CS (−5 s), during it (0 s), and after (5 to 30 s). Note that presentation of the fear signal increased response rate whereas that of the safety signal had the reverse effect. Diazepam injected at an anxiolytic dose had no effect. Adapted from Dantzer and Mormède, 1976).
With the situation (e.g., high cortisol levels are associated with a higher probability of engaging in passive coping, whereas high catecholamine levels are associated with a higher probability of engaging in active coping; Dantzer and Mormède, 1983). They also allow brain memory systems to differentially process for further use sensory aspects of the emotional situation and outcomes of emotional behavior (Mormède and Dantzer, 1978).

A full account of emotional reactions in farm animals requires at least the assessment of the extent to which the necessary synchronization between behavioral and physiological responses takes place. This type of research is unfortunately still relatively rare. In the case of chickens, for example, frustration has been defined at the behavioral (Duncan, 1970) but not at the physiological level, so that it is not yet known whether the operating characteristics of the emotional system at the sensory motor level are the same in mammals and in birds.

In Leventhal's theory, the third level of processing is the conceptual (Leventhal and Scherer, 1987). At this level, it becomes possible to reflect upon, abstract, and draw conclusions about the environment and one’s emotional responses to it. This is analogous to the meta-knowledge discussed before (Damasio, 1998), and it can be safely assumed that it needs a minimum form of abstraction and self-consciousness to be achieved. Therefore, the probability that this level is accessible to farm animals is unlikely.

Application of the hierarchical model of emotion to farm animals allows us to determine more precisely the type of emotional experience that is accessible to them. The case of sows in maternity stalls illustrates this issue very well. The nervousness and stereotypes pregnant sows develop just before parturition are often interpreted as indices of the frustration these animals are experiencing. It is said that sows feel frustrated because they cannot engage in the nest-building behavior they would normally present in the wild. However, based on the multilevel theory of emotion, frustration can develop only if sows are able to form schemata, in the present case a mental representation of what they are missing (e.g., adequate material for nest building). The path is open here for a logical trap. By definition, frustration can only occur in individuals that are missing something they have experienced earlier. Sows that are confined in gestation stalls are obviously likely to miss several features they have already experienced, such as the ability to move around and to interact with conspecifics. This can be a source of frustration, and the level of frustration confined sows experience is a function of the relative importance of the items they are missing. In order to assess this relative importance, the same type of procedure as that used by Mason et al. (2001) for mink can be put to work. However, once more, the positive results obtained with such a procedure will not demonstrate the existence of a frustration in a situation other than the one that has been set up.

Figure 3. Relationship between plasma cortisol levels and behavioral response to frustration in pigs. Pigs that had learned to get a food reward by pressing a panel with their snouts were put into the operant conditioning cage on the day of test with the food dispenser turned off. Open circles show for each pig the initial plasma cortisol levels, measured just before the start of the session, and closed circles the plasma cortisol levels measured 30 min after completion of the frustration session. Note that the number of responses emitted during the session was correlated negatively to initial (dotted line) but not to final (interrupted line) plasma cortisol levels. Adapted from Dantzer et al. (1980).

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Because of this synchronization process, changes in circulating hormones can be used a posteriori to assess whether the behavioral response to the situation is truly indicative of an emotional state. This possibility has been very elegantly made use of by Mason et al. (2001) to show that the way mink value different resources in a closed-economy set-up does not necessarily imply that the lack of preferred resources is detrimental to welfare. In their experiment, urinary cortisol levels increased only when mink were prevented from getting access to a water pool, but not when they were unable to visit an alternative nest site or an empty cage, two resources with lower incentive value than the water pool. Elevations in urinary cortisol of mink denied access to the water pool were of the same magnitude as those observed in mink deprived of food. Activation of the autonomic nervous and neuroendocrine systems serves to fuel the motor components of the emotional response. However, it is not its sole role. By their action on the brain, hormones influence the way animals cope with the situation (e.g., high cortisol levels are associated with a higher probability of engaging in passive coping, whereas high catecholamine levels are associated with a higher probability of engaging in active coping; Dantzer and Mormède, 1983). They also allow brain memory systems to differentially process for further use sensory aspects of the emotional situation and outcomes of emotional behavior (Mormède and Dantzer, 1978).

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for the experiment. The mink that were studied in the
Mason et al. experiment had no previous experience
with the swimming pool. In order to learn to push open
a door so as to get access to the swimming pool, they
obviously had to develop some representation of what
a swimming pool is and what it means to their welfare.
The fact that subsequent blockade of access to the swim-
mimg pool door caused behavioral agitation and in-
creased urinary cortisol levels was clearly indicative of
a state of frustration. However, these findings do not
imply at all that mink that are raised as fur animals
and have never seen a swimming pool are frustrated
when there is no swimming pool in their cage. Such a
conclusion is condemned to be logically flawed as long
as mink have not been shown independently to be able
to form mental images of something they have never ex-
perienced.

The appropriate vocabulary here is therefore that of
motivation, or need, not that of emotion. To come back
to sows in maternity stalls, they are likely to be in
the same state, in relation to the hormonally induced
changes in their internal milieu, as are hungry animals
in relation to their energy status. Hunger is a motiva-
tion, not an emotion. The fulfillment of a need takes
place at the level of sensory-motor processing. It obvi-
ously has an affective dimension that is generally posi-
tive, but such an affective state is independent of the
ability to form schemata. Being hungry is certainly
aversive in most situations and will therefore be ac-
tively avoided. However, being hungry is a necessary
but not a sufficient condition for frustration because
frustration does not occur just because of the lack of
food but because of the lack of expected food.

This type of reasoning must not be pushed too far,
however; otherwise it leads to another trap, that of
dogmatism. Engrained in the multi-level theory of emo-
tion developed by Leventhal (Leventhal and Scherer,
1987) is the possibility that when an emotion takes
place in a system that has the capacity of forming mem-
ories, the brain in that case, it will leave memory traces
that, under certain conditions, can be reactivated by
only part of the conditions that initially triggered the
emotion. In other words, processing of information at
one level of the multilevel process that is at the source
of emotion, even when this level is the most elementary
one, may trigger the full-blown emotion. As a typical
example, agoraphobic patients can develop a panic at-
tack when exposed to a place in which they feel trapped.
However, the same pathological emotion will also de-
volve when they are exposed to alkalosis, whether pro-
duced by hyperventilation or by sodium lactate infusion
(Maddock, 2001). The explanation here is that under
the effect of these treatments, panic patients experience
visceral sensations that are reminiscent of those associ-
ated with the panic episode. It can be imagined that a
similar process takes place in animals that have been
repeatedly exposed to strong or repeated emotional ex-
perience, especially in unpredictable and uncontrolla-
ble conditions. In the case of sows in maternity stalls,

the triggering factor would be the restlessness and en-
hanced arousal associated with the beginning of partu-
rition, and the resulting emotional state would be that
of the frustration already experienced during confine-
ment in gestation stalls. There are several direct and
indirect ways of testing this possibility. An obvious ap-
proach is to verify that the postulated emotional state
develops less easily in those animals that are exposed
to the situation but have had limited opportunity to
previously experience the same emotional state than
in those animals that have already had ample opportu-
nity to experience it. However, such an experiment is
not necessarily easy to set up. An indirect approach
would be to search for evidence of the plastic changes
in the brain that underlie the expression of such a phe-
nomenon. At the neurobiological level, the process that
allows a full emotion to develop in response to a weak
stimulus that normally has no effect on its own is known
as sensitization. When the initial stressor is sufficiently
intense, the neural circuitry that mediates the corre-
ponding emotion may undergo a long-term increase in
sensitivity (Antelman et al., 2000). The cellular and
molecular basis of this sensitization process has been
elucidated in several neurochemical systems in vivo
(Bremner et al., 1996; Post and Weiss, 1997), and even
in simpler animal models such as the gill-withdrawal
reflex of aplysia (Cohen et al., 1997). In neurobiological
terms, however, what is relevant for emotion is not
the nature of the biochemical process per se but where
exactly it takes place in the brain.

The previously delineated description of emotional
states has been carried out hardware-free (i.e., without
paying any attention to the neural basis of emotion).
This attitude was certainly very popular until two de-
cades ago. However, it has been superseded now by
the recent developments of research on emotion and
cognition in neuroscience. The reductionist power of
neuroscience has made clear that mental states are
ultimately activities of the nervous system and are not
formed at the cellular level, as was wrongly claimed by
early neurobiologists, but rather at a certain level of
organization of this system, that of the connectivity
between different brain structures. There is already
evidence that the basic elements of an emotional behav-
ior are organized in the brain stem. This is the case,
for instance, for the oro-motor patterns of taste-induced
disgust and pleasure that can even occur in anence-
phalic newborns (Grill and Norgren, 1978). However,
the effect of experience enlarges the range of stimuli
that are able to trigger these basic responses, and this
process takes place in the visceral limbic brain (Yama-
 moto et al., 1994). It is even possible to assess which
neural structure is involved in processing environmen-
tal cues associated with specific emotional states. In
the case of a conditioned taste aversion that requires
the learning of an association between a novel taste
stimulus (the conditioned stimulus, or CS) and visceral
malaise (the unconditioned stimulus, or US), the CS-
US association seems to take place in the parabrachial
nucleus, whereas the gustatory cortex modifies the strength of this association depending on the novelty of the taste stimulus, and the amygdala is indispensable for the expression of conditioned taste aversion (Yamamoto et al., 1994). In the case of conditioned fear, the amygdala seems to be necessary for forming representation of discrete emotional stimuli, whereas the hippocampus plays a key role when it is necessary to form a representation of the context in which the emotional response has taken place (LeDoux, 1996).

Needless to say, this type of research is still in its infancy in farm animals, with the noticeable exception of the neural basis of the mental representation of social stimuli in the ovine brain (Kendrick, 1991; Kendrick et al., 1997). There is no reason why the study of farm animal welfare should stay away from the move toward the construction of an emotional brain and ignore the way the neuronal architecture of the brain of farm animals enables them to represent the world. This is not just for academic purposes, as exemplified by results from research on pain in animals. The study of pain has benefited very much from the development of new techniques for measuring pain-related behaviors that allow an individual to care for the damaged part of its body and promote recovery (Bolles and Fanselow, 1982). These pain-related behaviors can be easily observed in animals that are inflicted with chronic pain, in the form of arthritis induced by injection of adenvant or paw inflammation elicited by local injection of formalin. From this perspective, chickens seem to display species-specific pain-related behaviors that serve a protective function similar to those observed in rats. However, whereas removal of the telencephalon eliminates pain-related behaviors in rats, it fails to do so in chickens that have been given an intra-articular injection of sodium urate crystals (Gentle, 1997). Although decerebration is a very crude procedure that needs to be complemented by more precise determination of the neural structures that are activated by nociceptive stimuli, using for instance the expression of early activation genes that are characteristic of neural activation, these findings, if they are confirmed, might imply that pain-related behaviors are organized in the brain stem in chickens whereas they are organized at higher levels of brain functioning in rats. Brain stem structures only allow sensory-motor processing, so it is unlikely that chickens form schemata of the pain they display behaviorally, and their mental experience of pain is therefore probably not the same as that of mammals.

Implications

Research on farm animal welfare has become very conventional. The quest for indicators of welfare is the norm and sets the pace for elaboration and revision of recommendations and regulations. In the near future, progress in deciphering the genome of farm animal species is likely to result in the replacement of behavioral indicators by molecular markers of cellular damage and death. However, what all these indicators mean in terms of well-being will remain elusive as long as there is little or no research on the basic components of well-being: perceptions, representations, and feelings. It is certainly time for agricultural research to address this question directly, especially because suitable strategies are now available as a result of recent advances in psychology and neuroscience.

Literature Cited


Cognition studies with pigs: Livestock cognition and its implication for production

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ABSTRACT: The purpose of this paper is twofold. First, it discusses in general terms how animal production can be affected by the animals’ cognitive abilities; second, it aims to introduce our work on pig cognition. We suggest that livestock cognition does not only affect production indirectly through its effects on livestock welfare, but also that cognition can have direct effects. Direct effects are evident when cognitive abilities limit feed intake, for example, or in the recognition of groupmates or offspring. We illustrate such direct effects with two case studies from pig production: voluntary feed intake after weaning and production losses associated with aggression in groups. Voluntary feed intake after weaning is affected by preweaning experiences, weaning age, and postweaning practices. Some studies suggest a link between early environment and cognitive development in piglets, as has previously been demonstrated in other species. We suggest this as a possible contributing factor to low feed intake immediately after weaning. The other case study centers on aggression in groups of pigs. Several studies indicate that some social assessment and recognition take place between individuals, allowing them to judge each other’s aggressiveness and to avoid fighting once a dominance hierarchy has been established. However, the regrouping of previously familiar pigs can also lead to high aggression levels. This suggests that pigs may be able to form only short-term social memories, or that some aspects of their social memory are disrupted before regrouping. Our work shows that pigs have well-developed spatial memory abilities, which can be disrupted by common management procedures. If this were also the case for social memory, it could help explain increased aggression levels in previously familiar pigs after routine procedures. We also show that pigs are able to adjust their foraging behavior depending on the presence or absence of a subordinate, exploitable co-forager that knows where food is. This ability has potential implications for the way feed is best dispensed to pigs such that all group members can maximize their intake.

Key Words: Animal Behavior, Livestock Farming, Pigs

Introduction

In modern production systems, farm animals are constantly and inadvertently presented with many learning and memory challenges. Consider as an example chickens housed in large groups in free-range or barn systems. We rely on their learning and spatial memory abilities to locate important resources such as food, water, nesting areas, or familiar subgroups (Mendl et al., 2001). Similarly, at weaning under commercial conditions without the provision of creep-feed, piglets have to learn instantly how to acquire food from unfamiliar sources. This is in stark contrast to natural conditions, in which the weaning process is prolonged and gradual, allowing the piglets to explore sources of solid food over many weeks before they have to rely exclusively on them (Held and Mendl, 2001). In single-space feeder systems, the learning challenge can be even greater. The weaners may have to work out how to operate the mechanism that releases the feed before they receive their first postweaning meal (e.g., Pluske and Williams, 1996). In addition to these spatial memory and operant conditioning abilities, the recognition of conspecifics as familiar or unfamiliar, as dominant or subordinate to oneself, or as own or other offspring (e.g., Kendrick et al., 1997) is also likely to be important if animals are to thrive in modern production systems.
Our paper has two main aims. First, it discusses how livestock productivity can be affected by the animals’ cognitive abilities. Postweaning growth-check in weaners and production losses linked to aggression in groups of pigs serve as case studies. Second, the paper briefly reviews some of our recent work on cognition in pigs.

Livestock Cognition and Implications for Production

Until recently, the word cognitive was predominantly used to describe mental processes that require at least some form of mental representation of the processed information (Shettleworth, 1998). Or, put differently, it referred to mental abilities that involve information manipulation and storage beyond making simple stimulus-response connections. For example, considerable effort has been devoted to investigating whether animals, as humans, store information about the spatial layout of their environment as mental spatial representations or so-called cognitive maps (Tolman, 1948), or whether they attribute mental states to others (review on primates by Heyes, 1998).

We use a broader definition of cognitive here to include all mental processes animals use to acquire information about their environment, to store and recall it, and to use it in their decision making (cf. Shettleworth, 2001). This encompasses learning and memory abilities, but also what may be called “higher” cognitive abilities, such as forming cognitive maps, which are indicated by unlearned, complex, and flexible behavior patterns (e.g., finding new routes home from an unfamiliar release site).

How, then, can livestock cognition affect production? We suggest that it does so not only indirectly by the positive and negative effects it has on livestock welfare, and thus productivity, but that it can also have direct effects. In our distinction, “indirect” effects occur when cognition, or its failure, leads to some form of stress response, which may be associated with suffering and compromised welfare and may negatively affect productivity. “Direct” cognitive effects, on the other hand, result in the animals’ not functioning appropriately with direct consequences for their productivity (e.g., failure to find food). They may also have welfare-related implications for productivity, but do not necessarily or always.

The relationship between the cognitive abilities of farm animals and welfare has already been discussed (see most recently Dantzer, 2001). We know that lack of predictability of and control over the variable aspects of the animals’ environment increases the physiological symptoms of stress (Weiss, 1971; Wiepkema and Schouten, 1990) and associated loss of productivity such as decreased daily weight gains (e.g., de Jonge et al., 1996) or reproductive disorders (Varley and Stedman, 1994). For the environment to be predictable to an animal in the first place, not only must the environment have some predictable properties, but the animal must also realize that it does. To have control over its environment, the animal must learn and understand how the environment works and how the environment can be changed to its benefit. And to this end, the animal must be able to perceive, store, and use appropriately the pertinent environmental information.

We want to emphasize again that in our view welfare is crucially linked to suffering, which implies at least some subjective awareness (see Dawkins, 1990), though the study of cognition as we refer to it here does not concern itself with the subjective emotional experiences of the animals. However, knowledge of how much farm animals understand about their surroundings, how they use information about their physical environment and about the behavior and intentions of their groupmates can help us understand how they are negatively or positively affected by their surroundings. For example, social stress induced by common husbandry procedures such as mixing of unfamiliar animals or social isolation from familiar individuals is one of the most potent sources of stress in farm animals (Zayan and Dantzer, 1990). The extent to which animals suffer in social environments is likely to be affected by their “social cognitive” abilities, that is, their ability to assess, monitor, and predict the behavior and intentions of their groupmates (Wiepkema and Schouten, 1990).

As another example, one might consider animals that are capable of forming only short-term memories. They would be unlikely to suffer from memories of negative experiences in the more distant past. Similarly, if animals were unable to form expectations based on events in the past in the absence of present external and internal (for example physiological) stimuli, it would be unlikely that they suffered because their expectations are not met (Nicol, 1996). The cognitive abilities of livestock can thus inform us about the sorts of environments, or situations, in which the animals might suffer and in which their welfare may be compromised.

Direct effects are evident where cognitive abilities limit feed intake, for example, or recognition of groupmates or own offspring. In the following, we illustrate such direct effects with two case studies from pig production.

Postweaning Growth-Check in Piglets

The first is an experiment by Pluske and Williams (1996) on the effects of feed and feeder type on postweaning feed intake. Piglets were weaned at about 30 d and put into weaner groups of nine piglets each. Their feed intake and growth rates were measured for 4 wk after weaning. Feed was dispensed either from single-space feeders wet and dry, or only dry or from multispace feeders. To operate single-space feeders, the piglets had to operate a latch mechanism with their snouts to make feed drop into a trough. Piglets in the “wet and dry” treatment group had to coordinate the flow of water from a drinker inside the bowl with the delivery of food into the bowl. Multispace feeders were
conventional troughs with enough feeding spaces for all nine weaners to feed at the same time. The expectation was that voluntary feed intake would be greater in single-space feeders, because fighting at the feeders would be reduced, because potential attackers could not reach the feeding piglet’s head or ears (Pluske and Williams, 1996). Pluske and Williams also predicted that adding water to the feed would increase voluntary feed intake even further. However, against expectation, there was no difference in feed intake or weight gain over the 4 wk after weaning. In the 1st wk after weaning, the feed intake was actually 27% higher in the multispace treatment than in the two single-feeder treatments. Weight gain in the 1st wk after weaning was significantly lower in the single-space feeder treatment with wet and dry feed (Pluske and Williams, 1996). As mentioned above, weaners had to learn how to operate the single-space feeders, and with the “wet and dry” feeders they also had to learn how to coordinate water flow and food delivery. Pluske and Williams observed that it took the piglets about a week to learn how to use the single-space feeders. They suggest that this led to the initial postweaning growth-check and concluded that any potential increase in feed intake caused by lower aggression levels at the single-space feeders was overridden by the piglets’ problems with learning how to operate these feeders (Pluske and Williams, 1996).

Young commercial weaners often show a characteristic growth-check in the 1st wk after weaning, which is thought to be associated with abrupt weaning at ages when piglets would still be nutritionally dependent on the sow under natural conditions (cf. Pajor et al., 1991). One of the main factors limiting growth immediately after commercial weaning is thought to be voluntary feed intake (Pluske et al., 1995). Voluntary feed intake, in turn, may be determined by cognitive processes such as learning, as suggested by Pluske and Williams’ (1996) study. It might also be affected by the disruption of proper cognitive functioning through separation stress or neophobia (cf. Mendl, 1999). Under natural conditions, the number of sucklings begins to fall after the 1st wk after birth and continues to decline gradually (Jensen, 1988; Jensen and Recén, 1989). The sow begins to terminate more and more sucklings (Newberry and Wood-Gush, 1986; Jensen and Recén, 1989), and she spends increasing amounts of time away from the nest to forage and feed (Jensen and Redbo, 1987; Stangel and Jensen, 1991). The frequency of sucklings continues to decrease steadily, with the steepest fall during the first 4 wk (Jensen, 1988). Feeding on solids by the piglets is well established when they are 4 wk old and increases considerably between the 6th and 10th wk after birth (Newberry and Wood-Gush, 1985; Jensen, 1995). In the Petersen et al. (1989) study, for example, piglets started to graze when they were between 24 and 36 d old and to feed on pelleted feed between 28 and 39 d of age. For the piglets, the natural weaning process is thus accompanied by increasing experience of new sources of food and gradual nutritional changes.

One common practice thought to decrease the postweaning growth-check by facilitating a more gradual change in diet and increasing preweaning experience of new food sources is the provision of supplementary creep feed during lactation. Piglets typically start to eat it when they are 2 to 3 wk old (e.g., Pajor et al., 1991). However, there is large within- and between-litter variation in the amount of feed consumed before weaning, and the effect of providing creep feed on postweaning feeding behavior and growth rates is not clear-cut (Pluske et al., 1995; Held and Mendl, 2001). Weaning age also affects voluntary feed intake immediately after weaning. Generally, all weaners tend to spend less time feeding on the day after weaning than on subsequent days regardless of weaning age. However, the younger the piglets are at weaning, the stronger is this effect (Held and Mendl, 2001). Efficient feed intake seems to develop gradually with age and experience, with the younger piglets taking longer to pick up feeding on solids (see also Appleby et al., 1991; Fraser et al., 1995). We suggest that not only age-dependent gut maturity, but also cognitive maturity, may contribute to this age effect.

Both preweaning experiences and weaning age affect the ability of piglets to cope with the weaning challenge. In general, weaning practices that mimic certain aspects of the natural weaning process ameliorate some of the behavioral problems in young commercial weaners such as low feed intake in the first few days after weaning (Fraser et al., 1995; Held and Mendl, 2001). Early indications are that piglets reared outdoors up to weaning, for example, spend more time feeding at weaning (and mixing) into straw yards than indoor-reared piglets (Webster and Dawkins, 2000; Cox and Cooper, 2001). Cox and Cooper (2001) also observed that outdoor-reared piglets fought less at weaning and mixing. The suggestion is that outdoor piglets have better-developed social and general cognitive skills than conventionally reared piglets. Similarly, de Jonge et al. (1996) found that female piglets reared under conventional indoor conditions up to weaning were more aggressive to each other when weaned into littermate pairs than piglets from enriched farrowing pens. These differences carried over into the later postweaning period and puberty, with the subordinates in pairs originating from conventional conditions (only) showing symptoms of chronic social stress (de Jonge et al., 1996). De Jonge et al. (1996) suggest as one possible explanation that rearing piglets in relatively barren conditions negatively affects the development of their social skills, leading to increased aggression levels. More direct indications for a link between rearing environment and cognitive development in pigs come from a study by de Jong et al. (2000). They found that pigs reared in standard farrowing and finishing pens had impaired long-term spatial memory abilities compared to pigs reared in larger pens with straw (de Jong et al., 2000). In rats,
humans, and nonhuman primates, a strong positive relationship has been established between social and physical environmental complexity early in life and cognitive development and level of cognitive abilities eventually attained (Rosenzweig et al., 1996). It has also been possible to link these effects to changes in brain anatomy and neurotransmitter expression (e.g., Ickes et al., 2000). It might, therefore, be fruitful for wider application to pig welfare and production to further examine the developmental cognitive mechanisms underlying the observed effects of preweaning environment on postweaning feeding (and social) behavior in pigs.

Production Losses Caused by Aggression in Groups of Pigs

A large proportion of production loss in weaners and group-housed, nonlactating sows can be attributed to aggression (e.g., Tan et al., 1991; Stookey and Gonyou, 1994). Some of the aggression observed directly relates to competition over access to resources such as drinkers or feeder spaces (cf. Gonyou, 2001). Another source is the establishment and re-establishment of dominance hierarchies after mixing and remixing (Meese and Ewbank, 1973; Puppe and Tuchscherer, 1994). At weaning, for example, when piglets are mixed into groups of non-littermates, an initial intensive period of aggression lasting approximately 2 h is commonly observed (e.g., Meese and Ewbank, 1973). This is associated with investigation of unfamiliar individuals by nosing the face, ano-genital region, and belly. The animal that eventually becomes top-ranking deals most of the aggression. Skirmishes and fights can continue for 24 to 48 h. The frequency of aggressive interactions falls at the same time as a stable social hierarchy emerges. The decrease in aggression and continued low levels are likely to be the result of the piglets’ recognition and memory of each other’s relative social status. During fighting, pigs may be able to assess each other’s relative competitive abilities (Rushen, 1988; Mendl and Erhard, 1997), and their efficiency at this social assessing may determine the frequency and duration of fights.

Various factors influence the speed with which a social hierarchy is established and aggression during mixing decreases. Weight asymmetry in weaner groups facilitates social assessment. Rushen (1987), for example, showed that fights during the first 2 h after mixing lasted longer in groups that consisted of evenly-sized piglets than in groups in which weights differed more. Similarly, Mendl and Erhard (1997) showed that it is possible to split weaner pigs into “fast” and “slow” attackers according to their individual aggressive characteristics. When pigs of the same aggressiveness (fast or slow) were mixed, the number of escalated fights was higher than when pigs of different aggressiveness were mixed. Again, this implies that some form of social assessment took place between individuals that allowed them to judge each other’s aggressiveness. Disruption of social assessment, recognition, memory, or other social cognitive functions might help explain why aggression can occur between previously familiar animals (Mendl, 1999).

Cognition Studies with Pigs

Spatial Memory

Our first experiment on pig cognition has centered on such disruption of cognitive processes and on how sophisticated the social cognitive abilities of pigs really are. Mendl et al. (1997) investigated whether pigs remembered the location of food hidden in one of 10 possible areas. The task required the pigs to search for and locate the food in their first visit to the arena (the search trial), to remember the location when returned to their home pens (retention interval), and to relocate it during a second visit (the relocation trial). As such it tested the pigs’ spatial memory abilities. Pigs did well in relocation trials. They found the food, making fewer errors than would be expected if they had been searching randomly. Pigs remembered food locations over retention intervals of 10 min and 2 h. However, how well they remembered depended on what happened to them during the retention interval. It has long been known that stressors can have deleterious effects on memory formation and recall (recent review in Mendl, 1999). Mendl et al. (1997) therefore tested whether this applied to spatial memory in pigs by presenting them with various treatments or “disturbances” in the retention interval. These were chosen to act as mild stressors or at least to lead to changes in arousal, which are also known to affect cognitive function (e.g., Kavaliers and Colwell, 1995; in pigs e.g., van Rooijen and Metz, 1987). “Disturbances” also mimicked common husbandry events: pigs were confined in a holding pen on the way back to their home pen for 3 min at the beginning of the retention interval, or for 3 min at the end when they were on their way back into the arena for the relocation trial; or they were placed into an unfamiliar isolation pen for the whole of the retention interval; or they received food in the isolation pen after the search trial and were then moved on to their home pen for the remainder of the retention interval; or they were allowed to explore an unfamiliar room for the duration of the retention interval. All disturbances negatively affected the performance of the pigs in the relocation trials. Pigs required more area visits, that is, they made more errors, before relocating the food than in control trials in which they had not been disturbed during the retention interval. The treatments, however, did not totally block or destroy memory of the food location. In “disturbance” trials, pigs still did better than they would had they been searching totally randomly (Mendl et al., 1997).

Laughlin et al. (1999) built on this to investigate whether a more complex spatial memory task might be more susceptible to interference from environmental stressors. Rather than requiring the pigs to remember
and relocate 1 out of 10 locations, they were tested in a win-shift task in a radial eight-arm maze. Four arms were baited with food, the pig was introduced into the maze, and it searched at random until it had found all four baited arms. It was then returned to its home pen for a 10-min retention interval before being allowed back into the maze for a relocation trial. Pigs were trained to a win-shift strategy, that is, they were rewarded for visiting the four arms that had not been baited in the search trial. Pigs, thus, had to remember four out of eight rather than 1 out of 10 locations. When the pigs reached criterion level of performance on the relocation task, tests proper started. There were four disturbance treatments, applied during the retention interval. Again, some were chosen to mimic common husbandry events that are thought to be potential stressors. In the “social encounter” treatment, the test pig spent the retention interval in a pen where it had contact with an unfamiliar pig through a barred gate; in the “novel” treatment, the pig was led to an unfamiliar outdoor area where it spent the 10-min retention interval; in the “maze” treatment, the pig was confined in the central part of the radial maze with all arms closed off; and in the “weigh” treatment, the pig was retained in weigh crate for 10 min then released back into the maze for its relocation trial. All except the “weigh” treatments significantly increased the number of arm visits in relocation trials compared to control trials without disturbance (Laughlin et al., 1999). These disruptive effects were stronger than in the study of Mendl et al. (1997), as the performance of pigs in the study by Laughlin et al. dropped to that expected of a randomly searching animal. One possible explanation for this difference is that more complex memory tasks such as remembering multiple sites rather than just one may be more susceptible to interference from environmental stressors (Laughlin et al., 1999).

These two studies suggest that even common husbandry events may act as mild environmental stressors that can have deleterious effects on spatial memory performance in pigs and may affect how efficiently they deal with their environment. If these effects extended to social memory, this would provide some explanation for the observation that even in previously familiar pigs aggression levels sometimes increase after temporary removal of individuals for routine management procedures (Luescher et al., 1990; Mount and Seabrook, 1993). Such procedures may be at least temporarily stressful enough to disrupt aspects of social memory and resultant social recognition necessitating the re-establishment of relative social status when the animal is put back into the group (cf. Mendl, 1999).

Social Cognition

Our work on social cognition has started by looking at how sophisticated the social cognitive abilities of pigs really are. How much do they understand about the behavior and intentions of others? Do they use this to their advantage, that is, having taken in information about others, do they change their behavior accordingly to their own benefit? Do they, for example, understand what others can and cannot see?

The first experiment addressed the question of whether pigs use the behavior of others in a competitive foraging situation to forage more efficiently (Held et al., 2000). We adapted the Informed Forager paradigm of Menzel (1974) to test the social tactics of two pigs foraging together for a hidden food bait. We formed eight pairs of one light and one heavy juvenile pig. Lighter pigs were subordinate in a food competition test, heavier pigs dominant. Pairs were housed together in their home pens. Every morning they were allowed to forage for food hidden in an arena. Initially, during training, they foraged alone to learn their respective tasks. Then, during testing, they foraged together. Both pigs learned to expect food in one location (bucket) out of eight possible ones in an open arena with wooden screens providing visual barriers between the food locations. In training trials, they searched the arena individually. A different bucket was baited with food at each trial. The subordinate pig in each pair visited the arena twice. The same bucket was baited in its second visit as in its first. In training, the subordinate member of each pair thus learned to search for the food in its first visit to the arena (search trial), then relocate the food location in its second visit (relocation trial). The dominant pig visited the arena only once and searched at random for the one bucket of the eight that was baited. The purpose of training, thus, was to turn the subordinate pigs into informed foragers or “I-pigs,” but keep the dominants naïve, or uninformed. When the I-pigs had reached criterion level in their relocation task we tested the two pigs of each pair together. The I-pig still got its solitary search trial, but for the relocation it was now paired with its uninformed, but heavier, partner. In pair trials, then, the subordinate knew where the food was hidden, the dominant did not.

What would the uninformed partner do in the pair trials: continue searching at random as in solitary trials during training, or use the knowledge of the subordinates to lead them to the food? We found that uninformed pigs abandoned searching for food for themselves and learned to follow their informed partners to the baited bucket (Held et al., 2000). Once at the baited bucket, they displaced the subordinates and monopolized the food bait. Following the informed subordinates dramatically increased the foraging efficiency of the dominants. In solitary trials, the dominants searched the arena randomly, that is, they visited as many unbaited locations before finding the baited one as expected of a randomly searching animal. When they followed the subordinates in pair trials, however, they visited significantly fewer locations before they reached the baited one (Held et al., 2000). This shows that pigs change their behavior in the presence of a companion that is a better forager and exploitable. Dominant pigs must have had some means of assessing relative forag-
ing efficiency, probably using their co-forager’s behavior as the source of information.

These skills are useful if one considers the natural behavior of pigs. Studies on feral and domestic pigs kept in seminatural conditions have shown that domestic pigs retain the social and foraging behavior of their wild ancestors (Graves, 1984; Wood-Gush et al., 1990). They forage for patchily distributed food in family groups in large home ranges (Krosniunas, 1979; Janeau and Spitz 1995). These family groups consist of one or several sows and their offspring with differentiated rank relationships between them (Mauget, 1981; Petersen et al., 1989; Mendl, 1995). Optimality models predict that under such conditions individuals would benefit from the ability to adjust their foraging behavior flexibly to the presence and behavior of other members of their group. The optimal tactics in terms of foraging returns for each individual depend on its social rank or relative competitive ability, and the resource distribution (Barta and Giraldeau 1998). Generally, when food is clumped dominant group members should specialize as scroungers by exploiting subordinates as food finders or producers (Caraco et al., 1989; Vickery et al., 1991). We would, therefore, expect domestic pigs to have evolved flexible social tactics, and the cognitive abilities that facilitate them, so as to maximize their individual foraging success. Good spatial memory abilities allow individuals to store for future use information about the location of profitable food patches. The ability to use to their own advantage the pertinent information held by another group member (knowledge exploitation) allows pigs access not only to food sources they found themselves, but also to those located by subordinate others.

The next experiment again looked at whether and how pigs use social information in a foraging task. Here we investigated whether pigs understand what another can or cannot see. That is, we tested the visual perspective-taking ability of pigs. A detailed analysis of the results is still outstanding, and we can therefore not draw any conclusions as yet. However, we have included the study here to introduce the type of experimental methodology that allows investigation of more complex social cognitive abilities in farm animals. We adapted a classic primate experiment (Povinelli et al., 1990) to test whether pigs base their foraging choice on the visual perspective of a companion. Visual perspective-taking experiments work on the assumption that animals with perspective-taking abilities will discriminate between individuals that can and cannot see some critical object or event (Heyes, 1998). We predicted that when pigs cannot see for themselves where food is being hidden they should follow an individual that had been able to see where the food was rather than follow one that had not.

Subject pigs initially learned that they had to watch and see where a human trainer went to know which of four corridors contained food. Over differing numbers of training trials, the test pigs learned to enter the corridor that they had seen the trainer enter. During this training phase, the pigs were also given the experience of not being able to see the baiting event when a visual barrier was placed in front of their start box. Once they had reached criterion level on the training task they were tested in an unrewarded probe trial with two companion pigs in the start boxes on either side. Companions were trained to always enter one particular corridor regardless of the movements of the baiting trainer, and also regardless of whether their view of the arena was blocked by a visual barrier or not. In tests, a visual barrier was then placed in front of the test pig in the middle and in front of one companion, the “blind” companion. The other, “seeing,” companion had full view of the arena and corridor entrances. The test pig in the middle could not see the arena, but it could see the “blind” and “seeing” companions on either side, and it could see that one had a visual barrier in front, the same as itself, and the other did not. While the visual barriers were in place, the trainer crossed the arena rattling the bucket noisily to indicate that baiting of a corridor was taking place, then exited the arena quietly to the left or right. After the visual barriers were removed the two companions were released and entered the two corridors that they had been trained to enter. Once they had entered, the test pig was released. Where would it go?

The hypothesis under test was that test pigs will discriminate between “seeing” companions that have visual access to the arena and “blind” ones that do not, if they were able to take the companions’ visual perspectives. And the resultant prediction was that test pigs would follow “seeing” companions more often because they understood that only these would lead them to the food. A positive result would show the pigs’ understanding of the behavior of their conspecifics to be a lot more complex than previously assumed. As such it would drastically broaden the range of social situation pigs might perceive as stressful. In situations in which they cannot see, for example, they might use “seeing” others as their source of information with resultant expectations of their environment, which may subsequently be thwarted.

Implications

Modern production systems rely on the ability of livestock to learn and remember how to use unfamiliar equipment, where to find important resources, and so on. That is, they rely on the animals’ cognitive abilities. Cognition affects production indirectly through its association with subjective awareness, stress, and welfare. Production may also be directly affected when the cognitive faculties of livestock are underdeveloped or disrupted. Our work shows that pigs have good spatial memory abilities that can be disrupted by common management procedures. If this extended to social memory, it could help explain increased aggression levels in previously familiar pigs after routine procedures.
We have also found that pigs adjust their foraging behavior depending on the presence or absence of a subordinate, exploitable co-forager that knows where the food is. This ability has potential implications for the way feed is best dispensed to pigs such that all group members can maximize their intake.

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Beta-Adrenergic receptor agonist modulation of skeletal muscle growth

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ABSTRACT: Mechanisms by which ractopamine and other beta-adrenergic agonists stimulate skeletal muscle growth are discussed. Oral administration dose-response studies in surgically altered laboratory animals provide evidence that indirect endocrine-mediated effects are not an essential component of efficacy. Results from age-comparison studies in laboratory animals and livestock species provide evidence that metabolic maturity of skeletal muscle may be a critical factor with regard to efficacy, suggesting that receptor presence and density are important. Temporal studies demonstrate the rapidity of responses associated with protein and lipid metabolism changes, and that progressive decline in rate of anabolic response in skeletal muscle results from chronic administration. Associated results that demonstrate progressive beta-adrenergic receptor density reductions are observed and suggest, likewise, that protein accretion rate and muscle growth rate responses are receptor-mediated. Measurement of in vivo metabolic effects resulting from continuous systemic infusion has been conducted in relatively few experiments. Detailed blood flow and hind limb net flux data are available for a single beta-agonist, cimaterol. Kinetics studies and close arterial infusion of cimaterol in the hind limb of growing cattle demonstrate large transient increases in amino acid extraction from the circulation and similar patterns of net uptake when compared with the contralateral control saline-infused hind limb. Predictions of differential net effects on protein accretion using integration of essential amino acid net flux measurements are corroborated by quantitative documentation of protein mass differences in individual muscles from treated and control hind limbs. Definitive descriptions of specific pathway mechanism(s) of action for increasing protein synthesis have not as yet been reported. Therefore, additional research is required for elucidation of cellular and intracellular components of mechanism(s) of action.

Key Words: Beta-Adrenergic Agonists, Growth, Muscles

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Introduction

Rapid preferential increase in skeletal muscle protein mass is the most striking response to oral administration of select phenethanolamines in laboratory and farm animal species. Dose-dependent increases in weight of individual muscles have been observed in rapidly growing rats, mice, rabbits, lambs, cattle, pigs, chickens, and turkeys (Anderson et al., 1991; Moloney et al., 1991). Although up to 40% greater weight of muscles has been observed in treated sheep and cattle, magnitude of response varies greatly among phenethanolamines studied and is influenced by age, species, sex, diet, breed, time to reach plateau, and other factors (Beermann, 1993; Mersmann, 1998). Percentage of weight or protein mass increase also varies somewhat from muscle to muscle, and in a few instances a significant response was not observed in a small number of muscles. Because these compounds reduce body fat without altering organ or bone mass, they are also referred to as repartitioning agents. These repartitioning phenethanolamines are classified as beta-adrenergic receptor (βAR) agonists because they share structural similarities and pharmacological properties with the endogenous catecholamines epinephrine and norepinephrine, and many of their metabolic or physiological responses can be reduced or blocked by βAR antagonists (Barnes, 1995). The objectives of this paper are to highlight our current state of knowledge regarding the mechanisms underlying βAR agonist effects on skeletal muscle growth and to identify key areas in which new research efforts are needed. Results from studies in several species provide clarification of effects on muscle fiber histology and histochemistry and patterns of RNA, DNA, and protein accretion. Inferences are drawn from these results for effects on cellularity and cellular metabolic changes. Influences on aspects of protein synthesis and degradation, as they pertain to protein accretion in muscle growth, are also described.

Indirect vs Direct Actions

The complexity of hormonal influences on skeletal muscle growth make it necessary to separate possible
indirect, endocrine-mediated actions of βAR agonists from direct, βAR-dependent mechanisms of action. Indirect modes of action of βAR agonists include possible perturbations in circulating concentrations, sensitivity, and/or responsiveness to hormones known to influence skeletal muscle growth. Surgically altered animal models that exhibit lack of specific metabolic hormones have provided additional insight. Assessment of direct βAR-mediated effects on skeletal muscle includes close (direct) arterial infusion of βAR agonists and saline in contralateral hind limbs, pretreatment or cotreatment with general and βAR subtype-specific receptor antagonists in vivo, and in vitro incubation of agonists and antagonists in myoblast, satellite cell, and myotube cultures. Variation in results between in vitro and in vivo studies has provided equivocal results, however. Several lines of evidence support involvement of βAR in mediation of muscle growth responses. Selectivity and binding kinetics of phenethanolamines for βAR subtypes have been demonstrated (Colbert et al., 1991; Spurlock et al., 1994; Smith et al., 1990). Temporal changes in down-regulation or desensitization of betaadrenergic receptors is observed with chronic βAR agonist administration (Smith, 1989). Myoblast and satellite cell culture studies provide demonstration of activation of βAR signal transduction pathways (Shappell et al., 2000), and blockage of responses with nonselective and selective antagonists implicate βAR dependence (Reeds et al., 1988; MacLennan and Edwards, 1989). Use of more recent technologies to create knockout and receptor-modified animal models provides strong evidence for receptor-mediated mechanisms.

Effects on Muscle Cellularity

The anabolic effects of βAR agonists on muscle include muscle fiber hypertrophy, changes in muscle fiber type frequency, and differential rates of muscle RNA, DNA, and protein accretion. No evidence of muscle fiber splitting or increase in fiber number has been reported. Percentage increases in average fiber cross-sectional area are similar to percentage increases in muscle weight in lambs (Beermann et al., 1986; Kim et al., 1987) and rats (Maltin et al., 1986), although some changes in fiber type distribution have been observed. In general, the increase in hypertrophy of type II fibers accounts for the increase in muscle mass without any quantitative change in muscle length. Similar changes have been observed in pigs fed 20 ppm ractopamine (Aalhus et al., 1992). No in vivo increase in myotube or muscle fiber number has been reported in βAR agonist-treated animals. Lack of response in very young nursing lambs (Williams, 1989) and other species suggests that either muscle fibers lack sufficient βAR number or function to respond early in life or that fractional growth rate in very young muscle fibers is at the maximum.

Results of temporal studies show that 25% increases in RNA concentration and 85% increase in total mass of RNA occurred in parallel with 30% increases in the total weight and protein content of hind limb muscles in lambs fed 10 ppm cimaterol for 3 wk (O’Connor et al., 1991b). During this same time interval DNA concentration was reduced by 42% and total DNA content of the same muscles was unchanged. After 6 wk of treatment, differences in RNA concentration and content disappeared, but muscle weight and protein content remained 25% higher in treated lamb muscle. DNA concentration remained 25% less. These results suggest that stimulation of satellite cell proliferation and incorporation into growing muscle fibers is not an essential component of fiber hypertrophy. Although ractopamine has been shown to elicit a 30% increase in proliferation rate, and in protein and DNA concentrations in cultured mouse C2-C12 myoblasts (Shappell et al., 2000), this in vitro effect is lost after successive passages of the cells, and ractopamine failed to increase DNA or protein in myotubes derived from the C2C12 cells. Grant et al. (1990) observed an increase in proliferation, but not fusion, of chick breast muscle satellite cells incubated with ractopamine. These results were confirmed in studies using turkey satellite cells (McFarland et al., 1995; Shappell et al., 2000) and porcine satellite cells (Cook et al., 1995). Shappell et al. (2000) concluded “that in turkeys, ractopamine may not work directly through the β-adrenergic receptor of muscle cells (and c-AMP) to stimulate changes in muscle carcass traits, but possibly through extramuscular effects, such as increases blood flow and amino acid uptake by muscles.” In summary, in vitro studies fail to provide substantial evidence in support of βAR-mediated stimulation of satellite cells as a means by which muscle hypertrophy is initiated by feeding βAR agonists in growing animals.

Indirect Effects of βAR Agonists

Stimulation of skeletal muscle growth by βAR agonists may involve modulation of normal endocrine influences on growth and metabolism. Many studies were conducted to investigate these possibilities. Feeding cimaterol to growing lambs increased growth hormone and T4 concentrations and decreased IGF-I concentrations after 6 wk (Beermann et al., 1987). In subsequent studies, no change in IGF-I, decreased T4, and markedly decreased (50%) insulin concentrations were observed after 3 wk of treatment (O’Connor et al., 1991a). Young et al. (1995) also reported no change in IGF-I following chronic administration of clenbuterol to sheep. In cattle fed cimaterol, an acute decrease in growth hormone concentration was followed by a chronic increase in growth hormone and a decrease in IGF-I (Chikhou et al., 1991). Dawson et al. (1993) observed no significant differences in growth hormone or IGF-I concentrations in steers fed cimaterol. The normal episodic pattern of growth hormone secretion was absent in the steers fed cimaterol, however. A similar result was observed in lambs fed a high-energy diet with or without cimaterol administration (Beermann, unpublished data).
Anderson et al. (1991) suggested that the repartitioning effects of phenethanolamines may be due in part to opposing effects on insulin sensitivity in adipose tissue vs skeletal muscle. Ractopamine reduced sensitivity to insulin of adipocytes from rats (Hausman et al., 1989) and pigs (Liu and Mills, 1990). Budohoski et al. (1987) observed increased sensitivity to insulin in soleus muscle receiving chronic treatment with βAR agonists. Beermann (1987) noted no change in sensitivity to insulin in lamb hindquarters, using insulin challenges, despite a 50% reduction in circulating insulin concentrations. More refined studies using the hyperinsulinemic and euglycemic clamp techniques in cattle demonstrated a transient (Eisemann and Bristol, 1998) and chronic (Sternbauer et al., 1998) decrease in insulin sensitivity with clenbuterol administration. Although results available to date do not support significant changes in insulin sensitivity as the mechanism by which skeletal muscle growth is stimulated by βAR agonists, more definitive studies are required to clarify these relationships in muscle.

The anabolic response of muscle in endocrine-altered animals to βAR agonist administration adds support for mechanism(s) independent of hormone modulation. Muscle growth is significantly increased in animals with genetic growth hormone deficiency (Bates and Pell, 1991), in hypophysectomized rats (Thiel et al., 1987), and in diabetic (McElligot et al., 1987), adrenalectomized (Buttery and Dawson, 1987), and hypothyroid rats (Beermann, unpublished data). Additive effects of clenbuterol and growth hormone have been demonstrated in veal calves (Maltin et al., 1990). Likewise, cotreatment of pigs with salbutamol and growth hormone (Hansen et al., 1997) and ractopamine and growth hormone (Jones et al., 1989) resulted in additive responses, suggesting separate mechanisms of action account for the independent effects. In summary, indirect effects of βAR agonists, especially effects on endocrine-mediated influences on muscle growth, appear to be negligible in accounting for the hypertrophic responses. Evidence in support of this conclusion is found in analysis of results from studies in which direct βAR-mediated effects were investigated.

**Direct Effects of βAR Agonists**

Close arterial infusion of cimaterol for 21 d increased the rate of blood flow and extraction of essential amino acids from the circulation in the hind limb in a transient manner. Uptake of amino acids by the hind limb exhibited a large acute increase, followed by a gradual continuous increase to a maximum of 160% of controls on d 14, and then a decline during the last 7 d of infusion. Fractional rates of protein accretion were 61 and 130% higher in cimaterol-infused hind limbs on d 7 and 14, respectively. Calculation of cumulative net protein accretion rates in the treated and contralateral saline-infused hind limb predicted 10 to 15% differences in protein mass of the semitendinous and semimembranous muscles, respectively. These differences were confirmed with proximate analysis of the muscles taken on d 21 of the experiment. Close arterial and systemic infusion of clenbuterol in sheep provided similar responses (Aurousseau et al., 1993) and confirm results obtained from cattle fed clenbuterol in which net flux across the portal-drained viscera, the liver, and hindquarters was studied (Eisemann and Huntington, 1993).

The other approach taken by many to assess direct βAR-mediated effects of beta agonists is to demonstrate dependence on βAR functionality in relation to a variety of response variables (Barnes, 1995). At present there are three subtypes of βAR, designated β1, β2, and β3 (Liggett and Raymond, 1993). Distribution and density of βAR subtypes in mammalian tissues is known for several laboratory animal species (Minneman et al., 1979), but as mentioned earlier, few studies provide information for livestock species (Smith, 1989; Spurlock et al., 1994; Bridge et al., 1998).

Pretreatment and cotreatment of animals with general or selective βAR antagonists proved effective. Reeds et al. (1988) used propranolol, a nonselective β1 and β2 antagonist, and altenolol (β2-specific) in combination with clenbuterol feeding in rats. Dosages of the antagonists were 10 and 100 times the concentration of clenbuterol. Effects of clenbuterol on heart weight, fat deposition and energy expenditure were reduced with the antagonists, but the muscle hypertrophy response was not. Similar results were obtained by MacLennan and Edwards (1989) when similar doses of clenbuterol and propranolol were orally administered to rats. Muscle growth response was reduced in an additional treatment group that received intraperitoneal injection of propranolol with subcutaneous administration of clenbuterol. Blockage of the muscle growth response provided evidence for involvement of the βAR. Unfortunately, these experiments do not reveal which cell types the βAR are active in. Therefore, these results do not directly differentiate direct βAR-mediated and indirect actions or effects.

Choo et al. (1992) conducted similar studies in which the β2-specific antagonist ICI-118,551 blocked the anabolic responses of clenbuterol in rats. To date, similar studies have not been reported for livestock species, but other evidence for βAR dependence is available.
These include quantitative measurement of cAMP response in skeletal muscle slices, cultured myoblasts, and myotubes (Silence and Matthews, 1994; Shappell et al., 2000) and documentation of desensitization or down-regulation of βAR in muscle tissue following chronic exposure to βAR agonists (Smith, 1989; Spurlock et al., 1994).

**Effects of βAR Agonists on Protein Synthesis and Degradation**

Early investigations failed to provide evidence for increased fractional rates of protein synthesis during significant elevations in protein synthesis rates in rats (Reeds et al., 1986) or sheep (Bohorov et al., 1987) fed clenbuterol, leading to the suggestion that reduction in protein degradation rates accounted for the muscle growth observed. Similar conclusions were reported by MacRae et al. (1988), but the possibility exists that increases in fractional protein synthesis rates are transient. This is supported by the steady increase from 1 to 14 d, and then a dramatic decline during the subsequent 7 d in net amino acid flux across the hind limb in cattle treated by the close arterial infusion of cimaterol (Byrem et al., 1998). Using the Snell Dwarf mouse as a sensitive model, Bates and Pell (1991) demonstrated that clenbuterol and growth hormone both increased whole-body and muscle fractional protein synthesis rates. They noted, however, that growth hormone treatment exhibited a larger response. Bergen et al. (1989) observed an increase in fractional protein synthesis rate from 4.6 to 6.7%/d in muscle of pigs fed 20 ppm ractopamine. Similar results were observed by Culham et al. (1990) using labeled lysine instead of tyrosine.

Alternative measures that support an increase in protein synthesis include measurement of mRNA abundance for myofibrillar proteins such as actin, myosin, and so on. Several investigators using this approach observed significant increases in response to feeding phenethanolamines. α-Actin mRNA abundance was increased by feeding ractopamine to pigs (Bergen et al., 1989; Helferich et al., 1990; Grant et al., 1993). Increased α-actin mRNA abundance was also observed in muscle of sheep fed the beta-agonist L-644,969 (Koohmaraie et al., 1991). Smith and co-workers observed elevated myosin mRNA abundance in cattle fed clenbuterol and ractopamine (Smith et al., 1989; 1995). These results are interpreted as evidence for increased rate of transcription in muscle as well as increased stability of RNA that would lead to greater rates of mRNA synthesis in muscle fibers. Whether these events are linked to protein kinase A activation via cAMP is not known.

Protein degradation is usually determined by differences between measured fractional protein accretion and synthesis rates, rates of urinary 3-methyl histidine excretion, or by measurement of protease activities in muscle tissue (Goll et al., 1998). Common among results of many studies is the indication that muscle protein degradation may be reduced or not affected in animals administered phenethanolamines that enhance muscle growth rate. Examples include total body and urinary excretion of 3-methyl histidine, indicative of a 25% reduction in fractional degradation rates in rats fed cimaterol for 7 d (Eadara et al., 1989); a 27% reduction in fractional degradation rate of skeletal muscle proteins in steers fed L-644,969 (Wheeler and Koohmaraie, 1992), increased calpastatin mRNA in muscle of steers receiving close arterial infusion of cimaterol (Sun et al., 1994), and elevated calpastatin activity in sheep and bovine muscle of animals fed the beta-agonist L-644,969 (Kretchmar et al., 1990; Koohmaraie et al., 1991; Wheeler and Koohmaraie, 1992; Pringle et al., 1993; and Killefer and Koohmaraie, 1994). Similar effects were reported by Bardsley et al. (1992) and Parr et al. (1992). Ractopamine-fed pigs fail to exhibit increased calpastatin activity or mRNA, however (Ji et al., 1991). Because accurate direct methods for measurement of protein degradation rates are not available, definitive conclusions regarding effects of repartitioning phenethanolamines cannot be made at this time.

**Implications**

A rapid increase in fractional rate of muscle protein synthesis occurs with oral administration of β-agonists, and some, but not all (ractopamine), may reduce fractional protein degradation rates. This appears to be a receptor-mediated response, rather than an endocrine-dependent one. A critical area for research is the need to identify specific β-receptor subtypes in muscles of livestock species and determine their role in growth enhancement. Subtype-specific agonists and antagonists must be used to investigate mechanism(s) of regulation for these phenethanolamines. New technologies such as creation of β-receptor subtype gene knockout animals, use of specific antibodies to β-receptor subtypes, and use of transgenic approaches to alter their function, or their expression, will reveal the details of the mechanisms by which these repartitioning phenethanolamines enhance muscle growth and reduce fat accretion.

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**Beta-Adrenergic receptor modulation of adipocyte metabolism and growth**

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**ABSTRACT:** β-Adrenergic receptor (βAR) agonists reduce body fat in mammals and birds. Synthetic lipid metabolism is decreased in βAR agonist-treated animals or in agonist-treated adipocytes in vitro. Degradative lipid metabolism is increased by βAR agonists in adipocytes in vitro and in vivo. The βAR agonist effects are blocked by βAR antagonists. In mammalian tissues, there are at least three distinct βAR subtypes; β-1 (β1AR), β-2 (β2AR), and β-3 (β3AR). Individual tissues have different proportions of subtypes. For example, greater than 85% of the βAR in rat heart is β1AR, in guinea pig lung is β2AR, and in rat adipose tissue is β3AR. Subtype distribution within a tissue varies with species (e.g., human heart has 65% β1AR and porcine adipocytes have less than 10% β3AR). There is species variation in the amino acid sequence of a βAR subtype. Thus, it is expected that some βAR agonists would have different effects in the same tissue in different species because of different βAR subtype distribution and(or) amino acid sequence. In support of these concepts, the pharmacology of βAR agonists and antagonists in adipocytes is in many cases species-specific. Cloning of individual βAR subtypes allows determination of the pharmacology of subtypes from that species. For example, the pharmacology of the cloned porcine β1AR, β2AR, and β3AR indicates selected agonists or antagonists can be used to assess the proportion of βAR subtypes. Nucleic acid sequences of the subtypes were used to prepare probes to quantify the subtype mRNA. The pharmacological and mRNA data agree rather closely and indicate porcine adipocytes contain over 70% β1AR. The effects produced by a βAR agonist (or antagonist) on adipose tissue in vivo depend not only on the species and the adipocyte βAR subtype distribution, but also on the pharmacokinetics and pharmacodynamics of the compound in that species, including blood flow to the tissue, and the multiple metabolic and endocrine effects of the compound in other tissues of the body. In short, it is expected that individual βAR agonists would have somewhat different effects in different species.

Key Words: Adipocytes, Beta-Adrenergic Receptors, Growth, Metabolism

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**Introduction**

Understanding the mechanisms by which β-adrenergic receptor (βAR) agonists modulate adipocyte metabolism and growth requires familiarity with the family of membrane-bound βAR subtypes. This paper describes the physiological functions and biochemical characteristics of these receptors, including subtypes, tissue distribution, and species variation. This information provides the basis for discussing animal responses to oral administration of βAR agonists and effects on adipocyte metabolism and fat deposition. Secondary vs primary mechanisms of action are also discussed.

β-adrenergic Receptors

The βAR are cell-surface receptors that interact with stimulatory G-proteins (Gs-proteins) to activate the enzyme adenylate cyclase. Adenylate cyclase synthesizes cAMP, the intracellular messenger for responses to βAR. The physiological ligands for the βAR are the neurotransmitter norepinephrine and the adrenal medullary hormone epinephrine. Norepinephrine, in addition to being a central nervous system and peripheral sympathetic nervous system neurotransmitter, is present in the plasma and can act as a hormone. There are a large number of synthetic analogs of norepinephrine and epinephrine, some of which are agonists (bind to the receptor to activate it and stimulate βAR-mediated activity), some of which are antagonists (bind to the receptor, but do not activate it, and thus compete with agonists and inhibit βAR-mediated activity), and some of which are partial agonists (bind to the receptor and partially activate it). The βAR are present on almost
every cell type and control an exceptionally large number of physiological and metabolic functions. Examples are regulation of heart rate and contractile force, blood pressure, bronchial muscle tension, uterine contraction, and glycogen and lipid degradation. As functions of norepinephrine, epinephrine, and synthetic analogs were explored, incredible complexity arose that gave rise to the concept of more than one type of receptor. First, α-adrenergic receptor (αAR) and βAR functions were separated, then the βAR was separated into two subtypes, the β1AR and β2AR. Later, the αAR was separated into subclasses and, finally, evidence was accrued for a β3AR.

The βAR is a continuous protein chain, >400 amino acids in length. It contains seven relatively hydrophobic segments that traverse the cell membrane (transmembrane domains) and are connected by three extracellular and three intracellular segments or loops. Also, there is a N-terminal extracellular tail and a C-terminal intracellular tail. The ligand-binding site is composed of amino acids contributed by several of the transmembrane domains. The binding of the G-proteins occurs primarily through intracellular loop 3. Phosphorylation is one mechanism by which receptor activity is diminished, and there are phosphorylation sites on the C-terminal segment. Selected reviews about βAR structure and function include: Stadel and Lefkowitz (1991), Caron and Lefkowitz (1991), and Strosberg (1992, 1993, 1997). Reviews with emphasis on agricultural species are Mersmann (1989b, 1998), Mills and Mersmann (1995), and Moody et al. (2000).

Animal Responses

The use of βAR agonists to alter body composition of growing animals raised for meat production was reported in the 1960s (Cunningham, 1965). Beginning in the early 1980s, synthetic βAR agonists were shown to affect body composition in several species, including cattle, chickens, pigs, sheep, and turkeys (Ricks et al., 1984). It was not until late 1999 that a βAR agonist, ractopamine, was approved in the United States for use in one of these species, the pig. Oral administration of any of a number of βAR agonists usually causes an increase in daily gain accompanied in many cases by a slight decrease in feed intake with a consequent improvement in efficiency of gain. The striking observation is that βAR agonists preferentially increase skeletal muscle protein mass, which is usually accompanied by a decrease in adipose tissue mass, with little or no change in internal organ size. All of these responses are quite variable and depend on the species, perhaps the breed, the animal age, the sex, the specific βAR agonist used, the dose, the diet, and many other factors that vary in the numerous published studies. There are multiple studies of the effects of βAR agonists on animal growth; among the summaries of these results are Hanrahan (1987), Bergen and Merkel (1991), Beerman (1994), and NRC (1994). A rather complete tabular summarization of studies in various species using a variety of βAR agonists is noteworthy (Moloney et al., 1991), as is a summarization of multiple studies on one agonist, ractopamine, in pigs (Watkins et al., 1990). Attempts to amalgamate data across species and agonists, albeit a gross oversimplification, indicate a hierarchy of responses across species with sheep > cattle > turkeys > pigs > chickens (Mersmann, 1998; Moody et al., 2000). Perhaps one contributing factor to this hierarchy is that some species are closer to their maximal growth response because of intense selection for growth rate; consequently they respond to a lesser extent (e.g., chickens respond much less than sheep).

Factors Leading to Variable Responses

In addition to the variable response observed in different species, even when administered the same βAR agonist, there is considerable variation caused by the use of different βAR agonists. This is to be expected because an individual agonist has not been tailored to all the species in which it has been studied. The rate of absorption, the metabolism of the agonist by various organs, and the excretion rate of the agonist or its derivative(s) dictate the concentration achieved and maintained over time in the plasma, and ultimately at the target organ sites. The many aspects of these pharmacodynamic properties of the agonist, coupled with the blood flow to the target organs, dictate the pharmacokinetic properties of the agonist. For a given βAR agonist, many of these pharmacodynamic properties are expected to vary among species.

The pharmacodynamic properties of a particular βAR agonist administered to a particular species are expected to be influenced by genetic-, sex-, and age-caused variation in drug metabolism and delivery systems. Furthermore, the βAR population on target organs or cell types may be expected to vary not only with species, but also with age and perhaps with breed or sex. Variations in the βAR number on a target cell would be expected to cause variation in the response to a βAR agonist. Examination of the response to a βAR agonist within a species must use a dose × response design because the response of one variable (end point) may have a different relationship to dose than the response of another end point. Thus, for ractopamine-fed pigs, the half-maximal response for improvement in gain is achieved at ~1.5 mg/kg feed, whereas the half-maximal response for improvement in dressing percentage is achieved at ~10 mg/kg feed (Moody et al., 2000). Likewise, comparison of a given βAR agonist across species can only be validly accomplished when the studies utilize a dose × response design because a dose that may be maximal in one species may be far less than maximal in another species. Factors influencing response to βAR agonists have been discussed previously (Mersmann, 1989b, 1995, 1998).

Dietary components may influence absorption of the drug, they may modify the transport of the drug, or they
may increase or decrease the metabolism or excretion of the drug. With an anabolic agent such as a βAR agonist, the protein content of the diet must supply sufficient essential amino acids for optimal protein synthesis to allow expression of the anabolic properties of the βAR agonist on muscle synthesis (Mitchell et al., 1991; Dunshea, 1993; Moody et al., 2000).

**Fat Deposition**

Mammals fed βAR agonists generally have decreased carcass fat, as indicated by backfat thickness or trimmed fat from commercial cuts (Moloney et al., 1991). As genetic selection for lean carcasses has continued, there is less subcutaneous fat, particularly in pigs. Thus, because the control pigs have less fat, a treatment to reduce fat deposition is more difficult to detect. Regardless, in most βAR agonist-treated animals, there is a numerical decrease in carcass fat, even if the data do not always achieve statistical significance. When comparative slaughter techniques are employed to calculate deposition rates, the rate of muscle or protein deposition is increased, whereas the rate of fat deposition sometimes is not significantly reduced (Mitchell et al., 1991; Dunshea, 1993; Chwalibog et al., 1996). If measured at a constant time (age), the βAR agonist-treated animals weigh more and have more muscle mass; thus, even an unchanged rate of fat deposition translates to a lesser percentage of fat per animal. If measured at constant weight, the βAR agonist-treated animals have more muscle mass; even with an unchanged fat deposition rate, there is less fat mass because the βAR agonist-treated animals grow faster and are measured at a younger age. The overall conclusion is that βAR agonists decrease carcass fat in growing mammals and birds.

**Adipose Tissue Lipid Metabolism**

The βAR agonists markedly increase adipocyte degradative lipid metabolism. Activation of the βAR causes an increase in cAMP that activates protein kinase A, which in turn phosphorylates hormone-sensitive lipase. Phosphorylated lipase is the activated form that initiates the degradative process, lipolysis. Fatty acids are produced and, to a large extent, exported from the adipocyte to be used as oxidative fuels by other tissues. Fatty acid synthesis and the esterification of fatty acids into triacylglycerol, the primary energy storage in the adipocyte, are both inhibited by βAR agonists. Thus, an increase in catabolic and a decrease in anabolic lipid metabolic processes in the adipocyte would both lead to decreased hypertrophy of the adipocyte with a consequent decrease in fat deposition. Much of these data have been summarized (Smith, 1987; Mersmann, 1989b, 1995, 1998; Mills and Mersmann, 1995).

The synthetic βAR agonist isoproterenol and the physiological agonists norepinephrine and epinephrine each increase adipocyte degradative lipid metabolism and decrease synthetic lipid metabolism in vitro. One enigma is that, overall, the βAR agonists that cause changes in body composition, including decreases in fat deposition, are not particularly potent or effective agonists to modulate adipocyte lipid metabolism in vitro (Mills and Mersmann, 1995). These results may represent artifacts of the studies in vitro because the βAR agonist clenbuterol, which does not increase porcine adipocyte lipolysis in vitro, increases plasma fatty acid concentrations when infused in vivo (Mersmann, 1987; Hu et al., 1988). An increase in plasma nonesterified fatty acids usually results from an increase in adipocyte lipolysis.

**βAR Subtypes**

There are three well-documented βAR subtypes: β1AR, β2AR, and β3AR. Evidence for these subtypes initially came from classic pharmacological studies of organ, tissue, and cell systems using not only norepinephrine and epinephrine, but also numerous synthetic agonists and antagonists. These approaches were followed by ligand binding to membranes from various tissues. It became obvious that certain tissues contained primarily one receptor subtype. For instance, rat heart contains mostly β1AR (> 90%), guinea pig bronchi contain mostly β2AR (> 85%), and rat adipocytes contain mostly β3AR (> 90%). These tissues, or membranes prepared from them, were prototypes used to study an individual βAR subtype with minimal interference from other subtypes. The individual βAR subtypes were eventually cloned and expressed in cells without endogenous βAR so that the properties of a single βAR subtype could be studied without interference from other subtypes. Using prototypical tissue or membrane preparations and, later, cloned subtypes expressed in cells, individual agonists and antagonists could be classified regarding their specificity for a subtype. A few agonists and antagonists were discovered that had considerable specificity for a single subtype. Thus, CGP 20,712 is considered a β1AR antagonist, ICI 118,551 is considered a β2AR antagonist, and BRL 37,344 is considered a β3AR agonist. These subtype-specific agonists and antagonists have become classic reagents to classify the βAR subtypes in other tissues and species. However, such results must be considered tentative because the subtype specificity of these classic reagents is based solely on their interaction with prototypical receptors. Usually nothing is known about the subtype specificity of the classic agonist or antagonist in the species of interest. Overviews of the βAR subtypes with emphasis toward agricultural species are Mills and Mersmann (1995), Mersmann (1995, 1998), and Moody et al. (2000).

The βAR subtypes have now been cloned from a number of species. These include the porcine β1AR (Cao et al., 1998), β2AR (Liang et al., 1997), and β3AR (Smith and Mills, personal communication) and the bovine
β1AR (Ha et al., 1999), β2AR (Einspanier et al., 1997), and β3AR (Pietri-Rouxel et al., 1995). The β1AR is the largest of the three subtypes with approximately 460 amino acids. The β2AR has approximately 420 amino acids and the β3AR has approximately 410 amino acids. The homology for the three subtypes within a given species is usually between 45 and 60%, whereas the homology for a given subtype is rather high across species (usually > 70%). Although there is strong homology for a given subtype across species, the variation in amino acid sequence allows for considerable variation in ligand binding or functional properties of these homologous receptors. Consequently, it should not be assumed that a classic agonist or antagonist designated as specific for a βAR subtype (based on activities with prototypical receptors) will have the same subtype specificity in another species. For example, cloned human, mouse, and bovine β3AR expressed in Chinese hamster ovary (CHO) cells respond to propranolol (a classic βAR antagonist) in different ways; propranolol is an agonist for the mouse β3AR but a partial agonist for the human and bovine β3AR (Pietri-Rouxel et al., 1995).

Tissue Variation in Distribution of βAR Subtypes

Although the prototypical tissues contain a predominant proportion of a single βAR subtype (e.g., rat heart has > 90% β1AR), other tissues have a more equal distribution of the β1AR and β2AR subtypes. The β3AR has a limited tissue distribution, being present at high concentration in adipose tissue of some species (e.g., rats but not humans or pigs), and is expressed at substantial levels in selected areas of the gut (Mersmann, 1998). Considering only the β1AR and β2AR, in humans there is approximately 35% β1AR in adipose tissue, 27% β1AR in the lung, and 20% β1AR in the liver (Sano et al., 1993).

The βAR subtypes may change with growth/age of the animal. For example, undifferentiated preadipocytes from the rodent-derived clonal cell line 3T3-F442A have predominantly β1AR with essentially no β3AR, whereas the differentiated adipocytes have > 90% β3AR (Feve et al., 1991). Thus, the age of an animal may dictate the response to an exogenous βAR agonist because the βAR are less developed, or the proportion of the βAR subtypes may be altered during development. Of course, many other physiological responses of the animal may change with age to modify the pharmacodynamic and pharmacokinetic properties of a βAR agonist in vivo.

βAR Subtypes in Agricultural Species

Compared with a prototypical tissue wherein a single βAR subtype predominates (e.g., rat heart with ≥ 90% β1AR), the proportion of that receptor subtype in the same tissue from another species may be lower. For example, based on mRNA concentrations, the pig heart has 72% β1AR and pig lung has ~ 67% β1AR, rather than the > 85% β2AR in the prototypical guinea pig lung (McNeel and Mersmann, 1999). Based on ligand-binding studies, bovine muscle has almost exclusively β2AR (Silence and Mathews, 1994), whereas bovine (Silence and Mathews, 1994; Van Liefde et al., 1994) and ovine (Bowen et al., 1992) adipose tissue have predominantly β2AR. These ligand-binding results must be considered tentative because a single classic β1AR and β2AR antagonist was used to classify receptor subtypes and there has been no verification that the antagonists used have any specificity for the bovine or ovine β1AR or β2AR. Extensive pharmacological measurements using porcine adipose tissue, isolated adipocytes, and ligand binding to adipocyte membranes have clearly indicated that the βAR present do not respond to classic βAR subtype-specific agonists or antagonists, as do prototypical βAR subtypes (Mersmann et al., 1993; Mills and Mersmann, 1995). The cloned porcine β1AR (Cao et al., 1998) and β2AR (Liang et al., 1997, 2000) have been expressed in CHO cells so that the pharmacology of a single porcine βAR can be assessed. The uniqueness of the pharmacology of these porcine βAR subtypes has been verified; the classic β1AR antagonist CGP20712 is highly specific for the porcine β1AR, but the classic β2AR antagonist ICI 118,551 has no specificity for the porcine β2AR, whereas a classic β3AR agonist, BRL 37,344, is relatively specific for the porcine β2AR (Scott Mills, personal communication). These results clearly indicate the species specificity of the pharmacological response of a βAR subtype and also force the conclusion that use of classic βAR subtype-specific agonists or antagonists to classify βAR subtypes in other than the prototypical species produces, at best, tentative conclusions.

Using compounds specific for the cloned porcine β1AR and β2AR, it has been estimated that porcine adipocytes have ~75% β1AR (Scott Mills, personal communication). Using quantitative measurement of the mRNA for porcine βAR subtypes, it has been estimated that porcine adipocytes contain ~73% β1AR, ~20% β2AR, and ~7% β3AR (McNeel and Mersmann, 1999). Based on mRNA concentrations, the proportion of βAR subtypes in other pig tissues was estimated (McNeel and Mersmann, 1999), but these results have not been verified by ligand binding. There are no reports of βAR subtypes in cattle or sheep tissues using appropriately controlled mRNA measurements or ligand binding assessments using agonists or antagonists verified as specific for the βAR subtype of interest.

Secondary Mechanisms

In addition to direct effects on adipocytes, systemically delivered βAR agonists can have a number of secondary effects that could alter adipocyte metabolism and consequently growth. Blood flow to a variety of tissues is increased in the presence of a βAR agonist; this has been demonstrated in cattle (Eisemann et al.,
1988), sheep (Beermann et al., 1987), and pigs (Mersmann, 1989a). The concentration of a number of hormones may be altered; some of these can directly or indirectly affect the adipocyte. For example, the lower plasma insulin in sheep chronically fed a βAR agonist might lead to decreased lipogenesis and increased lipolysis (Beerman, 1987). Metabolic rate may be increased by βAR agonists, although chronically treated calves (Zimmerli and Blum, 1990), pigs (Yen et al., 1991), and sheep (Rikhardsson et al., 1991) do not have elevated metabolic rates. These and other secondary mechanisms have been discussed previously (Beerman, 1987; Mersmann, 1989b, 1995, 1998).

Conclusions

Although there is considerable evidence for effects of several βAR agonists on adipocyte lipid metabolism, both in vitro and in vivo, in cattle, pigs, and sheep, we will not know the quantitative effect of a βAR agonist on lipid metabolism in a particular species until there are measurements of isotopic flux. Likewise, although there are data suggesting βAR subtype specificity of particular agonists or antagonists in cattle and sheep, we cannot discern the correctness of these speculations until the pharmacological properties of the cloned βAR subtypes from those species are measured. Examination of the properties of the cloned porcine βAR and β2AR has allowed verification of the distribution of subtypes in porcine adipose tissue and has proven the unique pharmacology of the porcine βAR subtypes.

Implications

The diversity of β-adrenergic receptors, the diversity of receptor subtype tissue distribution, and the pharmacology of receptor subtypes imply that individual β-adrenergic agonists would have somewhat different effects in adipocytes and adipose tissue of different species.

Literature Cited


Implications of feedback regulation of beta-adrenergic signaling

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ABSTRACT: Receptor-mediated signals are tightly regulated by feedback inhibition and act to prevent signal overload and to reset the receptor to a changing environment. Short-term regulation (uncoupling) of beta-adrenergic receptors (βAR) involves receptor phosphorylation and uncoupling of the receptor from the G protein Gs. Chronic exposure to ligand leads to reduced receptor number (down-regulation), which results from a combination of receptor internalization and degradation, and decreased mRNA abundance. The extent of βAR regulation is subtype-specific with a rank order of β2AR > β1AR > β3AR. Differences between species are expected also because amino acid sequences differ. Uncoupling and down-regulation of βAR in pig tissues has been demonstrated in vivo and in vitro, although skeletal muscle exhibits a blunted response compared with adipose tissue and changes in mRNA abundance have not been observed. Desensitization presents a challenge especially in the treatment of human disease and may well limit the effectiveness of βAR ligands used to promote livestock production. Pigs fed βAR ligands show a rapid response in growth and feed efficiency that tends to peak during the first 7 to 10 d but declines thereafter toward zero by approximately 6 wk. A similar pattern was reported in rats fed clenbuterol and was accompanied by a 50% reduction in βAR in skeletal muscle. Feeding clenbuterol every 2nd d prevented the decline in the response to clenbuterol and gave a growth response that was equivalent to daily dosing. These data suggest that strategies to prevent or circumvent βAR down-regulation may prolong the agonist response. Intermittent dosing of pigs may present logistical problems. An alternative approach may be to incrementally increase the dose of βAR ligand to compensate for the decline in response or to augment the ligand response by inhibiting the inhibitory G protein Gi.

Key Words: Beta-Adrenergic Receptor, Pigs, Regulation

Introduction

Living organisms operate in a state of imbalance and the neural and endocrine systems have evolved to modify the rates of physiological processes to maintain homeostasis. Whether we have binged on chocolate-chip cookies, fasted for 10 d, or suddenly felt the need to run a marathon, these two systems interact to fine-tune metabolic rate. One of the hallmarks of both regulatory systems is the short-lived nature of the signals produced. The half-life of neurotransmitters is measured in seconds, whereas that of circulating hormones may be minutes to days. The rationale for the need for a system that is short-lived is to permit our systems to reset in order to meet the next challenge. The short-lived nature of chemical messengers extends to receptor molecules and signaling responses. Redressments in these systems are multifaceted and include uncoupling of receptor responses from signaling events, degradation of receptors, and up- and down-regulation of signaling molecules that affect the primary signaling pathway.

The need to regulate can be appreciated by considering several examples of disruption of regulation, including goiter, which results from overstimulation by thyroid-stimulating hormone when thyroid hormones are deficient (Hetzel, 1983), tumor growth due to mutations in signaling molecules (Sebolt-Leopold et al., 1999), and cholera, which results from overstimulation of G-protein signaling cascades (Fishman and Atikkan, 1980). Endocrine signals are tightly regulated so that animals can adapt to changing needs and to prevent the development of pathologies associated with unchecked signaling.

Beta-Adrenergic Receptors and Signaling

The beta-adrenergic (βAR) belong to a large family of seven transmembrane-domain proteins that couple
and signal through guanine nucleotide binding proteins (G-proteins). Three βAR subtypes have been cloned and all signal in a similar manner. The binding of agonist promotes the interaction between the intracellular domains of the βAR and the heterotrimeric G-protein Gs (Strosberg et al., 1993). This interaction catalyzes the exchange of GTP for GDP in the Go subunit and leads to the dissociation of Go from Gβγ. The activated Go activates adenylyl cyclase, catalyzing the synthesis of cAMP from ATP. The cAMP in turn activates protein kinase A (PKA), leading to subsequent phosphorylation events. Activation of adenylyl cyclase is terminated by the hydrolysis of GTP by an intrinsic GTPase and Go recombines with Gβγ. Opposing the stimulatory effect of Gs proteins on adenylyl cyclase is the inhibitory action of hormones that signal through Gi, including the α2-adrenergic and adenosine receptors.

The ability of βAR ligands to increase cAMP is measured in terms of potency (sensitivity) and efficacy (maximum response) and can be modified by altering any of the inputs affecting adenylyl cyclase activity. For instance, chronic treatment with a βAR antagonist increases the density of βAR in the plasma membrane and results in an increase in sensitivity (Glaubiger and Lefkowitz, 1977), whereas chronic treatment with a βAR agonist reduces the density of βAR and reduces sensitivity (Pequer et al., 1984). The response to βAR can also be increased by ligands that signal through Gi (Cumbay and Watts, 2001). In this case, the increased response is not a result of increased density of βAR, but rather a component of G-protein signaling. In contrast, conditions in which Gi is elevated result in reduced efficacy of βAR ligands (Tepe and Liggett, 2000).

**Desensitization of βAR Signaling**

Desensitization is defined as the attenuation of response despite continued presence of the stimulus and has been demonstrated in a variety of systems. One early report from the Lefkowitz group demonstrated that frogs given four doses of isoproterenol over 24 h had greater than 50% reduced stimulation of erythrocyte adenylyl cyclase (Mukherjee et al., 1975). Similar changes were induced in adipocytes from hamsters given once-daily subcutaneous injections of epinephrine for 6 d (Pequer et al., 1984). The primary alteration was a reduced maximal response to isoproterenol for the stimulation of glycerol release, cAMP accumulation, and adenylyl cyclase activity, with no appreciable change in sensitivity to isoproterenol. Reduced responsiveness of adipocytes has been observed also in rats with a norepinephrine-secreting tumor (Prokocimer et al., 1988). However, in this instance reduced sensitivity to isoproterenol was more pronounced than was reduced maximal response. The effects of chronic elevation of catecholamines shown for adipocytes and erythrocytes appear to be a general phenomenon and likely extend to most, if not all, tissues that express βAR.

The βAR ligand-mediated desensitization has been demonstrated in several in vitro systems, including ventricular strips (Temma et al., 1985), adipocytes (Mills and Orcutt, 1989; Ding et al., 2000), and a variety of cell lines (Su et al., 1980). The primary alteration is at the level of the βAR itself or βAR-Gs coupling, because adenylyl cyclase activity assessed by direct activation or via Gs is not impaired under conditions in which signaling through the βAR is reduced (Mukherjee et al., 1975; Hausdorff et al., 1990). Increased inhibitory activity of Gi was ruled out in studies in which Gi was inactivated with pertussis toxin, but recent studies have implicated some role of Gi in contributing to the reduced signaling through adenylyl cyclase (Tepe and Liggett, 2000).

**Mechanisms of Agonist-Induced Desensitization**

Multiple mechanisms contribute to desensitization and can be divided into acute “uncoupling” responses and chronic “down-regulation” responses (Figure 1). Uncoupling of the βAR from Gs prevents signaling to adenylyl cyclase and represents the post-stimulation sequence that prepares the βAR for re-stimulation. Uncoupling is initiated within seconds to minutes of agonist exposure and the extent of uncoupling is closely related to the potency of the ligand to stimulate adenylyl cyclase (Su et al., 1979; Su et al., 1980). Desensitization by partial agonists is directly related to their ability to activate adenylyl cyclase, whereas antagonists do not induce uncoupling (Su et al., 1980). Uncoupling is further characterized as being quickly and completely reversible upon agonist removal, does not require the synthesis of new protein, and does not involve a change in receptor density (Su et al., 1980; Hausdorff et al., 1990).

The primary mechanism for uncoupling involves phosphorylation of the βAR, which interferes with coupling to Gs. In addition, the uncoupled βAR has a reduced affinity for agonists that decreases the signaling response at submaximal ligand concentrations. Two kinases are involved in βAR phosphorylation. The first is a true “feedback” regulation by PKA, which is activated by cAMP from adenylyl cyclase (Hausdorff et al., 1990). Phosphorylation by PKA alters the conformation of βAR and its affinity for Gs. Because cAMP is a second messenger for a number of hormones, regulation by PKA can phosphorylate and uncouple the receptor involved in initiating the signal (homologous regulation) or other G protein-coupled receptors (heterologous regulation) (Richelsen and Pedersen, 1985; Hausdorff et al., 1990). A second family of kinases, the G-protein coupled receptor kinases (GRK), includes soluble enzymes that mediate only homologous desensitization. The specific enzyme that phosphorylates Ser and Thr residues in the carboxy tail of the βAR is βARK1 (β-adrenergic receptor kinase 1). The βARK1 enzyme phosphorylates only agonist-occupied βAR, or that con-
Figure 1. Cellular signals involved in β-adrenergic receptor uncoupling and down-regulation. Initial steps in desensitization are similar for uncoupling and down-regulation. Agonist binding leads to phosphorylation of the βAR by the kinases PKA and BARK I (A). The βAR subsequently binds β-arrestin (βAR-Arr), which effectively uncouples the receptor from further G-protein activation (Gsα). The βAR is reactivated and recycled to the plasma membrane following dephosphorylation in intracellular vesicles. (B) Down-regulation differs from uncoupling in that internalized βAR are degraded in lysosomes and mRNA abundance for βAR may be decreased. Both processes contribute to a reduction in total βAR in the plasma membrane.

formation of the βAR induced by agonist binding (Liggett and Lefkowitz, 1994).

The sequence of events that results in βAR phosphorylation has been determined (Liggett and Lefkowitz, 1994). Upon ligand binding and Gs activation, Gsα associates with adenyl cyclase, leaving Gs(βγ) tethered to the membrane in close proximity to the βAR. The βARK1 enzyme binds Gs(βγ), effectively targeting the kinase to the βAR. The agonist-occupied receptor has a high affinity for βARK1, resulting in phosphorylation of multiple residues. Phosphorylation by βARK1 increases the affinity of the βAR for one of the arrestin family of proteins (β-arrestin). The binding of β-arrestin causes steric hindrance of βAR association with Gsα and interrupts signaling. Receptors are subsequently reactivated by a process that involves sequestration and internalization into cytoplasmic vesicles, dephosphorylation, and recycling to the plasma membrane (Jockers et al., 1996; Kallal et al., 1998). Desensitization may also involve activation of Gi and inhibition of adenylyl cyclase (Tepe and Liggett, 2000). It has been shown that PKA phosphorylation of βAR increases the affinity for Gi, thus effectively switching signaling pathways from Gs to Gi.

Down-regulation is defined as a decline in the total number of βAR and contributes to desensitization from chronic exposure to agonists. Down-regulation develops more slowly than uncoupling, taking hours to days in cell culture systems (Su et al., 1980; Hausdorff et al., 1990) or in vivo (Mukherjee et al., 1975; Pequerey et al., 1984). The rate of decline in βAR binding sites is related to potency and efficacy of the drug (Su et al., 1980; Hausdorff et al., 1990). High concentrations of full agonists cause a more rapid decline in βAR binding, but even low concentrations of full agonists and partial agonists lead to loss of βAR number that is equivalent to that induced by a full agonist. Antagonists do not cause down-regulation, and in fact they have been shown to induce a compensatory increase in βAR number and responsiveness (Glaubiger and Lefkowitz, 1977).

Recovery from down-regulation is also slower than that from uncoupling, taking days in cell culture (Su et al., 1980). The total βAR protein content of a cell is the sum of the rates of synthesis and degradation, and it seems that both processes may contribute to the decline. Degradation of βAR involves endocytosis and hydrolysis in lysosomes. The process of endocytosis requires βARK1 and β-arrestin, the latter of which binds to caltherin in coated pit regions of the plasma membrane and initiates endocytosis (Lefkowitz, 1998). If βARK/β-arrestin are involved in both uncoupling and down-regulation, it is not clear whether these processes are always linked or a switch is made to induce down-regulation. It now appears that endocytosis is far more complex than simply βAR degradation and includes βAR reactivation and the activation of alternative signaling cascades (Lefkowitz, 1998).

Down-regulation of βAR occurs in cell lines expressing βAR genes that lack promoter elements, indicating that changes in expression are not required for down-regulation. Nonetheless, chronic exposure to βAR ligands leads to a decrease in mRNA abundance for the β1AR and β2AR (reviewed by Liggett and Lefkowitz, 1994) and likely contributes to the full decline in βAR protein.
Subtype Differences

Phosphorylation is a key element of desensitization, so it is logical that subtype difference in phosphorylation may determine rates and extent of desensitization. For the human βAR, the β2AR contains two potential PKA sites and 11 βARK sites, whereas the βAR has only one PKA site and 10 βARK sites. The β2AR is the most divergent, having no PKA sites and only three βARK sites (Hausdorff et al., 1990). Small differences have been noted between the β1AR and β2AR (Zhou et al., 1995), but the β2AR is resistant to short-term uncoupling responses (Granneman, 1992; Liggett and Lefkowitz, 1994). Chronic down-regulation of the β3AR may not involve the mechanisms outlined above because it appears to be absent in some cell types (Nantel et al., 1993; Liggett and Lefkowitz, 1994) but has been shown to develop slowly in others (Nantel et al., 1993). The pig βAR have been cloned and the putative phosphorylation sites are similar to those found in human βAR (Liang et al., 1997; Cao et al., 1998; Smith et al., 2000). The pβ1AR has one potential PKA site and 10 Ser + Thr residues in the carboxy tail for βARK phosphorylation. The pβ2AR may have only one PKA site and 14 Ser + Thr residues. We would predict, therefore, that desensitization would be similar in the pig as described for other species. The pβ3AR is similarly deficient in potential phosphorylation sites and its regulation would be expected to differ from the β1AR and β2AR.

Desensitization of Pig Tissues

Clenbuterol and cimaterol are two βAR agonists that induce muscle hypertrophy in rodents and are accompanied by a down-regulation of βAR in muscle tissue (Rothwell et al., 1987; Kim et al., 1992). Cimaterol similarly induced βAR down-regulation in pig skeletal muscle (Smith, 1989). Chronic feeding of ractopamine to swine reduced βAR in adipose tissue 25% after 1 d and up to 50% by 7 d (Spurlock et al., 1994). Curiously, however, significant βAR down-regulation was not detected in skeletal muscle and only trends for a decrease were observed. Smith (1989) also did not detect down-regulation of βAR in skeletal muscle of pigs fed ractopamine. Why do the adipose and muscle tissues appear to differ? One possibility is that βAR subtypes are distributed and regulated differently or that ractopamine preferentially targets one subtype. Indeed, the β3AR accounts for 75% of the βAR in adipose tissue and only 50% in skeletal muscle (Liang and Mills, 1999; McNeel and Mersmann, 1999). It is unknown whether these subtypes respond differently to elevated ligands, but ractopamine does not show specificity for one subtype over the other. Another possibility is that ractopamine might stimulate the synthesis of new βAR protein in skeletal muscle and effectively mask down-regulation. In adipose tissue, the decrease in βAR is consistent with the observed 40% decrease in rates of lipolysis and a twofold decrease in sensitivity to ractopamine (Mills et al., 1990). In vitro incubation of pig adipocytes with isoproterenol reduced total βAR binding sites 40% but did not affect mRNA abundance for either the β1AR or β2AR (Ding et al., 2000).

Implications of βAR Desensitization

There is little question that desensitization can affect physiological processes and therapeutic approaches to the treatment of disease. For instance, a decrease in βAR density and responsiveness to catecholamines in heart muscle may precipitate heart failure (Choi and Rockman, 1999). Furthermore, βAR agonists are often administered to counteract desensitization in heart muscle, but the treatment may instead hasten desensitization and the loss of effectiveness of administered drugs (Colucci et al., 1981).

Animals treated with βAR agonists exhibit growth patterns indicative of desensitization. Weight gain in rats fed clenbuterol was increased 20% over the first 7 d, but the response diminished to zero by d 14. A similar pattern for weight gain was shown for pigs fed ractopamine (Williams et al., 1994) or L-644,969 (Convey et al., 1987). Maximal responses were observed in the first week to 10 d followed by a decline in the response to each drug to near zero by wk 7. Further, we favor the idea that down-regulation of βAR in adipose tissue prevents full expression of the βAR response and may lead to little or no change in the rate of fat accretion (Dunshea et al., 1993; Liu et al., 1994). If desensitization limits the effectiveness of βAR ligands, it is doubtful that effects are fully lost because removal of the ligands from the diet invariably results in a reversal of the favorable change in body composition (Jones et al., 1985; Mills and Orcutt, 1989).

Circumventing Desensitization

The question of greatest interest is, does desensitization limit the effectiveness of βAR agonists to modify growth and composition, and how can desensitization be prevented or overcome? One approach tested in rats was to feed clenbuterol every 2nd d, thereby allowing the βAR system an opportunity to reset (McElligot et al., 1989). Intermittent feeding seemed to prevent desensitization because growth rate was stimulated by clenbuterol to a similar extent at each supplement interval over 14 d, whereas rats fed clenbuterol continuously showed no response by d 14. Overall, growth rate and skeletal muscle gain were the same in the two groups, but the intermittently-fed rats received 50% less clenbuterol. It is not known whether intermittent feeding is advantageous over longer time periods. A second approach may be to incrementally increase the dose of drug to compensate for the decline in response. Drs. Schinckel and Richert at Purdue are taking this approach to determine whether a greater response can be achieved with ractopamine.
Compensatory desensitization is a well-characterized response to chronically elevated agonist concentration that results in a net loss of beta-adrenergic receptors (βAR) from the plasma membrane and reduced tissue response. The ability of βAR agonists to affect pig growth and alter body composition may well be limited by βAR desensitization. Experimental approaches should be investigated to determine the extent to which desensitization limits drug response, and to develop practical approaches to optimize the effectiveness of exogenously administered compounds. Three βAR subtypes have been cloned from mammalian species and most tissues express more than one subtype. It is not known which βAR subtypes are linked to growth responses in the pig or how βAR agonists affect the balance of synthesis and degradation of each subtype in different tissues. Answers to these questions may lead to targeting strategies that improve the efficacy of βAR ligands.

**Implications**

Compensatory desensitization is a well-characterized response to chronically elevated agonist concentration that results in a net loss of beta-adrenergic receptors (βAR) from the plasma membrane and reduced tissue response. The ability of βAR agonists to affect pig growth and alter body composition may well be limited by βAR desensitization. Experimental approaches should be investigated to determine the extent to which desensitization limits drug response, and to develop practical approaches to optimize the effectiveness of exogenously administered compounds. Three βAR subtypes have been cloned from mammalian species and most tissues express more than one subtype. It is not known which βAR subtypes are linked to growth responses in the pig or how βAR agonists affect the balance of synthesis and degradation of each subtype in different tissues. Answers to these questions may lead to targeting strategies that improve the efficacy of βAR ligands.

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Communicating value to cattle producers: Issues, opportunities, and looking ahead

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ABSTRACT: Price systems in the beef industry have failed to communicate needed changes to producers. The lack of alignment between what is produced and what consumers want and are willing to pay for pushed beef demand down nearly 50% from 1980 through 1998. Ineffective grades allowed the price-driven system to fail, and current public policy blocks needed changes in quality grades for fresh beef. Product attributes of importance to consumers, such as tenderness, have not been identified and brought into the pricing process. In the presence of a failed pricing system, producers have looked to pricing grids, contracts, and vertical alliances to be paid for value and for investments in genetics and technology. The future will see continued competition between price-based systems and non-price means of coordination and quality control. If grades are not modernized and new technology brought in to allow more attribute identification, the price-based system will continue to disappear. Producers will need to look at alternatives and find the approach that allows them to participate in a beef system that profits from better serving a discriminating and changing consumer. Packers have revised their business models as contractual arrangements and alliances have allowed them to coordinate what they buy with needs for new consumer-friendly products and to accomplish at least a modicum of quality control. Once low-cost commodity operations, the large beef packers are now more nearly quality-oriented. The huge investments in new products and markets they have made are the catalysts that have turned the beef demand picture to the positive. Those investments are important to the industry and will set the future of the beef industry for the year 2010 and beyond. The future of beef can be very positive if needed changes are made to ensure the consumer is better served.

Key Words: Communication, Contracts, Coordination, Prices

Introduction

Demand for beef decreased dramatically from the late 1970s through 1998. The primary reason for the decreases was a growing divergence between the fresh beef offering and what the consumer wanted as consumers’ lifestyles changed. Beef lost over 30% of its market share and cattle inventories decreased from over 132 million head to 91 million head. Many producers were forced out of business and others consolidated to reduce costs. The prices consumers were willing to pay were not sufficient to support a beef industry that had grown to 43 kg in per capita consumption, retail weights, in 1976. By 1993, the inventories were much smaller and per capita consumption was down to 30 kg (Livestock Marketing Information Center, 2000c).

In theory, the price system should keep such a divergence from happening. Price premiums and discounts are supposed to communicate to producers and prompt needed changes in production. In practice, the price system failed as a communication mechanism. Cattle were being sold on broad averages, with little or no price differences for value. Important product attributes such as tenderness were not identified by the quality grades, and price premiums or discounts cannot be generated if tenderness is not identified and brought into the price discovery process. In the presence of a failed pricing system, producers will increasingly look to non-price systems such as vertical alliances for more accurate identification of cattle value and for potential returns to investments in new genetics and new management practices. Cattle producers of all sizes will need to understand the new approaches in order to evaluate whether and how those approaches fit their particular needs and operations.

Background

The value of calves from beef cow herds is derived from beef consumers’ dollars. It is a derived value that, in the long run, will compensate cattle producers as a
residual claimant. The beef system can be described as a supply chain that adds value as the product moves up toward the consumer. Middlemen try to extract a per-animal margin, and retail price minus the combined margins determines the calf price to producers. The individual producer is a residual claimant and has no power to set selling prices.

In the current marketplace, one firm may perform two or more of the economic functions along the supply chain, but the net result is the same. Consumers place a value on the fresh beef offering and decide whether to buy. If beef is offering the quality, consistency, and convenience the consumer is looking for, prices get bid up. If the fresh offering falls short in ways of importance to consumers, the packages stay in the counter and prices are pushed lower. The ability to always extract a margin sufficient to cover all costs weakens in moving from the retailer down through the cattle feeder, but all the "middlemen" want to extract targeted per-animal operating margins.

If all the middlemen margins were constant over time, producer-level prices would move directly with changes at the consumer level. But the margins between the producer and the consumer are not constant. They tend to move up with overall price inflation as labor, packaging, fuel, refrigeration, and transportation costs increase. Figure 1 shows wholesale, retail, and total price spreads for beef across recent decades. The spreads are in dollars per hundredweight, retail weights.

The price spreads are reported by the USDA and the "farm-wholesale" margin is essentially the packer/processor margin and the "wholesale-retail" margin or spread is the margin extracted by the retailer. It is clear that the price spreads have increased over time. Either costs, profits to middlemen, or some combination of the two are increasing. The expanding spreads are one source of downward pressure on producer prices (Livestock Marketing Information Center, 2000c).

The other primary source of downward pressure on producers’ calf and cow prices comes from decreases in consumer-level prices. The price consumers pay to clear the market is pushed down from supply-side pressure when seasonal and cyclical forces increase slaughter levels. The prices consumers will pay for the quantity being offered are also pushed down when they do not like the offering and demand decreases. The supply-side pressures on price are related to time, and although they can last for several years as the cattle cycle moves through the liquidation phase, they do eventually come to an end. When decreasing demand is the problem, the price pressure will last as long as the consumer is dissatisfied with the product offering. Demand will decrease until the problem is fixed and until the sector moves to a “consumer-driven” status.

Sustained problems on the demand side mean the communication system inherent to any marketplace is not working. As lifestyles and eating behavior change, what the consumer wants and is willing to purchase will also change. There must be a communication channel to send a message to producers, a message that both identifies the needed changes and provides an economic incentive for producers to make new investments and adjust their production programs. If there are no effective communications and no recognizable set of economic incentives, what producers offer can increasingly diverge from what consumers want. A market failure has then occurred, and this “failure” is the dominant feature of the beef business in the United States during the decades of the 1980s and 1990s.

Pricing Systems

Price-driven marketplaces with separate profit centers between the producer and consumer dominate the historical literature on the markets in any food sector. In theory, the consumer will send a message, a price premium or a price discount, down through the various profit centers to the producer. Price is bid up at retail on any product offering that finds favor with the consumer. The display counter empties, and the retailer bids up the price to get more of that particular product offering. Increasing prices and profits pull new investments into the sector, and growth in terms of increasing per capita consumption, is seen. The pattern in beef in the 1960s and into the early 1970s was one of growth, and increasing demand was the catalyst.

When retailers have to lower price to get the consumer to take the product offering, just the opposite occurs. Lower prices are pushed down toward the producer, and downsizing, disinvestment, and a loss of market share are the inevitable results. Dissatisfaction with the product offering brings decreases in demand, and producer-level price decreases can be significant and sustained.

Before turning to what is needed to prompt correct valuations and prices to beef cattle producers, it is useful to look at what happens when there is no effective communication in price-driven systems. It is problems...
in this pricing dimension that cause market failures in economic systems.

A Look at Demand

Demand is the schedule of quantities that consumers will take at alternative prices. If this schedule is plotted with price on the vertical axis, the curved line that results slopes down and to the right. Any price/quantity combination along the line represents the same level or strength of demand. If demand is not changing due to changes in preferences, in incomes, or in prices of substitutes, then any increase in quantity to $Q_2$ will bring a market-clearing price, $P_2$, that is below the earlier $P_1$ price. If quantity decreases due to seasonal or cyclical influences, the smaller quantity, or $Q_3$, will clear the market at a higher price than $P_1$, price $P_3$. Quantity and price change over time with no change in demand. In particular, quantity as measured by per capita consumption can change, and will change, with changes in per capita supply, but such changes in no way indicate whether the level or strength of demand has changed.

Figure 2 illustrates these possibilities. If $Q_1$, $Q_2$, and $Q_3$ are measuring per capita consumption, it is apparent that per capita consumption, which is a measure of per capita supply, can change while demand is constant. A new set of price-quantity coordinates is representing a different level of demand only if they are not on the curve labeled “Demand” in Figure 2.

Figure 3 presents a scatter plot with inflation-adjusted prices of Choice beef at retail on the vertical axis. Per capita consumption as a measure of quantity is on the horizontal axis. The average prices paid for the yearly quantity offered are identified by years in the plot. It is apparent that any negatively sloping line running through 1998, for example, is far below the demand line running through 1980, 1985, or even 1990. Any move down and to the left is a decrease in demand, and the new demand line is below the prior line. If that pattern persists over time, low prices will force producers out of business, reduce per capita supply and per capita offerings, and the result is a loss of market share. That loss is apparent in the decrease in per capita consumption from near 43 kg in 1976 to 30 kg in 1993.

Table 1 presents a demand index developed for the Beef Promotion and Research Board as a part of an industry demand study launched in 1997. The index was calculated using 1980 as a base period (index value of 100) and it declined to 51.45 in 1998. To facilitate monitoring any progress from the 1997 study date, a transformed index with 1997 $= 100$ is also shown in the table. In 2000, the index with 1997 $= 100$ suggests demand was 6.7% above demand in 1997.

The dramatic and sustained decline in demand, running unabated from 1979 or 1980 through 1998, is evidence of a massive market failure. There was no significant response to consumers’ changing wants and no significant and badly needed modification of the fresh beef product offering for nearly 20 yr.

A Failed Pricing System

The beef pricing system of the 1980s and 1990s appears to have failed in its role as a communication system. Many fed cattle sell each week in a few hours at one average price with no significant price discrimination in spite of a huge variation in final quality and value of fed cattle in any pen and in every feedyard. Producers who have invested in superior genetics, production technology, and management expertise get little or no reward if they sell at the average price. There is a subsidy flowing from producers of the high-value cattle in the overall quality and value distribution to producers of the low-value cattle. Schroeder and Graff (2000) estimate the subsidy at $30 per animal.
Table 1. Beef demand index, 1980 through 2000

<table>
<thead>
<tr>
<th>Year</th>
<th>Per-capita consumption, lb</th>
<th>Deflated price, cents/lb</th>
<th>Constant demand price, cents/lb</th>
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*Source: Original calculation. Per capita consumption data and nominal prices can be found at the Livestock Marketing Information Center (2000; http://lmic1.co.nrcs.usda.gov/, Members Only section, spreadsheet SUMQ.xls and RETMT.xls). The Consumer Price Index used to deflate the prices is available at the Bureau of Labor Statistics (http://stats.bls.gov/cpihome.htm).

The reasons for the long-running decrease in beef demand are widely known, and they are associated with the effectiveness of the price system (Schroeder et al., 2000). Moving through the 1980s, consumers were increasingly concerned about fat and cholesterol levels and they were willing to pay for convenience in the form of a reduction in meal preparation time (Purcell, 1993). Perhaps most important, consumers of fresh beef or beef entrees in their favorite restaurant wanted a consistent, high-quality eating experience. Instead of consistency, consumers were treated to a fresh beef offering with Choice cuts that were often tough. A “quality concerns” strategy workshop that examined the findings of the national beef quality audit conducted in 1991 ranked excessive external fat, excessive seam fat, low overall palatability, and inadequate tenderness numbers 1 through 4 in the top 12 list of concerns about beef quality (NCA, 1992).

The failure of the pricing system to provide coordination between what is produced and what consumers want has roots in both the public and private sectors. Public quality grades for beef are administered by the Agricultural Marketing Service (AMS) of the USDA on a user fee basis. The policy of AMS is to change the grades for any food or fiber product only when the industry demands change. The last significant change was in the late 1970s when the industry supported a move to “flatten” the marbling requirements against age of the animal. The argument was that declining age of the steer and heifer at slaughter would compensate for lack of marbling. To the extent that marbling is correlated with tenderness, this reduction in marbling requirements for the Choice grade may have contributed to the tenderness problem of the 1980s and 1990s.

The economic purpose of grades in any food product is to identify and categorize the product attributes of importance to the final consumer. In beef, if any attribute such as tenderness varies significantly within a grade such as Choice, the necessary conditions for effective price signals are not met. There is no price signal mechanism for consumers to use in sending a message to either encourage production of tender beef or discourage production of tough beef. There is no categorization within Choice beef to which a price signal can be attached. A market failure results and consumers simply walk past the beef counter in the grocery store and order something else at the restaurant, even at their favorite steakhouse. The study by Lusk et al. (1999) indicated that consumers will pay significant premiums for guaranteed tenderness in beef, but tenderness is not identified as part of the quality grade specifications.

Across the 1980s and into the 1990s, the beef quality grades have been inadequate and outdated. Without reference to the widespread concern about consistency across USDA graders, the grade specifications were simply not sufficient. The volatile industry reaction to the late 1990s move to get B-maturity cattle out of the Choice and Select grades made the USDA and AMS leaders even more cautious about changing grades, and the beef quality grade program continues largely un-
changed since the 1970s. Helming (1996) stated that the USDA grading system stifled development and use of branded beef products and blocked value-based beef production and pricing from becoming a reality. Helming (1996) wanted to see the public grades replaced with private grades that included specifications on product attributes such as tenderness that influence the quality of the consumer’s eating experience. However, this call for a dramatic change was buffered by observations on the usefulness of the quality grades in selling to other countries, and exports were starting to grow rapidly in the middle of the decade. There was no widespread support for elimination of public grades and no proposal for new approaches emerging from private firms along the supply chain.

The beef industry of late 2001 will likely not demand a change in grades. Those cattle owners feeding cattle with overall quality below the mean level of the quality distribution are receiving a significant subsidy. This part of the feeding industry will not want a change such as tenderness scores within the Choice and Select quality grades. They fought the proposed change in the B-maturity issue.

The public sector that includes federal agencies and the land-grant university system, perhaps predictably because of long-standing USDA policy, has been slow to make progressive change in the beef grades. As a result, the price-driven system could not prompt the vertical coordination and related quality control so necessary to improvement in the offerings to the consumer market, especially in fresh beef. Market share for beef declined sharply across the 1980s and 1990s. Cattle producers were forced out of business as inflation-adjusted retail prices plunged, even in the presence of declining per capita offerings, and prices were forced down at the cow-calf level.

The private sector reluctance to make changes was predictable and grows out of the way the sector has been structured under the traditional price-driven system. There are a number of profit centers between the original cattle producer and the consumer. Inter-level relationships have been adversarial for decades. Producers and producer groups complained when told by industry experts that they should make sure the new product development work was done and pointed fingers at the packers. But the large packers were following a business model of being the low-cost provider of commodity beef, and they were efficient in that role. The packers had no strong motivation to spend billions of dollars on new product lines when the raw material supply (fed cattle) was heterogeneous, unpredictable, and variable in quality and value. Without quality control to allow them to brand and stand behind their products, the large packers could see no way to build a fence around the benefits of investments in new products and in new markets. The industry drifted and needed corrections were not made.

### The Move to Non-Price Systems

The recent move to non-price means of coordination and quality control was very predictable. The profit opportunities coming from better serving consumers, long ignored, were becoming so apparent that they demanded attention. In-house analysts at the large packers were looking at the massive decline in demand and starting to analyze what could happen if that trend could be reversed. In pork, where grades and the price system had suffered a similar market failure, the move away from price-driven systems occurred at an incredible pace. The largest firm, Smithfield Foods, Inc., acknowledges publicly that some 70% of their kill is from their own genetics in company-owned and contract production programs. As the company achieved a measure of coordination and quality control, they were able to meet a company goal to move into export markets such as Japan, and company profits surged. The message was not lost on other meat packers and processors.

In beef, smaller firms in the further processing business moved first into pre-cooked product and attacked the problems of quality inconsistency and too much time in meal preparation. Contracts, price grids, vertical alliances, and other forms of non-price coordination were developed to help processors buy what they needed for a new product line. Non-price approaches to vertical coordination and quality control are now a reality. As the price-driven system is increasingly being abandoned, processors are identifying and buying the genetics and the quality control they need to serve the consumer with a new and branded product offering. In 2001, the large packers have largely abandoned a business model built around being a low-cost commodity operator and are using price grids, contractual procurement, vertical alliances and quality control and are offering branded and cooked product lines.

It is not impossible for the price-driven system to come back and compete with these non-price systems, but it is not likely to happen. At a minimum, it would appear that the quality grades would need to be modernized or widely used private sector replacements would need to be developed, and neither of these developments appears to be very likely. Instead, vertical alliances are sorting carcasses using in-house measures of tenderness to identify carcasses acceptable for branded and quality-assured product lines. Because these processes and procedures are developed with private monies, there will be less interest in participating in open-market, price-driven systems in which prices are averages and do not reflect the premiums that can be generated from branded beef products.

### What Producers Will Need to Do

Producers looking to be paid for value will have, therefore, two broad approaches they can follow. They can campaign hard to fix the price system to give it a chance to compete with the non-price approaches, or
they can go to the contracts, grids, and vertical alliances.

The price system will not be easy to fix. It will need a change in grades toward a more refined identification of product attributes that influence value to the consumer, and a corollary move to objective and high-tech measures will be essential. Any progressive proposal for change splits the cattle-feeding sector and seed stock producers. Firm-level profits and opportunities to increase those profits are still usually seen as more important than a progressive change for the industry as a whole. That was clear in the sometimes bitter dialogue surrounding the move away from B-maturity cattle. With leading meat scientists saying tenderness is a key factor in consumer acceptability and describing USDA quality grading as “mass inspection” and lacking in precision, those feeding the B-maturity cattle still put their bottom line first and some tried to block the change (Tatum et al., 1999). In the near term, the chances of an industry consensus to incorporate tenderness scores or other more refined measures in the quality grades are small. The price-based system will, in all probability, continue to languish and falter.

In the presence of a failed price system, producers need to look at the non-price coordination opportunities to learn what will be valued in a consumer-driven marketplace, and try to offer what consumers want. Depending on geographical location and the constraints that geography place on genetic mix, the need is to find an opportunity that will reward producer-level investments in technology and management expertise. Individual animal identification and feedback is essential and is increasingly available. No one grid or contract arrangement or alliance will fit every producer’s resource base and opportunities, so there is a need to look and compare. Fortunately, the alliances recognize the reality of geographical and other influences on genetic mixes, and the alliance within a producer’s region will probably fit some or most producer needs. The best situation, arguably, is one in which producers get a significant share of the “premium pool” associated with high-quality cattle moving into premium-priced, branded product lines, and some vertical alliances are offering producers who maintain ownership of their cattle a share of those premiums. It is this set of premiums for high-quality and branded product lines that can expand the number of consumer dollars shared across all participants, and competing for more of those consumer food dollars is very important (Hudson and Purcell, 2001).

**Implications**

The move to non-price systems for beef products will not block all opportunities to make needed changes to give the price-driven system a chance. Modernization of beef grades, including taking into account varying levels of tenderness, would provide needed quality control. The price-driven model can be effective if it has the grades, technology, and policies to allow it to work. In the meantime, it will be the non-price alternatives that offer some chance of “pricing to value,” and it will be the price grids, contract arrangements, and vertical alliances that will likely continue to grow in importance. Producers wishing to be compensated for high-value cattle will need to take a look. If better coordination and quality control is the result of these new systems, both the individual cattle producer and the beef industry as a whole will face a more promising future.

**Literature Cited**


Using genetic tools to meet market targets without sacrificing maternal performance

M. W. Tess

ABSTRACT: Changes in beef production/marketing systems are creating incentives for beef producers to improve carcass quality. Current grid marketing schemes are characterized by premiums for carcasses that excel for marbling and(or) retail product and by large discounts for noncompliance factors. Economic incentives for producers to select for tenderness may be on the horizon. Effective tools are available for producers to genetically tailor cattle to specific markets. New DNA markers for carcass trait QTL will help cattle producers identify genetically superior animals at younger ages. Markers will be used most efficiently when marker genotype information is incorporated directly into the computation of EPD, and after potential epistatic interactions and genotype × environment interactions are characterized for each QTL. Limited research has not identified risks associated with maternal performance due to selection for increased marbling or tenderness. However, selection for increased lean yield carries risks of older age at puberty, increased mature size, decreased fertility, and possibly increased maternal calving difficulty. Systems research indicates that reduced fertility would have large negative effects on profitability. To avoid detrimental effects on maternal traits, genetic management should consider EPD for multiple traits as part of a systems approach. Managers will deal with increasing amounts of information and detailed monitoring of production costs will become increasingly important to success. Structured crossbreeding, exploiting heterosis and breed strengths, should be used to increase profitability of production systems. Management strategies to reduce phenotypic variation in market groups and to match genetic potential with nutritional management are expected to increase competitiveness in grid marketing schemes.

Key Words: Beef Cattle, Carcasses, Genetics, Maternal Transmission, Systems

Introduction

U. S. beef production and beef marketing are changing. Beef production systems are becoming more product-oriented rather than commodity-oriented. Value-based marketing is being stimulated by technologies such as electronic identification and Internet commerce. Production segments are becoming more coordinated, sometimes by formal business alliances, sometimes by improved information transfer and measurement of value.

Industry changes are providing new incentives for genetic changes in carcass traits. Developing technologies are providing new genetic tools for making these changes. Cow-calf producers are challenged to genetically tailor cattle to meet new and dynamic markets, yet continue to manage cattle and natural resources in a sustainable manner.

My objectives are 1) to identify the economic aspects of carcass quality and the traits that will likely receive increased attention in future breeding programs, 2) to anticipate how important maternal traits might change in response to selection for different aspects of carcass quality, and 3) to discuss genetic tools and their application in meeting these new carcass targets without sacrificing maternal performance.

Review and Discussion

Economic Incentives for Genetic Change

Grids. Current marketing systems for fed cattle reflect value differences associated with several traits, most of which are measured after slaughter (USDA, 2001). Primary traits include USDA quality grade and USDA yield grade. Quality grade, largely determined by marbling, is intended to be a measure of palatability (USDA, 1997). Yield grade, determined by carcass weight, longissimus muscle area, fat thickness, and kidney, pelvic and heart fat, predicts retail lean yield. Some systems recognize additional indicators of quality grade
and yield, such as breed identification and muscling. Quality grade and yield grade form the basis of most grid pricing systems (two-dimensional set of premiums and discounts) for individual carcasses and motivate price differentials paid for groups of cattle sold before slaughter. Magnitudes of these premiums and discounts vary seasonally in response to supply and demand factors (LMIC, 2001). Grid prices may also differ among alliances and(or) packers.

Grid marketing schemes normally take into account several compliance factors, measures that largely identify carcasses that cannot be marketed through mainstream channels. Compliance factors include extremes in carcass weight (light or heavy), undesirable levels of maturity, carcasses from bulls or dairy breeds, and dark cutters (USDA, 2001). Essentially, there are no premiums for compliance factors, only discounts. Generally, discounts for the most undesirable quality and yield grades (standard quality grade and yield grades ≥ 4), and for noncompliant carcasses are much larger than premiums paid for desirable quality grades and yield grades. Hence, these carcasses are referred to as “out-cattle” (i.e., cattle that do not fit the grid). Discounts for out-cattle are so severe that it can easily take two or more premium carcasses to balance one noncompliant carcass.

Grid marketing schemes provide incentives for beef producers to genetically improve quality grade and yield grade. In addition, there are strong incentives for producers to avoid marketing out-cattle. Because out-cattle are associated with extreme values for quality grade, yield grade, and carcass weight, the incentive to avoid out-cattle is largely an incentive to market cattle with less phenotypic variability.

**Niche Markets.** Utilizing coordinated networks or integrated systems some beef producers are targeting specialized or niche markets. Generally, these systems market beef products at the retail level with brand name identification. Examples include Laura’s Lean Beef (Laura’s Lean Beef, 2001), Montana Range (Leachman, 2001), and Coleman Natural Products (Coleman, 2001). Product definition varies among systems but usually focuses on a specific aspect of eating quality (e.g., tenderness or leanness) or food safety (e.g., free of antibiotics). Depending on the market niche, producers participating in these systems experience incentives for genetic change that may be different from those for producers marketing through mainstream channels.

Tenderness is considered a very important heritable palatability trait (Dikeman et al., 2001). Tenderness must be measured on cooked meat, and available technology to measure tenderness in commercial packing plants is considered too expensive (NCBA, 1998a). Therefore, there is currently no industry mechanism to provide information feedback to producers on a large scale. Except for production systems marketing branded retail products (e.g., Montana Range; Leachman, 2001), there is currently little economic incentive for producers to select for tenderness. However, due to the importance of tenderness to beef demand, it seems likely that affordable technology will be soon developed to address this issue, and economic incentives for producers to select for tenderness may be on the horizon.

**Genetic Relationships Between Carcass and Maternal Traits**

The components of quality grade and yield grade are moderately to highly heritable (Marshall, 1994; Shanks, 1999; Shanks et al., 2001); hence, selection is expected to be effective in changing these traits. Historically, carcass traits have not received much attention in the breeding plans of U.S. beef producers. As beef producers now focus on carcass traits, answers to important questions are needed: 1) Will selection for improved carcass characteristics lead to undesirable correlated responses in important maternal traits and 2) Will breed substitutions to improve carcass quality negatively affect maternal traits? Regrettably, few experiments focusing on selection for carcass quality have been conducted. Therefore, few correlated selection responses have been documented, and we must rely on less direct types of information. I will focus on three traits: marbling, retail product (or yield grade and its components), and tenderness.

**Marbling.** At the University of Nebraska, Angus sires with high and low EPD for marbling were randomly mated to MARC II composite cows. Progeny were evaluated for growth and carcass traits (Vieselmeyer et al., 1996) and palatability traits (Gwartney et al., 1996). Because heifers were slaughtered, this study provided no information on correlated responses in maternal traits.

Frazier et al. (1999) used field data to evaluate associations of Angus sire marbling score EPD with reproductive performance of females. Marbling score EPD was significantly associated with age at first calving; however, predictors were not consistent across states, even switching signs. Classifying sires into marbling score EPD categories produced inconsistent relationships with age at first calving. The authors concluded that marbling score EPD was not a good predictor of age at first calving or calving interval and suggested that selection for marbling should not affect these maternal traits.

Splan et al. (1998) estimated genetic correlations between male carcass traits and female reproductive traits. Genetic correlations between marbling score and age at puberty, calving rate, and calving difficulty were close to zero (Table 1), suggesting that little change would occur in these maternal traits in response to selection for increased marbling.

As the most popular U.S. beef breed (Taylor and Field, 1999), Angus has served as a benchmark for many breed evaluation studies. Angus cattle have higher marbling scores than most other beef breeds used in the United States (Cundiff et al., 1986). Breed comparisons have not identified problems with age at

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**Table 1: Genetic correlations between male carcass traits and female reproductive traits.**

<table>
<thead>
<tr>
<th>Trait</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at puberty</td>
<td>0.00</td>
</tr>
<tr>
<td>Calving rate</td>
<td>0.00</td>
</tr>
<tr>
<td>Calving difficulty</td>
<td>0.00</td>
</tr>
</tbody>
</table>

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**Shanks et al. (2001);**
puberty, calving difficulty, pregnancy rate, calf crop weaned, or maintenance requirements for beef breeds that rank high in marbling (Ferrell and Jenkins, 1985; Cundiff et al., 1986; Martin et al., 1992).

Retail Product. MacNeil et al. (1984) reported genetic correlations between retail product weight and age at puberty, conceptions/service, maternal calving difficulty, and mature weight (Table 1). Their results suggest that selection for increased retail product weight would lead to older ages at puberty, improved fertility, and increased mature size with no change in maternal calving difficulty.

Retail product percentage and retail product weight are not the same traits but are genetically correlated (0.46, Koch et al., 1982). Splan et al. (1998) computed genetic correlations between female traits and retail product percentage. Correlations reported by Splan et al. (1998) suggest that selection for retail product percentage will lead to no change in age at puberty, a small decline in calving rate, and a slight increase in maternal calving difficulty.

As components of retail product (or yield grade), fat thickness and longissimus muscle area are also of interest. Because breed associations report EPD for these traits, some producers may select for decreased fat thickness or increased longissimus muscle area. Genetic correlations reported by MacNeil et al. (1984) and Splan et al. (1998) indicate that selection for decreased fat thickness would negatively affect age at puberty, fertility, calving rate, and maternal calving difficulty. Selection for increased longissimus muscle area would have no effect on puberty or calving difficulty but would improve calving rate slightly (Table 1). Undesirable associations between maternal traits and retail product appear to be mediated through fat thickness.

Breed comparisons involving breeds that excel for retail product are confounded by the fact that some of these breeds also have high milk production. Restricting comparisons to breeds that have moderate milk but increased growth and lean yield suggests that heifers sired by these breeds tend to be about 1 mo older at puberty and have lower heifer pregnancy rates than breeds with less rapid growth and lean yield (Cundiff et al., 1986; Martin et al., 1992); however, most heifers from these breeds should still reach puberty before their first breeding season under good nutritional management. Means for calving difficulty and calf crop weaned were similar for breeds with moderate vs more rapid growth and lean yield (Cundiff et al., 1986). Bennett and Williams (1994) hypothesized that cows from larger, leaner breeds would require better nutritional management than more moderate types. Nugent et al. (1993) reported that these biological types of cows had shorter postpartum intervals in response to increased feed. Compared to progeny of sires from moderate breeds, progeny of sires from breeds characterized by rapid growth and high lean yield and dams of moderate types are expected to experience more calving difficulty and calf mortality, leading to reduced re-breeding rates in dams (Cundiff et al., 1986).

Feed requirements for maintenance account for over 70% of annual requirements for beef cattle. Many studies have attempted to estimate maintenance requirements for different breeds and biological types (Ferrell and Jenkins, 1985, 1985a,b). In some studies larger, leaner breeds had higher maintenance requirements (Mcal ME/kg^0.75) than more moderate types, but not in others. Ferrell and Jenkins (1985) concluded that maintenance requirements are positively associated with genetic potential for measures of production such as growth rate and milk yield. However, the relationship between maintenance and milk potential seems to be stronger than that between maintenance and growth potential, and U.S. feeding standards (NRC, 1996) do not adjust maintenance requirements upward for larger, leaner breeds. The lack of independence between estimates of maintenance and the efficiency of energy use for growth, and the change in efficiency of energy use for growth with changing energy intake makes estimation and interpretation of these parameters difficult (Ferrell and Jenkins, 1985a,b).

### Table 1. Genetic correlations between maternal performance traits and carcass traits

<table>
<thead>
<tr>
<th>Trait</th>
<th>Age at puberty</th>
<th>Conceptions/service</th>
<th>Calving rate</th>
<th>Calving difficulty</th>
<th>Mature wt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retail product wt</td>
<td>0.30</td>
<td>0.28</td>
<td>-0.02</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>Retail product %</td>
<td>-0.01</td>
<td>0.61</td>
<td>-0.13</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>Carcass wt</td>
<td>0.17</td>
<td>0.61</td>
<td>0.05</td>
<td>-0.31</td>
<td>0.21</td>
</tr>
<tr>
<td>Fat thickness</td>
<td>0.06</td>
<td>0.21</td>
<td>0.19</td>
<td>-0.36</td>
<td>-0.09</td>
</tr>
<tr>
<td>Longissimus muscle area</td>
<td>-0.29</td>
<td>0.21</td>
<td>0.19</td>
<td>-0.36</td>
<td>-0.14</td>
</tr>
<tr>
<td>Marbling score</td>
<td>0.04</td>
<td>0.15</td>
<td>-0.01</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>Warner-Bratzler shear force</td>
<td>0.04</td>
<td>-0.05</td>
<td>-0.14</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Taste panel tenderness</td>
<td>-0.32</td>
<td>0.07</td>
<td>-0.42</td>
<td>0.07</td>
<td></td>
</tr>
</tbody>
</table>

*Correlations involving retail product weight, conceptions/service, and mature weight are from MacNeil et al. (1984). Correlations involving retail product %, longissimus muscle area, marbling score, Warner-Bratzler shear force, and taste panel tenderness are from Splan et al. (1998). When two values are listed, the upper value is from MacNeil et al. (1984) and the lower from Splan et al. (1998). All carcass traits are adjusted to constant age.
Although easily classified as high retail product breeds (Wheeler et al., 1996), Belgian Blue and Piedmontese are distinct from other breeds due to their frequent expression of muscle hypertrophy (double-muscled), a condition caused by the effects of alleles at a single locus (inactive myostatin, Casas et al., 1998, 1999). Compared to homozygous normal animals, individuals carrying a single copy weigh more at birth but experience similar calving difficulty, have larger longissimus muscle area, less fat thickness, and greater retail product yield, yet do not express double-muscled (Casas et al., 1998, 1999). Heifers sired by Piedmontese bulls average 15 to 20 d younger at puberty than Angus or Hereford crossbreds (Thallman et al., 1999; Lammoglia et al., 2000). Pregnancy rates, calving and weaning percentages, and postpartum intervals to estrus for Piedmontese- and Belgian Blue-sired heifers appear to be similar to those for Hereford and Angus crossbreds (Freetly and Cundiff, 1998; Thallman et al., 1999).

**Tenderness.** Splan et al. (1998) reported genetic correlations between two measures of tenderness (Warner-Bratzler shear force and taste panel tenderness) and maternal traits (Table 1). Inconsistencies among correlations for shear force and taste panel tenderness make conclusions difficult; however, their results suggest that selection for increased tenderness should lead to less maternal calving difficulty and possibly younger age at puberty.

Differences in Warner-Bratzler shear force and(or) taste panel tenderness have been demonstrated among several breeds (Marshall, 1994; Wheeler et al., 1996). Generally, tenderness measures for F1 crosses have been within acceptable ranges. *Bos indicus* tends to be less tender than *Bos taurus* breeds. Two breeds that appear to excel for tenderness are Pinzgauer and Piedmontese (Marshall, 1994; Wheeler et al., 1996). The tenderness advantage for Piedmontese does not appear to be associated with the myostatin locus (Casas et al., 1998). Reproductive comparisons involving Piedmontese were reviewed above. Pinzgauer heifers tend to be about 2 wk younger at puberty and have higher pregnancy rates than Hereford and Angus crosses, whereas calving difficulty and calf crop percentages are similar for these breeds (Cundiff et al., 1986; Martin et al., 1992).

**Potentially Sensitive Traits in Range Cow-Calf Production Systems.** Based on this brief review, there is little evidence to suggest that selection for increased marbling or increased tenderness or that substituting with breeds that excel in these traits will lead to declines in maternal performance. It should be emphasized, however, that direct measures of correlated responses to selection have not been reported. On the other hand, selection for increased retail product is expected to lead to older ages at puberty for heifers, heavier mature weight, and possibly increased maternal calving difficulty. Selection for decreased carcass fat thickness is expected to lead to older ages at puberty, decreased fertility and calving rate, and increased calving difficulty. Breed comparisons suggest that compared to moderate breeds, breeds that excel for growth and lean yield are older at puberty, except for the double-muscled Belgian Blue and Piedmontese, which are younger. Breed comparison studies have not identified important differences in maternal calving difficulty or calf crop weaned due to increased growth or leanness.

It is important to know just how detrimental changes in these maternal traits might be to ranch profitability. Using systems analysis techniques (Tess and Kolstad, 2000a,b), Tess (1999) evaluated the effects of changes in several maternal traits on cow-calf enterprise profitability in a range environment. This study demonstrated that system performance was quite sensitive to performance levels for postpartum interval to estrus and mature cow conception rate (i.e., fertility). Postpartum intervals greater than about 70 d led to precipitous drops in gross margin. Gross margin declined in a nearly linear fashion with mature cow conception rate. Together, postpartum interval and conception rate largely determine calving rate. Profitability was relatively insensitive to calving difficulty rate. Increased age at puberty and decreased heifer conception rate led to higher replacement rates, yet their effects on gross margin depended on marketing strategies for cull heifers. If nonpregnant heifers were sold following the grazing season, gross margin was relatively unaffected, essentially shifting income from calves to yearlings. If nonpregnant heifers were given an additional year to breed, gross margin declined after age at puberty exceeded approximately 420 d. Similarly, if nonpregnant heifers were retained profitability declined in a nearly linear manner as heifer conception rate declined.

Most female reproductive traits have a minimum level of performance below which herd size cannot be maintained without purchasing replacements. The results of Tess (1999) suggest that the relationship between profitability and maternal performance is mirrored by the effects of maternal traits on calf weight weaned per cow exposed, or by weight sold per cow exposed. Any genetic or management change that decreases these measures is likely to be detrimental to ranch profit. Estimates of economic weights for fertility have consistently been positive (Kolstad, 1993; MacNeil et al., 1994; Koots and Gibson, 1998a,b).

Several researchers have studied the effects of mature size on beef enterprise profitability. Using systems analysis techniques, Kolstad (1993) found that increases in mature weight for maternal strains, independent of other growth traits, had negative effects on profit. Similarly, MacNeil et al. (1994) reported that the relative economic value of mature weight was negative for maternal strains and general-purpose strains in all production/marketing scenarios studied. Koots and Gibson (1998a) reported that mature weight had a positive economic value in general-purpose lines; however, in their model mature weight accounted for other growth traits. Further, the economic value of mature weight was sensitive to the marketing assumptions and
base trait means (Koots and Gibson, 1998b). Heavier mature weight represents added overhead in terms of feed for maintenance (per cow, Cundiff et al., 1986). For a given feed resource (e.g., rangeland), increasing feed requirements per cow will require reductions in herd size (Tess and Kolstad, 2000b). Cows that excel in rapid early growth but mature at lighter weights should be desirable in most systems.

**The Genetic Toolbox**

There are a variety of genetic tools currently available to beef producers, and new tools are sure to be developed. Just like a mechanic uses different tools for different jobs, beef producers should use genetic tools based on their effectiveness, ease of application, and cost.

**Breed Resources.** Breed differences in carcass traits have been reported in several studies (Marshall, 1994; Wheeler et al., 1996). For some producers, exploiting breed differences will be the fastest way to make genetic adjustments in carcass quality. If females will be used as replacements, choices among breeds should be based on maternal as well as growth and carcass traits (Cundiff et al., 1986). For some niche markets, production of animals that carry a single copy of the inactive myostatin allele may form an important component of the breeding strategy (e.g., Montana Range, Leachman, 2001).

**Expected Progeny Differences.** To practice effective selection within breeds, estimates of breeding value or EPD are needed. Compared to most growth traits, traditional performance and progeny testing for carcass merit is more difficult. Carcass traits cannot be measured directly on potential parents. Carcass measurements on cattle (i.e., progeny or other relatives of potential parents) marketed and harvested through mainstream commercial channels are expensive to collect. Ownership of calves can change several times prior to slaughter and cattle are typically moved to different locations during their lifetime; hence, maintaining animal identification and information feedback to the cow-calf segment (i.e., where breeding decisions are made) are difficult tasks. Nevertheless, carcass traits are moderate to highly heritable (Marshall, 1994; Shanks, 1999; Shanks et al., 2001) and several breed associations currently compute and publish EPD for carcass traits based on direct measures of carcass quality.

Current technology permits computation of adjustment factors for comparing EPD across breeds (across-breed EPD; e.g., Barkhouse et al., 1998) or by computing EPD for animals from different breeds using one multibreed dataset (multiple-breed EPD; Pollak and Quass, 1998). Across-breed EPD adjustments are currently not available for carcass traits.

**Ultrasound.** Problems associated with direct measures of carcass quality have motivated searches for traits that could be measured on live animals, especially potential parents, that could provide information on carcass quality. Real-time ultrasound has proved to be an effective technology to meet this goal (Wilson, 1992).

An ultrasound measurement made on potential breeding stock raised under ranch conditions (e.g., bulls or heifers at 1 yr) is not the same trait as the direct measurement made on carcasses from animals grown in a feedlot, but a genetically correlated trait that explains (or accounts for) some but not all the variation in the carcass trait. Estimates of genetic correlations between carcass measures and ultrasound measures are needed before EPD for carcass traits can be computed using ultrasound records (e.g., Moser et al., 1998). Hence, breed associations have taken one of four approaches to computing EPD for carcass traits: 1) using carcass data to compute carcass EPD, 2) using ultrasound data to compute ultrasound EPD, 3) computing separate EPD for carcass and ultrasound, or 4) using carcass and ultrasound records to compute a single carcass EPD (i.e., via the genetic correlations).

Due to the fact that ultrasound measurements are made on potential parents, one might predict that future carcass trait EPD will be essentially based on ultrasound measurements. However, developing technology related to source and process verification (i.e., electronic animal identification, animal tracking networks, and Internet data transfer) might facilitate a different course. If this electronic technology is widely adopted, and if the expense is low, direct carcass measures might eventually be the dominant source of genetic information on carcass traits.

**Genetic Markers.** Molecular genetic markers (i.e., DNA markers) have been reported for QTL affecting several carcass components, including rib bone and dressing percentage (Stone et al., 1999) and marbling score (Casas et al., 2001; GeneStar, 2001). Research also suggests the possibility of QTL for carcass weight, fat depth, longissimus muscle area, and retail product yield (Stone et al., 1999; Casas et al., 2000, 2001). The muscle hypertrophy locus (inactive myostatin allele) found in the Belgian Blue and Piedmontese breeds has been mapped (e.g., Fahrenkrug et al., 1999) and shown to affect longissimus muscle area, retail product yield, marbling, yield grade, fat thickness, and kidney, pelvic, and heart fat. Undoubtedly, additional markers will be discovered and validated for these and other traits (NCBA, 1998b). Markers that prove to be closely linked to important QTL (i.e., QTL having a large economic effect) or markers that actually map to the QTL locus will likely be rapidly commercialized (e.g., GeneStar, 2001).

Due to the part/whole relationship between QTL and the target trait, DNA markers explain a portion, but not all, of the genetic variation in the target trait. In other words (and similar to ultrasound), DNA markers account for part, but not all, of an animal’s carcass EPD. The utility of DNA markers is due to the fact that the genotype for the marker, and hence a portion of the EPD, can be determined early in life on potential parents. The most valuable markers will be those that
explain a significant portion of one or more EPD and can be economically assayed. Physiological measurements such as blood hormone concentrations could potentially have similar utility in providing early indicators of genetic merit. For example, Davis and Simmen (2000) found that bulls with lower serum IGF-I concentrations had higher marbling scores, quality grades, fat thickness, and yield grades.

In the future, it is likely that marker genotype information will be incorporated into national genetic evaluation programs. In other words, information from DNA markers will supplement performance information in computing EPD. As described for ultrasound, genetic correlations between marker genotype and the trait of interest will be needed in order to incorporate this information into the computation of EPD. If ultrasound and carcass measures are both used to compute EPD, genetic correlations between the QTL and both measures will be needed.

**Risks and Questions.** Marker-assisted selection will no doubt help beef producers be more competitive in the future. However, like most technology, it is accompanied by risk.

In the future, one can envision several DNA markers and possibly some physiological markers documented for each carcass trait, with private companies conducting assays for the markers. For a given trait, each marker will explain a portion, but not all of the EPD for an animal. To my knowledge no current genetic evaluation system explicitly includes marker genotype information in the analyses, but it is likely that such technology will be soon developed. Nevertheless, current carcass EPD (computed from direct carcass measurements and/or ultrasound) already account for some of the effects of any QTL that exist for the trait. In other words, QTL affect performance whether we know they are there or not, and performance differences are the basis of EPD.

Consider a beef producer who is considering using semen from a bull based on genetic merit for some carcass trait, and assume that marbling is the trait of interest. It is easy to envision a situation in which the bull under consideration has a marbling EPD, plus one or more known marker genotypes for marbling QTL. Regardless of whether the EPD was calculated using the marker genotype information, the genetic information provided by the EPD and that provided by the marker genotypes overlap (i.e., they are not independent). In such cases the marker genotype information is likely to be overvalued by the beef producer.

As mentioned above, some DNA markers detect alleles at loci that are closely linked to QTL, whereas others detect actual QTL alleles. Using current technology for linked markers, usually only heterozygous animals can be identified (i.e., animals that carry one, but not two, copies of the desirable allele). Hence, it is possible for an animal to carry both desirable QTL alleles but they could be undetectable. In the industry, heterozygous bulls are generating much attention. An obvious problem with heterozygous bulls is that only half their progeny will carry the desirable allele. More important, the danger is that producers will value these bulls highly when it is possible, if not likely, that other bulls within the same breed are genetically superior because they are homozygous for the desirable allele and/or because their net genetic makeup (EPD) is superior. Because QTL explain only part of the genetic variation for the target trait, it is possible for a bull to carry a desirable QTL allele yet not rank near the top of the breed for the trait.

Research relating to DNA markers has made great progress in a short time. Much effort has been expended to identify potentially useful markers, yet little is known regarding interactions involving QTL. In other words, for many QTL it is not known how or whether the QTL will interact with other QTL or the background genotype (epistasis), or whether the QTL performs the same in all production environments (genotype × environment interaction). For example, Casas et al. (2000, 2001) detected evidence of interactions between the myostatin gene and QTL affecting Warner-Bratzler shear force and fat thickness. Future research will likely address these questions. However, until these questions are answered for each QTL, there will be uncertainty in predicting their effects on performance.

Application of DNA technology in the beef industry faces obstacles and questions beyond the scope of this paper. Statistical procedures to incorporate QTL information into the computation of EPD are currently being developed. The computational complexity of these procedures may restrict the number of QTL that can be incorporated simultaneously. It may be necessary to validate that QTL (and their markers) are segregating in each breed. Private ownership of DNA technology and competition for business will limit information sharing. Cost/benefits of the technology to the beef industry may be difficult to calculate, and marketing of perceived benefits may drive application.

**A Systems Approach to Genetics and Management**

Similar to other industries, the beef industry is becoming more complex. Managers must deal with increasing amounts of information to be competitive. Coordinated and integrated production systems may need to supply beef products on a weekly basis to meet market demand. Calving in different seasons will make matching forage resources and nutrient demand more difficult (Reisenauer et al., 2001). Detailed monitoring of production costs will become increasingly important. Marketing strategies and genetic tools are just part of beef cattle management systems. Management from a total systems approach will be increasingly important to success.

As reviewed above, evidence suggests that producers breeding for increased lean growth risk loss of performance for some maternal traits, including age at puberty, fertility, calving ease, and mature size. Yet, the
research available regarding the relationships between maternal traits and marbling or tenderness is not extensive. Hence, uncertainty exists regarding how genetic emphasis on carcass performance will affect maternal performance. How do genetic tools fit into the management system to meet future markets?

**Multiple Trait Genetic Management.** First, it is important to emphasize that effective genetic management will be *multiple* trait management. In coordinated or integrated production systems profitability is determined by production efficiency in each production segment (cow-calf, background or stocker, and feedlot), plus end-product value. Carcass traits should never be the sole focus of genetic decisions. Markers (and possibly other indicator traits) will provide valuable early indicators of genetic merit. The industry will use markers most efficiently when information from marker genotypes is incorporated directly into the computation of EPD.

Fortunately, EPD are available for many important beef cattle traits. Widespread whole-herd reporting could facilitate genetic evaluation of additional maternal traits (Tess, 1999). Monitoring an array of traits in making selection decisions can prevent undesirable correlated responses. Most breed associations compute EPD for calving ease or birth weight, which can be used to avoid increases in calving difficulty. Some breeds compute EPD for mature weight, and most compute EPD for weaning weight, yearling weight, and carcass weight. These growth traits are highly correlated (Bullock et al., 1993; Northcutt and Wilson, 1993; Kaps et al., 1999); hence, monitoring EPD for these traits will help producers avoid unwanted increases in mature size. Grid discounts for extremely heavy carcasses provide further incentive to constrain mature size. Development of EPD for scrotal size and stayability will be useful in maintaining or improving age at puberty and fertility (Tess, 1999).

**Heterosis.** Second, the economic value of heterosis should be exploited, especially in reproductive females. Favorable heterosis effects for reproductive traits are well documented (Long, 1980; Cundiff et al., 1986; Gregory et al., 1992). Crossbreeding is an effective way of counteracting the potential increase in age at puberty expected from using breeds that excel for lean growth. Crossbred heifers reach puberty 1 to 3 wk earlier than purebreds (Gregory et al., 1991; Martin et al., 1992). Heterosis effects are desirable for most carcass traits except fat thickness and retail product percentage (Cundiff et al., 1986; Marshall, 1994).

Practical, structured crossbreeding systems and well-designed composite breeds permit breed differences and heterosis to be combined in a complementary manner and manage trade-offs due to genetic antagonisms (Gregory and Cundiff, 1980; Kress and MacNeil, 1999). Using systems analysis techniques, Lamb and Tess (1989) reported that two- and three-breed rotational crossbreeding systems produced about 11% more income than purebred systems in small herds. Davis et al. (1994) determined that maternal heterosis improved profit $70-cow⁻¹-yr⁻¹ for range-based cow-calf enterprises. Lamb et al. (1992a) found that rotational crossbreeding systems improved economic efficiency by an average of 16 to 17% over purebred systems. Tess and Kolstad (2000b) reported that a rotation of three composite breeds improved annual net income per cow by 12% and ranch gross margin by 6% when compared to the average of the same composite breeds managed as purebreds. Adding a composite terminal sire breed improved net income per cow and gross margin by 18 and 19%, respectively. Lamb et al. (1992b,c; 1993) found that rotational crossbreeding systems were economically more efficient than purebred systems in the feedlot segment and in integrated systems, regardless of the marketing end point.

Use of terminal sires probably gives producers the greatest flexibility in genetically tailoring cattle to specific market end points (Bennett and Williams, 1994). Terminal sire systems will be the most practical way of exploiting the advantages of animals that are heterozygous for single copies of QTL such as the inactive myostatin allele. Many producers, especially those managing small herds, find terminal sire systems difficult to implement due to problems associated with bull/cow ratios, generation of replacement heifers, and variation in performance between progeny of terminal sires.

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### Table 2. Reduction in phenotypic standard deviation (%) due to the production of various types of related calves

<table>
<thead>
<tr>
<th>Mating scheme</th>
<th>Additive genetic variance:</th>
<th>Dominance variance:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20.00</td>
<td>40.00</td>
</tr>
<tr>
<td></td>
<td>20.00</td>
<td>20.00</td>
</tr>
<tr>
<td>Multiple unrelated sires</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Sires = ½ sibs</td>
<td>0.63</td>
<td>1.26</td>
</tr>
<tr>
<td>Sires = ¼ sibs</td>
<td>0.78</td>
<td>1.57</td>
</tr>
<tr>
<td>Sires = full sibs</td>
<td>1.26</td>
<td>2.53</td>
</tr>
<tr>
<td>Sires = inbred full sibs (F = 0.25)</td>
<td>1.51</td>
<td>3.05</td>
</tr>
<tr>
<td>Single sire</td>
<td>2.53</td>
<td>5.13</td>
</tr>
<tr>
<td>Single inbred sire (F = 0.25)</td>
<td>3.18</td>
<td>6.46</td>
</tr>
<tr>
<td>Full-sib embryo transfer calves</td>
<td>7.80</td>
<td>13.40</td>
</tr>
<tr>
<td>Calves = clones</td>
<td>22.54</td>
<td>36.75</td>
</tr>
</tbody>
</table>

*Phenotypic variance = 100.00. No maternal effects.*
Genetic tools for carcass traits

Table 3. Effects of breed variation and sorting on the range in sale weights (kg)\(^a\)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>No sort</th>
<th>Sort off 5%</th>
<th>Sort off 10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uniform crossbreeding system</td>
<td>121</td>
<td>94</td>
<td>83</td>
</tr>
<tr>
<td>Inconsistent crossbreeding, maximum</td>
<td>137</td>
<td>107</td>
<td>93</td>
</tr>
<tr>
<td>performance difference among breeds</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Steer calves sold at weaning. 60-d calving season. Calves removed are those with extreme heavy or light weights.

Reducing Variation. The large discounts associated with nonconforming carcasses in most grid-marketing systems can be avoided by marketing phenotypically uniform groups of cattle. Hence, managers have incentive to limit genetic variation as well as variation caused by management and environmental factors.

Related animals are genetically more similar than unrelated animals. Table 2 shows the expected reduction in phenotypic variation (i.e., the range in phenotypic values or the standard deviation) by producing different types of related calves. Using related sires has relatively little effect on phenotypic variation, even when heritability is high. The production of full-sib calves (i.e., through embryo transfer) or clones could reduce phenotypic variation for traits exhibiting much genetic variation (additive and dominance variance) (Lamberson, 1994), but it is doubtful that either will be practical in the near future in beef cattle. Inbreeding helps reduce variation, but the loss of performance associated with inbreeding is too great for this to be a useful tool (Brinks and Knapp, 1975). Within-family variation does not appear to be affected by differences in EPD between parents (Bullock et al., 2000). Unfortunately, there are few practical tools to significantly reduce genetic variation within breeds.

Genetic variation associated with breeds and mating systems also can add to variation among calves. Table 3 illustrates the expected weight variation among calves from herds using what could be called “uniform” crossbreeding vs herds using “inconsistent” crossbreeding. Predictions in Table 3 were simulated based on performance differences among British and Continental beef breeds reported by the U.S. Meat Animal Research Center (Cundiff et al., 1986). Herds using rotational crossbreeding based on breeds with similar performance levels (i.e., the same biological type) will produce variation similar to purebred herds. Similarly, well-planned terminal-sire crossbreeding systems and straight-breeding systems based on composite breeds will also exploit heterosis without increasing calf variation. Across-breed EPD and multiple-breed EPD can be used to choose bulls with similar EPD from breeds that might have quite different performance means, although these tools are not yet available for carcass traits. Crossbreeding systems that indiscriminately use sires from different biological types and switch sire breeds frequently will produce more variable calves.

Variation in calf age contributes greatly to variation in phenotype. Table 4 summarizes expected differences in variation associated with differences in the length of calving season. The range in weaning weights expected among steers born over a 45-d period is approximately 118 kg. This difference increases by another 36 kg for calves born over a 120-d calving period. The obvious way to restrict the calving period is to restrict the breeding season. However, the real issue is the length of the calving period rather than the number of days bulls run with the cows.

Sorting off extreme animals prior to sale or shipment can be an effective tool to reduce phenotypic variation. Tables 3 and 4 illustrate the effects of sorting on weaning weight variation. Just as ultrasound is used in feedlots to sort animals into management/marketing groups, it seems possible that DNA markers might also be used this way. For example, knowing whether cattle are expressing a major allele affecting marbling might help beef producers better match cattle with specific pricing grids, or knowing whether or not cattle are expressing a major allele for tenderness might reduce the risk of guaranteeing branded products as tender. The utility of using DNA markers as management/marketing tools will depend on the cost/benefit of the information.

Table 4. Effects of calving season length and sorting on the range in sale weights (kg)\(^a\)

<table>
<thead>
<tr>
<th>Calving season</th>
<th>No sort</th>
<th>Sort off 5%</th>
<th>Sort off 10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>45 d</td>
<td>116</td>
<td>90</td>
<td>78</td>
</tr>
<tr>
<td>60 d</td>
<td>121</td>
<td>94</td>
<td>83</td>
</tr>
<tr>
<td>90 d</td>
<td>136</td>
<td>108</td>
<td>94</td>
</tr>
<tr>
<td>120 d</td>
<td>152</td>
<td>118</td>
<td>103</td>
</tr>
</tbody>
</table>

\(^a\)Steer calves sold at weaning. Uniform crossbreeding system. Calves removed are those with extremely heavy or light weights.
Implications

Information from DNA markers for carcass trait QTL will help cattle producers identify genetically superior animals at younger ages. Markers will be used most efficiently when marker genotype information is incorporated directly into the computation of EPD, and after potential epistatic interactions and genotype × environment interactions are characterized for each QTL. To avoid detrimental effects on maternal traits, genetic management needs to consider multiple traits as part of a systems approach. Structured crossbreeding, exploiting heterosis and breed strengths, should be used to increase profitability of production systems. Management strategies to reduce phenotypic variation in market groups are expected to increase competitiveness in grid marketing schemes.

Literature Cited


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