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Global Food Systems and Public Health: Production Methods and Animal Husbandry

A National Commission on Industrial Farm Animal Production Report

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The independent National Commission on Industrial Farm Animal Production (NCIFAP) was formed in 2006 to conduct a comprehensive, fact-based and balanced examination of key aspects of the farm animal industry. Commissioners represent diverse backgrounds and perspectives and come from the fields of veterinary medicine, agriculture, public health, business, government, rural advocacy, and animal welfare.

Since its inception, the NCIFAP, in consultation with other national experts, has conducted assessments of the industry’s impact on the public’s health, the environment, farm communities and animal health and well-being. The NCIFAP conducted public meetings around the country to gather information to produce specialized interim reports to help inform the commissioners and the public. *Global Food Systems and Public Health: Production Methods and Animal Husbandry* is one of the technical reports requested by the Commission and includes practical recommendations for policymakers, industry stakeholders, and the general public. Additional copies can be obtain from ____________________________

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Glossary of Abbreviations and Terms

ACSSuT, ampicillin, chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline resistant
AFO, animal feeding operation
AMI, American Meat Institute
APHIS, Animal and Plant Health Inspection Service
BASE, bovine amyloidotic spongiform encephalopathy
BSE, Bovine spongiform encephalopathy
bST, bovine somatotropin
CAFO, Concentrated animal feeding operations
CDC, Centers for Disease Control and Prevention
CFIA, Canadian Food Inspection Agency
CI, confidence interval
CID, Creutzfeldt-Jakob Disease
CNS, central nervous system
CWD, Chronic Wasting Disease
DHIA, Dairy Herd Improvement Association
DM, dry matter
DSI, Decision Strategies International
DT104, definitive type 104, *Salmonella enterica* serotype Typhimurium
EPA, Environmental Protection Agency
FAS, Foreign Agricultural Service
FDA, Food and Drug Administration
FFI, fatal familial insomnia
FMI, Food Marketing Institute
FSE, feline spongiform encephalopathy
FSIS, Food Safety Inspection Service
GMO, Genetically Modified Organisms
GSS, Gerstmann-Sträussler-Scheinker Syndrome
HA, hemagglutinin, a protein used to characterize influenza viruses
HACCP, hazard analysis and critical control points
HP, high pathogenic
HPAI, highly pathogenic avian influenza
IIC, Inspector in Charge
LP, low pathogenic
MBM, meat and bone meal
MDR, multiple drug resistant
MSM, mechanically separated meat
NA, neuraminidase, a protein used to characterize influenza viruses
NAHMS, National Animal Health Monitoring System
NASS, National Agricultural Statistics Service
NCCR, National Council of Chain Restaurants
NCIFAP, National Commission on Industrial Farm Animal Production
NPDES, National Pollutant Discharge Elimination System
NPIP, National Poultry Improvement Plan
NRC, National Research Council
OR, odds ratio
PCBs, polychlorinated biphenyls
PFGE, Pulse field gel electrophoresis
PRRS, porcine reproductive and respiratory syndrome
SE-PT4, *S. enteritidis* phage type 4 infection
RFID, radio frequency identification
SA, sialic acid
SAF, scrapie-associated fibrils
SE, *Salmonella enterica* serotype Enteriditis
SRMs, specified risk materials - high BSE infectivity tissues such as bovine brain and spinal cord
TME, transmissible mink encephalopathy
TSE, transmissible spongiform encephalopathy
USDA, US Department of Agriculture
USDHHS, US Department of Health and Human Services
USERS, US Economic Research Service
vCJD, variant form of Creutzfeldt-Jakob Disease
VNRT, variable number tandem repeat

**Average daily gain:** Pounds of weight gain per day (measure for beef cattle)
**Broiler:** A chicken raised for meat, usually young in age
**Culling:** Reducing or controlling the size of a group by removing some of the animals
**Economies of scale:** Reduction in the cost of producing something brought about especially by increased size of production facilities
**Egg elevator:** A device that receives eggs coming from multiple conveyor belts and puts them in position for further processing
**Feed-to-grain conversion rate:** Pounds of feed required to gain one pound of body weight (measure for beef cattle)
**Forage:** Plant material consumed by herbivores for nutrition. Includes both grasses and legumes (clovers, alfalfa)
**Growth efficiency:** Evaluated by average daily gain and feed-to-gain conversion rates
**Husbandry:** Production and care of animals
**Lairage:** A place where livestock are kept temporarily, eg, at docks or a market
**Metaphylaxis:** The timely mass medication of an entire group of animals to eliminate or minimize an expected outbreak of disease. Adjective: metaphylactic
**Monogastric:** Having a stomach with a single compartment
**Penta-resistant:** A bacteria that is resistant to five types of drugs (eg, ampicillin, chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline)
**Preconditioning (AKA backgrounding):** Preparation of 6- to 8-month-old range or pasture reared, recently weaned beef calves for entry into a feedlot and an intensive fattening program. Usually includes castration, dehorning, branding, and vaccination before weaning, and weaning before sale or entry to the feedlot. During this post-weaning period, the calf should become accustomed to feedlot feeds and conditions.
**Rumen:** Large first compartment of the stomach of a ruminant where feed is fermented
**Somatic cell counts:** Measure of bacteria-fighting cells found in the udder of cows; a normal count is below 100,000 cells/mL
"Spent" hen: at the end of the hen’s optimum egg production ability

**Transovarian:** transmission of a pathogen from an organism to its offspring by infection of eggs in its ovary

**Zoonotic:** Transmissible from human to animal or animal to human
Foreword

To explore and better understand the interface between animal health and production and public health, the NCIFAP posed the following questions:

a) What is the impact of food animal production on the global food system and public health?
b) What are the health consequences to both animals and people?

This report is a review of the five leading livestock commodities (referred to as industries) in the United States: laying chickens and eggs, broiler (meat) chickens, dairy cattle and milk products, beef cattle, and swine. Each commodity group section of the report consists of three parts: 1) a description of the commodity industry and at least one example of a disease of 2) humans and/or 3) animals associated with the commodity industry. For layers, *Salmonella enterica* serotype Enteriditis was chosen as an example because of its strong association with eggs. For broilers, avian influenza is reviewed as a risk to humans and animals. Although avian influenza can cause illness in birds, perhaps its greatest risk to animal health is the depopulation of flocks that occurs when certain strains of the virus are diagnosed. Several examples of diseases associated with dairy cattle are reviewed, including a discussion of the concept of production diseases. Bovine spongiform encephalitis (BSE or Mad Cow Disease) is included in the dairy section since this is the commodity where the disease has caused the most damage. *E. coli* 0157:H7 can cause very serious disease in humans and is reviewed as an example of a disease associated with beef cattle, even though it does not cause disease in these animals. Probably the most serious health risk to feedlot beef cattle is the group of agents and environmental factors known as Bovine Respiratory Disease Complex. Diseases of commercial swine are reviewed by life stages and production categories, and *Salmonella enterica* serotype Typhimurium DT104 was chosen as an example of a potential human pathogen.

To accomplish the charge to the writing team and answer the questions posed by the commission, government and industry databases and technical reports were reviewed. The peer-reviewed scientific literature was used to describe the diseases and conditions and their link to production methods and animal and human health. Several scientific papers have postulated a relationship between production method consequences to animal health and well-being, and public health and welfare. Elements that also impact this relationship include the use of antibiotics, antimicrobial resistance, and recycled animal waste. Discussions of these elements are covered in other reports developed for the NCIFAP and so are not included in any depth in this report. Also, a separate report was prepared for the NCIFAP that deals with additional public health elements and in more depth regarding the potential public health impacts of CAFOs. It is the hope of the writing team that this report will lead the reader to a better understanding of the intricate relationships between farm animal production and its benefits and risks.
Historical Perspective: Consumer Demand for Protein and Evolution of Industry

When humans first made their appearance in the historical record of the world, it was the hunter-gatherer lifestyle that supported and nourished societies. Such a system of food acquisition predominated for millennia, and it is estimated it probably supported a total of 4 million people worldwide (McMichael, 2004).

Then, approximately 10,000 years ago, some hunter-gatherers began to settle, planting crops and husbanding wild animals to the point of domestication. Crops were used almost exclusively for human consumption, and animals were kept extensively, that is, on range and without the benefit of additional cultivated foodstuffs. This pattern continued more or less uninterrupted until the end of the 18\textsuperscript{th} century, when there were about a billion people in the world. The system of agriculture operative at that time required 20,000 square meters of land to produce food for one person for a year. Thomas Malthus wrote, in 1798, in \textit{An Essay on the Principle of Population}, that human growth would soon outstrip the ability of the world to feed it. Fortunately, Malthusian predictions were not proved true, largely as a result of the change in agricultural systems from extensive to intensive.

\textbf{What has happened to agricultural food production since 1798?}

Today there are over 6 billion people in the world, and it requires only 2,000 square meters of land to produce enough food to feed one person for a year, a remarkable improvement from the systems in place only two hundred years ago (Trewavas, 2002). How did this occur? First, crop agriculture flourished due to technological innovations and interventions. And shortly after that, farmers discovered that animals could be congregated for more than subsistence, and the additional animals could be sold for profit.

Corn is an American plant, and is largely responsible for the growth of animal agriculture on this continent. In the 1800’s, as more and more fields were tilled and planted by our early settlers, farmers marketed the additional corn as a commodity, or when prices were low, corn could be fed to cattle and marketed as beef. Then the development of cheap and easy rail transportation facilitated the movement of this commodity. As urban centers grew throughout the 19\textsuperscript{th} century, there was demand for movement of food, and the introduction of refrigeration facilitated year-round transport of fresh and frozen meat products. Cities created lucrative markets for the sale of animal-based protein products, making it worthwhile to grow more animals or milk more cows than what was needed for consumption by the immediate or extended farming family. So locomotives took corn from the Great Plains and carried it to feedyards in Texas; trains carried the cattle to slaughter plants in Chicago, and then the meat from these animals was disseminated far and wide, also on rails.

In the 20\textsuperscript{th} century, improved grain yields accelerated the intensification of food production. It created the opportunity to either market corn as a raw commodity or as
value-added beef that drove the livestock industry in the United States. Cheap corn accelerated the drive toward the latter form of marketing corn. What made corn cheap? Corn is a crop that requires a great deal of nitrogen, and two events before 1950 promoted the application of usable nitrogen to growing corn. First, in the first two decades of the 1990s, German scientist Fritz Haber developed a process that combined nitrogen and hydrogen under intense heat to make a form of nitrogen that would be available for plants. Haber later won the Nobel Prize for his efforts. Second, factories that were built to make nitrogen-containing explosives for the war effort during World War II found that when peace was achieved, they had a significant surplus of raw product plus technologies for using that product. Some of these factories were converted to making nitrogen fertilizer (Pollan, 2006).

The numbers regarding corn yields tell a compelling story. In the 1950s, farmers could get 70-80 bushels of corn per acre of planted land. Fifty years later they could get 200 bushels per acre. As a result of availability of usable nitrogen, as well as genetic improvements to the crop itself, corn became inexpensive and abundant, suitable as a staple to feed to animals. Basically, cheap corn made intensive animal agriculture more profitable along with advancements in animal husbandry. Consequently, intensive feeding of livestock evolved from an opportunistic method of marketing corn to a profitable industry.

Outside of our American borders, where corn has been the supreme crop, similar changes were occurring in the developing world, albeit with slightly different crops. In the developing world, cereal production—not only corn, but also wheat and rice—increased dramatically, doubling over the last 40 years. This phenomenon, referred to as the “Green Revolution,” was brought about by improved seeds, irrigation, application of pesticides and use of nitrogen and phosphorous fertilizers (Tilman et al, 2002). The Green Revolution is another contributor to the outpacing of Malthusian predictions, and a great contributor to the huge global needs we have today to supply adequate human nutrition for more than 6.3 billion people. Although most of the products of the Green Revolution were important in supplying human nutrition directly (wheat and rice), corn also was a beneficiary of these technologies and allowed for intensive feeding of livestock.

What about global food animal production in 2007? Today, two-thirds of total animal production globally comes from monogastric animals—specifically, pigs and chickens. Both of these animals require cereal grains, the abundance of which is probably the main reason for their numeric success industrially.

Since 1960, global meat production has tripled; milk production has doubled, and egg production has increased four-fold (Delgado, 2003). Part of this is due to greater numbers of animals but also to genetic enhancement for improved growth, so that there is overall higher production per animal. Feed conversion ratios, defined as the measure of an animal’s efficiency in converting feed mass into increased body mass, continue to improve for all the livestock species. The change has been most dramatic in chickens. Whereas in 1960, a meat chicken could grow to 2.75 lb in 90 days with a 4:1 feed
conversion ratio, modern broilers can achieve 6 lb in 45 days, with a 2:1 feed conversion ratio (Aho, 1999). These improved feed conversion ratios and decreased time of life before slaughter have resulted in less impact of these animals on the environment in spite of the increased numbers of meat production animals.

**Global supply and demand of animal protein**

Currently, consumption of animal-based protein is unevenly distributed globally. For instance, in the United States, the average person consumes 124 kg of meat per year, whereas the global average is only 38 kg per person per year. The ten countries with lowest consumption are found primarily in Africa and South Asia, although in India, Sri Lanka and Bangladesh, this lower consumption of meat is offset by much higher consumption of milk (India, Sri Lanka) and fish (Bangladesh) (Speedy, 2003).

The main determinant of meat consumption is wealth, with two exceptions. Those cultures that subsist on herding may be poor overall but have abnormally high meat consumption, whereas those with religious proscriptions against eating meat may be low in meat consumption but better off in terms of wealth (eg, India).

There is a converse as well. Although one of the main determinants for meat consumption is wealth, it is also probable that in those countries where meat consumption is extremely low, increased meat consumption would improve wealth, as malnutrition due to an inadequate source of protein may be a serious and limiting factor to a productive economy (Speedy, 2003).

Today, world demand for animal protein is high and is increasing. Projections for consumption are staggering. A 2004 report indicated that between 2000 and 2030, global meat production was expected to increase by 1.9% per annum until 2015 and then by 1.5% per annum until 2030 (Steinfeld, 2004). Several other studies have documented that in the future, most of the demand for meat will come from the developing world, where large increases in overall populations, as well as rapidly increasing numbers of people with higher per capita incomes, create consumers with the ability to pay for a diversified diet. It is established that one of the first changes that happens when standard of living increases above poverty is a move from a diet of rice, beans, and corn to one that incorporates more animal protein, a phenomenon known as the “nutrition transition” which guarantees significant increases in animal-based food consumption from developing countries (Delgado, 2003).

Most of the recent growth in intensive agriculture and most of the projected growth for the next 30 years is in the developing world. More and more, intensive animal production facilities are being built or relocated in developing countries. South America and Asia are the biggest players in the increase in animal production. Although in South America, there is enough land mass to produce the cereal grains to feed livestock and/or to raise livestock extensively, in Asia, the most densely-populated continent, feed grain is imported from other parts of the world to support grain-based animal production that is almost entirely intensive.
These collective changes in agricultural production and distribution are referred to as the “Livestock Revolution.” The unspoken drivers of the Livestock Revolution are the relentless forces of globalization and the developing world’s emerging middle class, both of which facilitate movement and consumption of livestock products. Numerous structural changes are also associated with the Livestock Revolution, including: vertical integration, the introduction of large supermarkets in developing countries, regional concentrations of animals, and a move to place production facilities geographically at the furthest reaches of regulations (Steinfeld, 2004).

In summary, animal agriculture has experienced a “warp speed” type of growth over the last 50 years, with intensification resulting in an almost logarithmic increase in numbers and production output. The availability of high yield and inexpensive grains has fueled this increase and allowed for continually increasing rates of growth in order to feed the burgeoning human population. Animal-based protein consumption currently is disproportionate across various geographic areas and generally directly proportional to income levels. In the next 30 years, animal-based protein consumption will increase dramatically, in both overall numbers as well as increases on a per capita basis in the developing world. Coinciding with these changes will be the relocation of production facilities to the developing world.

**Global trends in American production in the last 30 years:**

**Imports/exports and the future of food animal agriculture**

Intensive animal production had its home in America, beginning with the swine industry in the 1930s and then expanding to poultry shortly after that. As mentioned previously, the ready availability of inexpensive grain and the rapid growth of an efficient transportation system made the United States the logical birthplace for the development of intensive animal agriculture.

Processing of large numbers of animals also had its home here. American slaughter plants were some of the first assembly line “factories” developed in the world. Indeed, Henry Ford got the idea for his first automobile plant from visiting a swine slaughterhouse, and went on to make an auto assembly line from what he saw as a “disassembly” line in the swine abattoir (Johnson, 2006).

From these early 20th century beginnings of intensive animal production and processing, US agriculture has experienced considerable modifications over the last two decades. The most notable changes are

- vertical integration,
- consolidation into large facilities, and
- restructuring of the supply chain.

*Vertical integration* entails one company or financial entity having control over all phases of production. Animals and slaughter plants are all owned by one company, and this company contracts with the people that we used to call farmers. Vertical integration began with the swine industry in the early 1990s when Smithfield Farms copied the vertical integration of the auto industry, an interesting turn of events given the reverse
The influence mentioned above. The poultry industry today is similarly integrated, with few total companies overseeing all of the chicken meat and egg production in the United States. The cattle industry is the least vertically integrated of the animal-protein producing industries in the United States.

Accompanying the trend to vertical integration has been the tendency to consolidate into large facilities. This was first observed, again with the swine industry, as the smaller producers were pushed to the economic periphery, being unable to compete with the efficiencies provided by a large corporation. The numbers speak for themselves regarding the consolidation of operations: in the United States, over the last two decades, the average number of animals per livestock operation has increased 1.6-fold for cattle, 2.3-fold for pigs, 2.8-fold for egg production, and 2.5-fold for broilers (Tilman et al, 2002). The large livestock or poultry operations are referred to as concentrated animal feeding operations (CAFOs), which are strictly defined according to environmental criteria set by the US Environmental Protection Agency (EPA) and the states in which the livestock entities operate. Permits must be maintained in order to operate a CAFO, and the restrictions can be stringent, which has added considerably to the costs of running a CAFO, further promoting larger enterprises, which tend to be more profitable and thus better able to afford higher operation costs.

The general public tends to consider farming as a way of life rather than as a business enterprise. However, the pastoral existence of animals and the humans who care for them is no longer much of a reality. Agriculture has always been a cornerstone of our national economy, and although today less than 2% of our population actually works on the farm, agriculture is still a big contributor to our economic vitality, largely through the production of exportable products. These exports historically have been robust, but recent transient downturns have occurred that resulted in some restrictions, (for example, bovine spongiform encephalopathy [BSE] fears). The trend is increasing again as these restrictions are relaxing. Agricultural exports of beef, pork, and broiler meat continue to expand, as high-end consumers in key countries recognize the unique value of specific American products (USFAS, 2006).

On the flip side, total import of agricultural goods also continues to increase. According to the US Foreign Agricultural Service (FAS, USFAS, 2006), in 1995, $9.5 billion worth of agriculture goods were imported into North America. That amount steadily increased to a total of $21 billion in 2006.

So, the gap between exports and imports has narrowed, and the United States is now, for the first time ever, poised to anticipate a trade deficit in the area of agriculture. Within the next five years, if trends continue, it is probable that we will be a net importer rather than exporter of agricultural goods, including animal products.

The global tapestry of trade has become increasingly intricate and complicated, and the United States is no exception to the sometimes incomprehensible pattern of product movement that has occurred. The World Trade Organization, now 12 years old, is ensuring that the highest quality product can be delivered at the least expensive price to
anywhere in the world, and the only barriers to that delivery must be scientifically based and related to health of animals or humans. The United States is experiencing both a major benefit and a major detriment as a result of the new rules of trade. Due to high level of national animal health status and other factors, US animal products are eligible for export to almost every corner of the globe. Low labor and environmental costs in the developing world, however, make US animal products less competitive as they have been in the past.

As mentioned in the previous section regarding the Livestock Revolution, there is a strong trend toward increasing intensive animal agriculture in Asia and South America, and buying animal-based protein from these regions will prove to be more economically attractive for US consumers. However, the Asian intensive animal industries do not have a readily available supply of feed, so it is likely that the feed grain industry in North America will continue to thrive as more grains are shipped to other countries to enhance their industrial food animal production.

It is interesting that although the American public is increasingly conscious of environmental concerns and “eating healthy”, we still consumed 25% of the world’s oil, and are considered the “fattest nation” on Earth (Frontline, 2004). The diet industry is worth $40 billion per year, more than the GDPs of 132 countries in the world (USCIA, 2007). And as the industrial animal production facilities move to South America and Asia, there are many hidden petroleum costs that are inherent in the transportation systems to not only get the meat and milk to our groceries but also to get the feed to the animals that are producing that meat and milk. Also, there is an interesting market trend occurring in the U.S. of “eating locally” by buying from producers (both plant and animal) in the immediate area of the consumer. However, such practices should be construed as being automatically safer or more environmentally friendly. A marginal producer may use more natural resources to get a product to market locally than a large producer thousands of miles away. Also, it has become more commonplace for animal-origin food products to be labeled with “process attributes” such as “free range,” “organic,” “natural”, “grass fed,” or “environmentally friendly,” etc. These process attributes may have little to do with nutritional value, microbial or chemical safety, efficiency of production or even animal welfare.

Can the world be fed?
There are two undeniable truths - agriculture has changed radically over the last two hundred years and the population of the world has increased logarithmically. We cannot turn back the clock to the hunter-gatherer days or even to the pastoral farming times of days gone by. So what are the present-day realities? It is estimated that agriculture as it is practiced today could probably be stretched to feed 8-10 billion people, which the world should reach around 2050 (Tilman et al, 2002). Where will this “stretch” occur? It is unlikely that there will be any further efficiency in the production of cereal grains through increased applications of fertilizer (Tilman et al, 2002), and environmental impacts of nitrogen fertilizer will be hard to circumvent. The competition for corn as a biofuel may result in the conversion of croplands from other grains to grow corn, but this remains controversial. Also, there is growing pressure from the World Trade
Organization to decrease farm subsidies to support these feed grains in the developing world, so there will probably be less croplands in the U.S. planted for corn to feed livestock. Globally, prices will increase, that will by definition result in a more efficient use of these feedstuffs. But to support the worldwide increase in animal production predicted by the Livestock Revolution, by 2020, production of cereal grains globally will have doubled what it was in 2000 (Delgado, 2003). All livestock sectors will grow but because poultry have the highest feed conversion efficiency, the poultry industry will likely expand to the greatest extent.

Exploration of economically viable aquaculture systems will continue. Fish have a very efficient feed conversion ratio, which will likely be exploited in the future. However, since these animals have not had the benefit of domestication and decades of selective breeding, there is not the comparable accelerated growth in fish that there is in livestock and poultry. Also, disease control programs are in a state of relative infancy compared to the other animal protein production industries, so it will be some time before aquaculture is competitive in replacing any of the other livestock sectors for most efficient production of food for humans.

Genetically modified organisms (GMO) is another realm that will be actively explored for production of food in the most efficient manner. GMOs that are perfectly suited to a specific soil or climate, or have enhanced nutritional value or pest resistance, are gaining acceptance. Chinese scientists are leaders in the development of such organisms, with recent patent registrations for over 250 new agricultural organisms, including transgenic rice resistant to three major pests, insect-resistant maize, and a tomato with enhanced shelf life (Huang et al, 2002). Similar studies in the developing world are not occurring at the same pace, probably because of the concern over consumer acceptance. But as the global population continues to expand and food security assumes a higher priority, there will likely be more genetically modified organisms (GMO) in agriculture all over the world.

**Overview of current food animal production systems**

**with a focus on CAFOs**

Concentrating Animal Feeding Operations (CAFOs) are used the world over, to grow animals for the production of human food. The term is pronounced “kay-foes” and is used to encompass a large assortment of animal collections. Commonly used words in animal husbandry that are all considered CAFO’s include: feedlot, dairy, hog barn, chicken house, fish farm, etc. CAFOs are heavily regulated, primarily by the Environmental Protection Agency, which also supplies definitions of CAFOs. First, the EPA defines all animal feeding operations (AFOs), as:

- a lot or facility (other than an aquatic animal production facility) where the following conditions are met:
  - Animals have been, are, or will be stabled or confined and fed or maintained for a total of 45 days or more in any 12-month period, and
  - Crops, vegetation, forage growth, or post-harvest residues are not sustained in the normal growing season over any portion of the lot or facility. (USEPA[a])
The primary term in an AFO is the word embodied in the middle letter – feeding. Animals that graze freely are not fed, and so are not included in an AFO definition. As animals are fed materials provided by humans, it is likely that their numbers will increase, and with that, environmental problems from waste will likely increase. Agricultural waste and waste water from any animal operation may have negative environmental effects through contamination of water bodies and land due to weather conditions and subsequent runoff, spills, leaks, or breaks (e.g., dams holding settling ponds), and animal access to streams.

To help ensure that the public and environmental health is not harmed by animal agriculture operations, the Environmental Protection Agency (EPA) regulates them through the Clean Water Act (USEPA, 2003b). Specifically, within the Clean Water Act, is the National Pollutant Discharge Elimination System (NPDES) program that prohibits “the discharge of pollutants into waters of the United States unless a special permit is issued by EPA; a state; or, where delegated, a tribal government on an Indian reservation.”

So, when does the EPA step in to regulate an AFO? The answer is simple – when the AFO becomes a CAFO. This happens when the concentration of animals reaches a certain density. CAFOs have strict government definitions and are further divided into medium and large CAFOs.

According to the EPA (USEPA, 2003b), a CAFO is

an AFO that is defined as a Large CAFO or as a Medium CAFO in the regulations, or that is designated as a CAFO by the permitting authority. Two or more AFOs under common ownership are considered to be a single AFO for the purposes of determining the number of animals at an operation, if they adjoin each other or if they use a common area or system for the disposal of wastes.

The US Environmental Protection Agency (2003a) further defines AFOs as large CAFOs if the AFO

stables or confines as many as or more than the numbers of animals specified in any of the following categories:
(i) 700 mature dairy cows, whether milked or dry;
(ii) 1,000 veal calves;
(iii) 1,000 cattle other than mature dairy cows or veal calves. Cattle includes but is not limited to heifers, steers, bulls and cow/calf pairs;
(iv) 2,500 swine each weighing 55 pounds or more;
(v) 10,000 swine each weighing less than 55 pounds;
(vi) 500 horses;
(vii) 10,000 sheep or lambs;
(viii) 55,000 turkeys;
(ix) 30,000 laying hens or broilers, if the AFO uses a liquid manure handling system;
(x) 125,000 chickens (other than laying hens), if the AFO uses other than a liquid manure handling system;
(xi) 82,000 laying hens, if the AFO uses other than a liquid manure handling system;
(xii) 30,000 ducks (if the AFO uses other than a liquid manure handling system); or
(xiii) 5,000 ducks (if the AFO uses a liquid manure handling system).
Medium CAFOs are defined in federal regulations (USEPA, 2003a) as such if the AFO meets two criteria:

I. The types or numbers of animals in the ranges as the type and number of animals that it stables or confines falls within any of the following ranges:
   (i) 200 to 699 mature dairy cows, whether milked or dry;
   (ii) 300 to 999 veal calves;
   (iii) 300 to 999 cattle other than mature dairy cows or veal calves;
   (iv) Cattle includes but is not limited to heifers, steers, bulls and cow/calf pairs;
   (v) 750 to 2,499 swine each weighing 55 pounds or more;
   (vi) 3,000 to 9,999 swine each weighing less than 55 pounds;
   (vii) 150 to 499 horses;
   (viii) 3,000 to 9,999 sheep or lambs;
   (ix) 16,500 to 54,999 turkeys;
   (x) 9,000 to 29,999 laying hens or broilers, if the AFO uses a liquid manure handling system;
   (xi) 37,500 to 124,999 chickens (other than laying hens), if the AFO uses other than a liquid manure handling system;
   (xii) 25,000 to 81,999 laying hens, if the AFO uses other than a liquid manure handling system;
   (xiii) 10,000 to 29,999 ducks (if the AFO uses other than a liquid manure handling system); or
   (xiv) 1,500 to 4,999 ducks (if the AFO uses a liquid manure handling system)

II. Either one of the following conditions are met:
   (i) Pollutants are discharged into waters of the United States through a man-made ditch, flushing system, or other similar man-made device; or
   (ii) Pollutants are discharged directly into waters of the United States which originate outside of and pass over, across, or through the facility or otherwise come into direct contact.

CAFOs are required to have a NPDES permit if they intend to discharge into the environment. Further, some states have additional regulations regarding the discharge of animal waste.

Producers are able to directly access the EPA’s regulations and requirements through a producer guide (USEPA, 2003b). It is important to note that industry organizations often provide assistance and further explanation of CAFO regulations and permitting processes through their own Web sites and literature. Examples of some of the industry organizations that make environmental information available to their members include the National Pork Producers Council\(^1\) and United Egg Producers\(^2\). Non-compliance with rules and regulations are in violation of the Clean Water Act, and penalties may result.

**Animal production economics**

The fundamental economic basis of animal agriculture is the realization of higher returns when fixed costs (labor and capital, etc.) are spread over greater units of product. The basic driver of economic efficiency is the dilution of fixed costs (animal maintenance costs as well as fixed cost at the farm level) by distributing them over more units of

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\(^1\) http://www.nppc.org/

\(^2\) http://www.unitedegg.org/environment.aspx
product. The trend to higher production and to consolidation into larger units has been consistent throughout the world and has influenced the development of societies over the history of mankind (Diamond, 2002). In the U.S., the trend has been particularly noticeable. At the founding of our country, approximately 98% of the population was directly involved in agriculture, while today it is less than 1.5%. As a nation, we currently spend less than 10% of our disposable income on the purchase of food, the lowest in the world, and efficient agriculture has been cited as one of the key factors in allowing the diversification and strength of our economy.

As an example, consider a cow producing 1 more pound of milk: The producer will still pay all the fixed costs (facility, labor, replacement, feed for maintenance, etc), and the only cost that will increase is the feed cost associated with the actual production, which is about $0.03/lb of milk production. For this additional pound of production in this example, the producer will get milk revenue of $0.13/lb. Each marginal pound of milk yields $0.10/lb of income over feed cost. Feed could actually double in price, and it would still be profitable to produce additional milk.

Economies of scale, comes into play at the enterprise level for a number of reasons. As herds/flocks increase in size, the input cost is lower based on bulk discounts and/or contract prices. Larger herds or flocks can better match the capacities of various aspects of the production system (milking parlor efficiency, labor, feeding etc.). Number and production increases must be matched with improvements in husbandry, including animal well-being and preventive measures. But what also must be taken into account are the externalities - costs of transportation and also disposal of wastes. However, it should be noted that as production per animal increases, which is the trend in modern agriculture, the impact on the environment per unit animal decreases.

**CAFO production methods**

As mentioned several times in this review already, large scale animal agriculture has become the norm in the United States. Advantages of CAFO production methods include increased production and efficiency and the provision of employment and monies into the local and regional economy. This results in less land used per animal and maximal use of available land, feed, energy, and personnel resources. Some land used for CAFOs is not suitable (eg, not fertile enough for crop production) for many other uses, which is another potential benefit. Animals are often housed inside, so inclement weather conditions may not have as much of a welfare, production, and economic impact when compared to outdoor production systems. From a veterinary standpoint, work with CAFOs involves primarily herd-health and epidemiological approaches, while individual animal health care is done by farm staff. Production of the desired end product, meat or milk, is typically obtained in a shorter time period using CAFO production methods. Animals are selected for specific traits, and bloodlines may become very concentrated, with little diversity. Thus, using CAFO production methods, a very uniform product is made available to the consumer. This is also an advantage to the processor (eg, uniform sized cattle, pigs, chickens, and fish). Because CAFO production methods produce many animals that meet a specific target weight and size, welfare during the slaughter/harvest
process may be improved. This is because the entire slaughter facility, from pens to all equipment for handling and processing, are built for the target weight and size.

There are also disadvantages associated with CAFO production methods. These include potential decreases in property values near CAFOs, adverse environmental effects, concerns regarding individual animal welfare, odor and other annoyance/nuisance problems, and worker and public health concerns, including environmental dispersal of antimicrobials and antimicrobial resistance (See individual Commodity/Species sections for additional discussions).

CAFO manure management must be carefully planned. Nutrients and pathogens in the manure can cause pollution of the environment and human health problems. The EPA regulates many aspects of manure management, through the NPDES, as described earlier. Control of the release of sodium, nitrates, and phosphorous into water systems is especially problematic.

Excessive phosphorus levels in surface waters may result in algae bloom and a reduction in aquatic life (Knowlton & Kohn, 1999). Similarly, excess levels of sodium in surface waters can cause eutrophication and lead to fish kills. Excessive levels of nitrates in drinking water can also cause serious illness in humans (Knowlton & Kohn, 1999).

Concerns also exist regarding the presence of pathogens in manure. Pathogenic zoonotic agents, including Campylobacter species, Listeria monocytogenes, Cryptosporidium parvum, Salmonella species, and E. coli O157, can be shed in food-animal feces (Jones, 1999; Pell, 1997). It is important that manure be stored and spread to minimize the risk of disease transmission.

**Selected federal and industry agencies**

The NAHMS³ was initiated in 1983 by the USDA and exists to provide information to domestic livestock industries by coordinating and conducting US-based studies focused on health and health management. Besides collecting and analyzing these data, NAHMS also works to disseminate the information and results on the health, management, and productivity of domestic livestock.

The Food Marketing Institute (FMI)⁴ represents food retailers and wholesalers concerned with food safety and defense. The FMI seeks to provide retailers and wholesalers pertinent information that will help them meet regulatory requirements and operate using best practices techniques. The FMI joined with the National Council of Chain Restaurants (NCCR)⁵ to develop and support programs that strengthen animal welfare. Their specific goals are:

- Consistency across the US retail sector
- Implementation of practicable and attainable guidelines based on science
- A measurable audit process

³ www.aphis.usda.gov/vs/ceah/cahm
⁴ www.fmi.org
⁵ www.nccr.net
• An ongoing advisory council of third party, independent animal welfare experts
• Improved communications across the supply chain on animal welfare issues.

The American Meat Institute (AMI)\textsuperscript{6} is considered the voice of the meat and poultry industry. This national trade association represents companies that process an estimated 70\% of our nation’s meat and poultry. The AMI works to inform governmental legislators and regulators as well as the media about activities that might impact the animal protein industry.

\textsuperscript{6} www.meatami.org
Selected CAFO Production Models

As models for food animal production, below are descriptions of poultry (layers and broilers), dairy, beef, and swine production systems. Each model represents specific complexity in the production cycle that will be considered in relation to potential impacts on human and animal health. This will be done by a discussion of at least one disease or condition that represents a potential risk to humans and at least one disease or condition that represents an animal health risk.

US poultry industry

The US poultry industry can be broadly divided into two categories: layers, egg producers, which spend most of their lives laying eggs; and broilers, which live only a short period of time before slaughter for the chicken meat that we buy at the grocery store or consume in restaurants. The major US poultry companies are fully integrated, which means that all aspects of production are controlled by the same corporate entity. In other words, the same company owns the hatcheries, where the young chicks will come out of their eggs and are then shipped to production facilities; feed mills; transportation; and processing plants, where the eggs are sorted and packed, or in the case of broilers, where the birds are killed and processed as whole chickens or cut into parts for retail sale. Some companies also have rendering plants for by-products. By-products are the inedible waste products of the slaughter plants. A rendering operation will cook these waste products under pressure until the inedible fats and oils and water are separated from the solids like proteins and fats. Primary breeder companies are those where the “grandparent” stock is kept - these are highly controlled facilities that keep the breed stock that is at the top of the production pyramid. Primary breeder companies are usually not integrated into the same production system that results in poultry meat or eggs; rather they are separate companies.

Layers

Most egg producers manage all aspects of their flocks and housing, including the raising, feeding and husbandry of birds as well as the marketing of eggs. Variations in management of layers are based on the breed selected, vaccination procedures, and methods of molting. Modern egg farms usually operate in a completely free market system with no government assistance programs or quotas. While these farms have grown to meet the market demand, they are still classified as “family farms” with the owner often on the farm making day-to-day decisions.

Size of the egg production industry – Currently, approximately 260 egg-producing companies have flocks of 75,000 hens or more, including 11 companies with more than 5 million layers. These 260 companies represent 95% of all the layers in the United States. Almost all layer flocks in the United States are housed indoors and in cages. About 240 million laying hens produce approximately 5.5 billion dozen eggs per year in the United States.

Layer raising, management, and egg production – The small producers, representing only 5% of the industry, usually take their eggs to a cooperative for packing. Specialty egg
producers may have their own packing and labeling for such products as organically-produced eggs.

The poultry egg production industry is vertically integrated, which means the company has control over almost all of the production process. However, as a general rule, layer companies do not own the breeder birds, which are the parent lines that supply the layer chicks. A typical rearing program will consist of hatching and placement, housing and caging, feeding, egg production, and egg collection.

**Hatching and placement**— Unless the operation produces fertilized eggs for a specialty market, chicks are sexed at the hatchery within a few hours of hatching, and only female chicks are used in the operations. Male chicks may be sold to be raised as meat birds or are destroyed at the hatchery. There are hatchery employees with the skill and training to differentiate the sex of day old chicks with great accuracy. Layer chicks (i.e., day-old, single comb white Leghorn chicks) are purchased from the primary breeder companies that operate the hatchery. At the hatchery, chicks are vaccinated according to the producer’s specifications (Table 1). Hatcheries deliver the chicks within one or two days of hatching. Chicks are not offered food during this time because the yolk sac contains enough nutrients to sustain them until they reach the layer premises. Upon arrival, chicks are placed in layer pens or houses with carefully controlled temperatures and raised on the floor until about 18 weeks of age, when the pullets (sexually immature laying hens) are moved to the laying facility to begin lay at about 20 weeks of age.
Table 1. Typical vaccination schedule for leghorns (Meunier & Latour).

<table>
<thead>
<tr>
<th>Age at Vaccination</th>
<th>Type of Vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day old</td>
<td>Marek's</td>
</tr>
<tr>
<td>15 days (1/2 dose)</td>
<td>Infectious Bursal</td>
</tr>
<tr>
<td>20 days (1/2 dose)</td>
<td>Infectious Bursal, Bronchitis, Newcastle, Infectious</td>
</tr>
<tr>
<td>25 days</td>
<td>Bursal (Typical brand name Combo Vec. 30)</td>
</tr>
<tr>
<td>30 days</td>
<td>Bursal (Typical brand name Combo Vec. 30)</td>
</tr>
<tr>
<td>49 days</td>
<td>Bursal (Typical brand name Combo Vec. 30)</td>
</tr>
<tr>
<td>10 weeks</td>
<td>Fowl Pox and Laryngotracheitis (commonly referred to as LT)</td>
</tr>
<tr>
<td>12 weeks</td>
<td>Combo Vac 30</td>
</tr>
<tr>
<td>13 weeks</td>
<td>Avian Encephalomyelitis (commonly referred to as AE)</td>
</tr>
<tr>
<td>16 weeks</td>
<td>Newcastle</td>
</tr>
</tbody>
</table>

**Housing, caging, and management (feeding, temperature, and vaccinations)**– Initially, chicks may be placed in layer cages or in pullet houses where they are reared on a floor covered with absorbent materials, such as wood shavings. Chicks that start in a pullet house remain there for approximately 10 to 15 weeks before being moved to a layer house. Beak trimming or debeaking (i.e., removal of a portion of the upper beak) is usually done at the hatchery or within the first week of placement. This is a standard procedure of the industry and is done to prevent damage due to pecking of cage-mates.

The most common type of layer housing for large commercial operations includes cages with several rows of tiered cages down the length of the house, ventilating fans at one end, and a manure pit underneath. A single layer cage may occupy as many as fifty chicks, but as they mature, cage density is lessened. Lighting and temperature conditions for a typical layer production period are adjusted over the next 16 weeks to ensure optimal growth and then to induce egg laying.

An automatic feed delivery system provides each cage with a measured but constant supply of feed, and there is a watering system with nipple drinkers throughout the cage system. Vitamins and vaccines or medications can be delivered through the watering system.

Vaccination programs are intensive until the birds are housed in the cages and may include additional water vaccination for Newcastle disease virus and infectious bronchitis.
virus after the birds are caged (Table 1). Vaccination through injection is not practical after caging because it is expensive to handle the birds, and handling stresses the birds, which causes a decrease in production of eggs. Records of production, feed consumption, medications, vaccinations, etc. are kept on all flocks. After the birds have completed one-to-two laying cycles, they are marketed as spent hens and usually used for pet food.

**Egg production**– A flock of layers will reach peak egg production (90+ percent) around 30 to 32 weeks of age. Percentage is calculated on an assumption that if each hen produced one egg per day, production would be 100%. Production declines to approximately 50% around 60 to 70 weeks of age. At this point, producers often molt the flock, which means using environmental stimuli to cause feather shedding followed by feather regrowth. During the period of molting, chickens will stop laying eggs. It takes approximately 10 weeks from the beginning of a molting program before the flock is back at 50 percent production, and post-molt production will increase to a peak of about 80 percent. Some producers will induce a second molt, but most producers send the hens, after the second laying cycle, to slaughter as “spent hens.” These are typically large carcasses and because of the age of the chicken, the meat tends to be a little stringy, so the parts are usually sold as stew meat or they are sent to create a processed product, such as chicken bologna. After the flock vacates the layer house, the house is stripped of all organic matter and sanitized before another flock enters the house (Meunier & Latour).

Because production is needed on a continuous basis, egg laying operations usually consist of birds of different ages, with young birds added at regular intervals. This means special care must be taken to avoid the introduction of diseases. Few people are allowed inside layer houses, and those that are allowed are screened for previous and current poultry contacts. Companies are unlikely to employ people who also have backyard flocks of chickens at home.

**Egg collection and processing**– Hens lay eggs onto a wire floor angled generally at 8-10° toward the front of the cage. This allows the eggs to roll to the front of the cage and onto a nylon belt. The belt transports eggs out of the house either to the egg processing facility or to a storage cooler (Meunier & Latour). Large scale commercial operations have automated egg collection systems that take the eggs to a central processing area where they are washed, visually inspected, graded and packed for distribution, and refrigerated (40-45°F) until ready for shipment. Visual inspection is designed to detect defects such as cracks and checks of the egg shell, and blood spots indicating bleeding inside the egg, usually at the time of ovulation. Intact eggs without detected flaws in the shells are shipped as table eggs for sale in grocery stores. Eggs with defects detected during inspection are discarded or can be sent for further processing including breaking and pasteurization. Such pasteurized eggs are sold to companies that produce bakery products.

**Egg production and the emergence of Salmonella Enteritidis as a public health risk**

The emergence of food-borne human infections caused by the *Salmonella enterica* serotype Enteritidis (SE) and by multiple-antibiotic resistant strains of *Salmonella* are
considered to be two major changes in the epidemiology of salmonellosis that occurred in the second half of the 20th century. This section reviews information on the global spread of SE, including the factors responsible for the emergence of these Salmonella strains, the public health impact, and the current policies for its control and prevention.

**Emergence of SE and its pandemic**– In the United States, SE steadily increased in frequency of isolation from being the sixth most common serotype in 1963 to the most frequently reported serotype in 1990. Since the 1970s, the incidence of SE infection and the number of related outbreaks has increased dramatically. By 1994, SE was the most commonly reported Salmonella serotype isolated from people, with an incidence of more than 10/100,000 of the population (Braden, 2006). In the northeast United States, epidemiologic and laboratory investigations incriminated shell eggs as the major vehicle for SE infection in humans. It was concluded that the eggs had been internally contaminated by transovarian transmission of SE in the laying hen due to infection of the hen’s ovary. Transovarian transmission was documented as a major mechanism for the contamination of eggs in several experimental studies (Lindell et al, 1994; Thiagarajan et al, 1994, 1996).

**Global spread of SE**– The factors responsible for the spread of SE are still unclear. One of the factors that may have been important for the epidemiological spread of this pathogen is the difficulty of detecting the contamination of the chicken: SE is known to colonize the intestinal tract of birds without causing obvious infection (Suzuki, 1994; Duchet et al, 1995). Several factors likely played a role in the emergence of this egg-associated disease in the United States and in many other countries. In an era of increasingly centralized large poultry farms that house tens of thousands of birds, the abilities of SE to cause symptomless infection of hen ovaries which allowed the transfer of the organism to the internal contents of eggs, and to persist in farm environments, allowed for its undetected and unchecked spread. Additionally, cross-contamination of foods and the practice of pooling hundreds of eggs for undercooked egg dishes in retail establishments allowed the contamination of large quantities of foods by a few infected eggs. In one case, tankers that were used for transporting raw eggs contaminated the mixture for a nationally distributed ice cream producer, resulting in an estimated 224,000 human cases of SE infection (Hennessy et al, 1996). Furthermore, the spread of infection within a flock through environmental contamination is enhanced by symptomless carriage of the organisms by even a few birds (Duchet et al, 1997, Gast & Holt, 1998). This is in addition to the fact that the presence of SE within contaminated eggs is difficult to detect until the bacteria exceed log 9.0 per egg (Humphrey, 1994).

**Farm practices**– The modernization of chicken farms and globalization of the bird breeding trade have also played a role in the spread of SE. For example, the most prevalent molt strategy in the Unites States is to remove feed until hens lose a specific amount of weight. However, hens molted in this way were found to be 100- to 1,000-times more susceptible to infection by SE and excreted significantly higher numbers of the organism in their feces (Holt, 2003). Several authors reported that other major risk factors were related to disinfection, lack of hygiene barriers, and feed mill processes (Henken et al, 1992; Davies & Breslin, 2003a).
**Rodent reservoirs**– Several authors have suggested that SE was introduced into poultry flocks by rodents where it is endemic, since in the past it was used intentionally to kill rodents (Henzler & Opitz, 1992; Friedman et al, 1996). SE was first used to control rodent populations during the Yersinia pestis outbreak in San Francisco in 1895 and then occasionally in Europe until 1960 (Rabsch et al, 2001). There is a correlation between the presence of Salmonella in mice and the contamination of poultry. Moreover, some recent reports have shown that several wildlife species, especially rodents, are involved in the maintenance of SE infection on farms (Davies & Breslin, 2003b; Garber et al, 2003, Liebana et al, 2003).

**Virulence evolution in Salmonella**– The dramatic increase of SE phage type 4 (SE-PT4) infection in Western Europe since 1980 suggests that it might have recently acquired new virulence genes. This hypothesis is strengthened by recent investigation of the molecular structure of SE from different sources, which indicated a likely common ancestor of SE that diversified with the organism spread (Saeed et al, 2006). It is possible, however, that SE emerged because it was associated with eggs, a new food source for contracting *Salmonella* infection. We can thus hypothesize that SE acquired new genes to increase the efficiency of its infection of the chicken reproductive tract. Recent reports have demonstrated that repeated passages through the reproductive tract of chickens after oral infection increased the ability of an SE strain PT13a to cause internal contamination of eggs, as opposed to serial passages through the liver and spleen that did not significantly affect the ability of this strain to cause egg contamination (Gast et al, 2003).

**Eradication of S. pullorum and S. gallinarum**– The analysis of SE isolates worldwide reveals the existence of two major evolutionary lineages: one found in western Europe, Japan and South America (SE-PT4) and another found in the Unites States, Canada, and the Slovak Republic (PT8 and PT13a) (Desenclos et al, 1996; Hickman-Brenner et al, 1991; Majtanova, 1997; Nunes et al, 2003). These geographical differences make the global spread difficult to completely explain as the spread of a single clone of the bacterium. It has recently been proposed that the eradication of S. gallinarum, a different and previously common infection of poultry, opened an ecological niche, which allowed the introduction of SE into poultry flocks (Baumler et al, 2000). Mathematical models predict that the coexistence of *S. gallinarum* and SE would prompt competition where the more transmissible bacterium will eliminate the other from the host population (Gupta et al, 1996) either as a result of adaptive immunity or as a result of microbial competition (Berchieri & Barrow, 1990).

**History of emergence of SE in the United States**– In the United States, the rapid increase in the incidence of human SE infection began in the northeast in the late 1970s. The infections spread to the mid-Atlantic states by the mid-1980s (St. Louis et al, 1988). During this period, 65 outbreaks of SE infection were investigated that involved at least 2,119 cases, 257 hospitalizations, and 11 deaths. In these investigations, eggs or egg-containing foods were implicated in 77% of 35 outbreaks of SE infection in which a food source was identified. Although eggs were already known to be a source of SE infection in
humans, these investigations established the shell egg as the most important vehicle for spread.

Salmonella serotypes have also been isolated from insects, rodents, and wild birds living on or around hen houses. Chicken manure and other moist, organic materials serve as additional sources in which Salmonella species can survive and grow for long periods. The high density of chickens on commercial farms serves to spread infection through direct contact with infected birds and with a contaminated environment (Gast & Beard, 1990). The facts that SE does not cause overt infection in chickens and that the chicken farm environment includes several niches for Salmonella make the control of the problem on the farm a difficult goal (Guard-Petter, 2001).

National surveys of SE in the United States— Between 1991 and 1995, microbiologic studies of SE infection in spent hens from egg-laying flocks were conducted by the FSIS (Ebel & Schlosser, 2000). A combined total of 711 flocks were surveyed in these two studies. For each flock, a sample from the gastrointestinal tract was collected from 300 spent hens at the time of slaughter. SE was identified in 35% of flocks tested, with the highest proportion (52%) of SE-positive flocks located in the northern United States. A microbiological assessment of SE environmental contamination of egg-producing farms was conducted by the NAHMS in 1999 (USDA, 2000). Two hundred farms in 15 states were selected. In total, 7% of farms tested yielded SE in at least 1 sample, with a range of prevalence by region from 0% to 17%. Among farms with SE isolated from the environment, contamination was widespread; positive samples were obtained from egg belts (48%), egg elevators (45%), walkways (18%), and manure (17%). Additionally, in 1991, the USDA’s Animal and Plant Health Inspection Service (APHIS) conducted a microbiologic survey of egg-processing plants. Of 278 liquid whole egg samples, 169 (61%) yielded Salmonella, of which 38 (14%) were the SE serotype (Ebel et al, 1993).

How common is SE contamination of eggs?— Although the frequency of SE in egg-laying flocks was reported to be high (>35%), the frequency of SE contamination of individual eggs is low, estimated to be ~1 in 20,000 eggs, on average, in the United States (Ebel & Schlosser, 2000). The total number of eggs produced in the United States is about 65 billion/year. Therefore, despite the low frequency of egg contamination, the number of contaminated table eggs was estimated to be more than 2 million per year in the mid-1990s, indicating a potentially significant source for human exposure. The frequency of SE contamination in eggs depends on the intensity of infection among hens in a flock and the timing of egg production relative to infection. In addition, how soon eggs are produced after an SE infection, and how heavily SE is colonized in the flock are important factors. It has been estimated that in an outbreak of SE infection associated with a restaurant, the frequency of SE-contaminated eggs served may have been as high as 1 in 12 (Vugia et al, 1993).

Role of human behavior in the epidemiology of SE infections— A key factor enabling the egg to be an efficient source of human infection is the manner in which people handle and eat eggs. Eggs are one of the few animal products that are frequently eaten raw or
undercooked. Raw eggs are usually components of breakfast eggs that are cooked so that the egg white and yolk are soft or runny, beverages such as eggnog and special diet or health drinks, homemade and restaurant-produced ice creams, salad dressings, mayonnaise, mousse, hollandaise sauce, and other types of foods containing eggs that are only lightly cooked. Case control studies were conducted to investigate the role of foods in the etiology of SE infections (Hedberg et al., 1993; Marcus et al., 2007). It was concluded that people with sporadic infections with SE were over 5 times more likely to have eaten raw or undercooked eggs and/or undercooked poultry in the 3 days before their illness, compared with healthy control subjects.

**Where does exposure likely happen?**— Of the outbreaks of SE infections from 1985-1999, 62% were related to exposure in restaurants or other commercial establishments (Patrick et al., 2004). One reason that commercial or other large-scale food preparation settings may be more frequently associated with illness is the practice of pooling large numbers of eggs for use in scrambled egg dishes or as components of batters (Sobel et al., 2000). When pooling eggs, one or a few contaminated eggs can contaminate a large amount of food under conditions that may enhance fast growth of the organisms that can potentially infect a large number of consumers of such dishes.

**Emergence of broiler consumption as a risk for SE infections**— Recently, Marcus et al. (2007) reported the result of a population-based, case-control study of sporadic SE infection in five of the Foodborne Diseases Active Surveillance Network (FoodNet) sites during a 12-month period in 2002-2003. A total of 218 cases and 742 controls were enrolled. Sixty-seven (31%) of the 218 case-patients and six (1%) of the 742 controls reported travel outside the United States during the 5 days before illness onset (OR 53, 95%; CI 23-125). Eighty-one percent of cases with SE PT4 had traveled internationally. Among persons who did not travel internationally, eating chicken prepared outside the home and undercooked eggs inside the home were associated with SE infections. Contact with birds and reptiles was also associated with SE infections (Table 2).

**Table 2. Recently investigated risk factors for SE infections in the United States (Marcus et al., 2007).**

<table>
<thead>
<tr>
<th>Exposure</th>
<th>All cases and controls</th>
<th>Domestic cases and controls only</th>
<th>International travellers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases exposed</td>
<td>Controls exposed</td>
<td>OR (95% CI) PAF</td>
</tr>
<tr>
<td>Egg outside the home</td>
<td>71/201 (35%)</td>
<td>123/735 (17%)</td>
<td>1.0 (0.7-2.1) 5%</td>
</tr>
<tr>
<td>Runny egg outside the home</td>
<td>22/71 (31%)</td>
<td>23/123 (19%)</td>
<td>1.0 (0.4-3.4) 1%</td>
</tr>
<tr>
<td>Egg inside the home</td>
<td>88/217 (41%)</td>
<td>393/747 (53%)</td>
<td>0.5 (0.3-0.8) n.a.</td>
</tr>
<tr>
<td>Undercooked egg inside the home</td>
<td>61/88 (69%)</td>
<td>191/393 (49%)</td>
<td>2.1 (1.1-5.9) 15%</td>
</tr>
<tr>
<td>Chicken</td>
<td>162/203 (80%)</td>
<td>518/733 (71%)</td>
<td>0.9 (0.5-1.6) n.a.</td>
</tr>
<tr>
<td>Chicken outside the home</td>
<td>115/162 (71%)</td>
<td>254/518 (49%)</td>
<td>2.6 (1.6-4.4) 35%</td>
</tr>
<tr>
<td>Bird in the home</td>
<td>17/212 (8%)</td>
<td>31/742 (4%)</td>
<td>2.7 (1.2-5.7) 5%</td>
</tr>
<tr>
<td>Lizard in the home</td>
<td>21/216 (10%)</td>
<td>24/742 (3%)</td>
<td>3.0 (1.3-7.1) 7%</td>
</tr>
<tr>
<td>International travel</td>
<td>67/217 (31%)</td>
<td>67/742 (9%)</td>
<td>62.3 (22.8-170.5) 30%</td>
</tr>
</tbody>
</table>

OR, Odds ratio; CI, confidence interval; PAF, population attributable fraction; n.a., not applicable.
The true burden of SE infections—The number of cases of SE infections, hospitalizations, and deaths; the identified food vehicle; and the place of preparation and consumption were among the information gathered by the CDC’s SE Outbreak Reporting System in 1985. A total of 997 outbreaks of SE infection were reported in the United States from 1985-2003 (Fig. 1), resulting in 33,687 illnesses, 3,281 hospitalizations, and 82 deaths. The number of reported outbreaks of SE infection in the United States increased from 26 in 1985 to a high of 85 in 1990, with a gradual decrease to 34 outbreaks in 2003. In addition, the number of cases in outbreaks each year has decreased, from a high of 2,656 in 1990 to a low of 578 cases in 2003. The one exception was 1994, a year in which >4,000 cases were attributed to an outbreak of SE infections caused by consumption of a contaminated, nationally distributed ice cream product (Hennessy et al, 1996).

Figure 1. Reported outbreaks of SE in the United States (1985-2003) (Braden, 2006).

A food vehicle was confirmed in ~44% of outbreaks of SE infection in the United States. Eggs or foods that contained egg ingredients were responsible for 75% of infection outbreaks from 1985-2003. Although the number of reported outbreaks of SE infection has decreased (Fig. 1), the percentage of outbreaks attributed to egg consumption was consistent from year to year (Fig. 2). Outbreaks of SE infection that were not egg-associated were due to a variety of other sources, including poultry products, raw almonds, alfalfa sprouts, pork, beef, and orange juice (Isaacs et al, 2005).
The incidence of reported, laboratory-confirmed SE infection began to increase from 1/100,000 population in the 1980s to 3.9/100,000 population in 1994. At that time, SE became the most frequently reported *Salmonella* serotype, representing 26% of all *Salmonella* serotypes reported in the United States. Although the incidence of SE decreased to 1.7/100,000 population in 2003, SE remains the second-most common *Salmonella* serotype reported (14% of all *Salmonella* serotypes in 2003). High rates were first seen in the northeast in the late 1970s, followed by the mid-Atlantic states (Fig. 3). In 1988, the incidence reached 9.2 and 10.5/100,000 population in the northeast and the mid-Atlantic states, respectively. In the Pacific states, the incidence reached 6.7/100,000 population in 1994. The incidence in the United States decreased by 56% from 1995 (3.9/100,000) to 2003 (1.7/100,000).
Surveillance data are based on laboratory-confirmed SE infections. However, laboratory-confirmed infections represent an underestimation of the total number of SE illnesses that occur in the United States each year because most clinical laboratories do not perform full serotyping, and at each step along the surveillance pathway, a portion of cases is lost. The CDC estimated these lost proportions by conducting surveys of ill people, health care providers, laboratories, and public health departments, and constructed a surveillance pyramid for salmonellosis (Fig. 4). Thus, an estimate of the true burden of diseases can be calculated when each lost portion is accounted for. For *Salmonella*, it is estimated that, for each laboratory-confirmed case, there are 38 cases that are missed (Voetsch et al, 2004). Taking the number of SE cases reported in national surveillance for 2003 (4,890), and applying the multiplier of 38, an estimated total of 185,820 cases of SE may have occurred that year in the United States.
Based on data provided by the SE Outbreak Reporting System and from national laboratory-based case surveillance, the CDC has estimated that SE-contaminated eggs accounted for approximately 180,000 illnesses in the United States in 2000 (Schroeder et al, 2005).

**Fluctuation or fall of the SE pandemic**—A current perception of the epidemiology of SE is that of a pathogen that has found a niche in commercially produced shell eggs and that causes major outbreaks in the United States and many other countries. In the early 1990s, while SE rates of infection in the northeast began to decline, the SE epidemic expanded to the Pacific region. Nationwide, the number of SE isolates reported to the CDC peaked at 3.8/100,000 population in 1995. Although the number of SE isolates reported to the CDC had significantly declined to 1.9/100,000 by 1999, this rate did not decline through 2001 and even increased in the southeastern regions. Although the number of culture-confirmed SE infections reported to the CDC declined in 1999, the number has not decreased since this date, and some regions have seen increases again with the appearance of SE-PT4 infections (USCDC, 2006; Cogan & Humphrey, 2003). An explanation for the current variations in Salmonella infections could be related to the frequency of SE in poultry flocks leading to flock immunity, which could have led to its decline. However, it is possible that, as a serotype becomes less prevalent, the number of immune individuals decreases, which could itself lead again to an increase in prevalence.

**Prevention and control of SE infection in the United States**—It must be stated that the reduction in the incidence SE infections in the United States should be attributed to the response of several agencies who are charged with food safety, including egg safety. The following agencies have played, over the years, a pivotal role: FSIS, NPIP, the USDA's
Agricultural Marketing Service, and FDA, which has had the regulatory authority to conduct inspections and investigations of egg producers.

The FDA and the CDC work closely in the context of egg-associated outbreaks of SE infection in humans to trace infected eggs to production flocks and to establish interventions aimed at halting and preventing additional human infections. In 1990, the FDA's Food Code was amended to include shell eggs as a "potentially hazardous food," indicating that proper cooking time and temperature controls are required to limit pathogenic microorganism growth. In 1996, the FSIS, in collaboration with the FDA, initiated a "farm-to-table" risk assessment of SE in shell eggs, which served as the basis for the federal and state Egg Safety Action Plan to address shell egg and egg product safety (USFSIS, 2005).

The three intervention policies aimed at the prevention of contamination of shell eggs by SE can be summarized as follows: the development of egg quality-assurance programs on farms, the rapid and sustained refrigeration of eggs from farm to consumer, and the education of consumers and food workers about the risks associated with pooling, handling, and consuming raw or undercooked eggs.

Egg quality-assurance programs on farms are comprehensive plans to limit SE contamination and spread in the farm environment. These voluntary programs usually include acquisition of chicks certified free of SE; control of pests (including rodents and flies, which may harbor or disseminate the organisms); restriction of access to and movement of personnel and equipment among hen houses; use of SE-free feed, cleaning and disinfection of hen houses between successive flocks; and microbiological testing for SE of the farm environment on a routine basis.

In most egg quality-assurance programs, repeated isolation of SE from a farm environment results in a diversion of eggs from that farm to egg-processing plants, where all egg products (i.e., pasteurized liquid egg or powdered egg products) are heat treated to reduce bacterial contamination. These programs have been shown to be effective in reducing rates of human SE illnesses (Muma et al, 2004). The FDA has proposed a regulation that would make egg quality-assurance programs mandatory for medium and large shell egg producers. This regulation involves new technologies, which are already used by some producers, that have been developed to address SE contamination, such as in-shell pasteurization of table eggs. This method of pasteurization applies a relatively low temperature to eggs for a prolonged period (compared with usual pasteurization methods), so as to reduce microbial contamination while preserving the liquid nature of the egg contents. According to a risk assessment developed by the FSIS, the number of SE-related illnesses in the United States could decrease by almost 70% if all shell eggs underwent pasteurization to achieve a 3-log reduction of SE count (USFSIS, 2005).

Furthermore, education of food workers and the public is important for the reduction of practices associated with high risk of exposure to SE infection. Physicians can play a role in SE control by educating patients of the risks associated with consumption of raw or undercooked eggs, the need to avoid contamination of other foods with raw eggs, and the
importance of hand washing after handling eggs. Supervisors in facilities that care for immunocompromised patients should establish a policy that only pasteurized egg products be served to patients. In addition, physicians caring for patients with possible *Salmonella* infection should follow the Infectious Diseases Society of America guidelines on submission of diagnostic specimens, including stool specimens. This will not only aid in the treatment of patients, but it will increase the completeness and accuracy of surveillance data that are important in recognizing outbreaks of SE infection and following surveillance trends of the burden of disease.

Interventions targeted to address these factors have been designed and implemented in many sectors of the egg industry. Although the epidemic levels of SE illness have decreased, there are still many cases and outbreaks of infection each year due to consumption of contaminated eggs. There is still much work to be done to reach the Department of Health and Human Services' (USDHHS) “Healthy People 2010” goal to reduce the number of human SE infections in the United States by 50%, compared with the number of infections in 1997 (USDHHS, 2000). A USDA risk assessment group concluded, after stakeholder input and thorough review according to OMB guidelines, that, based on the best available science, pasteurization and rapid cooling of eggs are predicted to be effective for reducing illnesses from SE in eggs and *Salmonella* species in egg products (USFSIS, 2005).

**Broilers**

Broiler chickens are those that are raised for meat. They are grown for about 6 weeks, at which time they are sent for slaughter. The broiler industry, like the layer industry, is integrated, which means that one company controls almost all aspects of production, from hatching through processing. The broiler industry has grown substantially over a 45 year period with the number of birds produced increasing from approximately 1.8 billion in 1960 to an estimated 8.9 billion in 2005. During this same time span, production increase can also be measured by the production of 4.3 billion pounds of ready-to-cook poultry in 1960 to an estimated 35.2 billion pounds in 2005 (Shelton, 2005). In 2006, production was 35.8 billion pounds with an estimated 8.9 billion birds in the eight leading broiler states (GA, AR, AL, MS, NC, TX, KY, MD) (USDA ERS, 2007).

The US poultry industry has an annual revenue of more than $40 billion. An estimated 500,000 people are employed directly by the industry, while those employed in the various allied industries, marketers, etc. count for many more. For most workers, their poultry industry job is their sole source of income. Raising poultry is a sustaining industry, especially for rural areas of the southern United States, and many farms raising poultry for the integrated poultry companies are family-owned, contract growing operations.

Efficient production by successful integrated poultry companies is based on detailed long-term plans and organization. Primary breeder companies must raise enough breeders to produce commercial multiplier flocks that will, in turn, produce sufficient eggs to hatch into broilers birds for commercial meat production. If any significant export market is lost, this pipeline would be dramatically disrupted. The birds already in the different
sectors—primary breeders, multiplier breeder and broilers—would still need feed, water and care, yet there would not be a ready market for the product, and the domestic market could not absorb this excess in product. In countries with large-scale commercial poultry operations, the decrease of domestic consumption after H5N1 infections in the country has been dramatic. The industries, both meat-producing chicken and turkey, and egg-producing, could be severely financially compromised due to the loss of the export market and the associated effects. Primary breeder companies, which supply the world with breeder stock, would be severely affected as well, as the export market would stop for this product.

The cycle is as follows: Primary breeder companies maintain all the “grandfather stocks” of chickens. These companies are usually not integrated with the rest of the industry and are the only part that is separate. Multiplier flocks supply eggs for the hatcheries. When the multiplier flocks need new stock, they buy them from the primary breeders. The eggs from the multiplier flocks are sent to the hatchery, where the eggs are carefully monitored, and one day after hatching, the chicks are sent to large chicken houses. In these chicken houses, all chickens of the same age grow together for about six weeks, at which time they are collected and transported to the slaughter plant. Details of each of these stages are listed below:

**Primary breeder industry**—The primary breeder companies in the United States provide the majority of broiler chicken and turkey commercial poultry genetics for the world. These companies distribute their stock to most countries, and their success depends on their reputation for healthy, quality products from the progeny of their parent flocks. Biosecurity is strict. Vaccination and veterinary care is delivered by veterinarians certified by the American College of Poultry Veterinarians, a specialty organization recognized by the American Veterinary Medical Association. The primary breeder industry, as well as all other aspects of broiler production, is enrolled in the National Poultry Improvement Plan (NPIP) for disease control. Under this program, flocks are continually monitored for disease surveillance.

**Breeders**—Integrated poultry companies own their own multiplier flocks to produce the eggs for hatching of broilers. These flocks represent a major investment and are necessary for all future birds to be raised to supply the company’s meat products. These flocks are maintained in much the same way that the primary breeders are, with strict biosecurity and a well-defined regimen of veterinary care. These breeder (or multiplier) flocks for production of broiler chicken hatching eggs are inoculated throughout the first 18 weeks of life with a variety of vaccines meant to protect the breeder flock and/or to pass immunity to the progeny. At 20 weeks of age, the pullets (young hens) are transported to the breeder farm. Production begins around 26 weeks of age and continues until approximately 63 weeks or so of age on the first round. Flocks may be molted for a second cycle of production. Samples, to test for pathogens such as *Salmonella*, are taken throughout the life of the flock.

Hens are housed with roosters with an 8-10:1 ratio in houses with slat areas to provide the hens a place to rest.
Houses used for broiler breeder flocks of any stage of life are normally thoroughly cleaned and disinfected after each flock. The litter is removed, and the house is washed down inside and disinfected. All feeders and drinkers and the lines to each are disassembled, washed, and disinfected. All feed is removed from the farm, and the bins are cleaned and disinfected. A rest period for the farm breaks any possible disease cycle.

**Hatcheries**—In addition to being members of the NPIP hatchery programs, hatcheries are maintained under the company biosecurity program. These programs have details for cleaning and sanitizing the equipment, building, and transport vehicles. Broiler eggs are held in the egg room of the hatchery for an ideal 3-5 days before they are set in temperature and humidity-controlled machines. After 18 days of incubation, the eggs are hand-transferred through an automated vaccinating machine. This machine punches a tiny hole in the top of each egg and deposits a vaccine to provide the embryo with its first vaccination. The eggs are put into the hatcher for an additional 3 days. When the chicks are removed from the hatcher, they are processed by vaccinating with an automated spray, counted and placed in baskets for delivery to farms.

The hatchers are scraped to remove down and manually-scrubbed of all organic debris and sanitized after every hatch. All equipment, including any vehicles for transport, is treated similarly.

**Placement**—Houses for placement of newly-hatched poultry are prepared in advance with ample feed and water available. The house is pre-warmed to provide a good environment for starting the flock. All poultry is fed with several formula changes throughout the growing period, and flocks receive a special feed for starting out. Heat is provided to the flock for varying periods depending on the outside temperatures and conditions. Ventilation is provided by the use of fans and curtains. Bedding is usually made from rice hulls or wood shavings.

**Grow-out**—The care and management of the farm is handled by the farm manager, but oversight is provided by the service man or woman employed by the company who visits the farm weekly and reports problems to the company veterinarian or consultant. Unlike some of the other animal industries, in the broiler industry, the “farmer” merely provides the land with the houses to maintain the birds and the labor to oversee their successful growth. The health of the birds is the primary focus because healthy birds are necessary for good feed conversion into meat and good processing results at the inspection station in the plant.

**Feed mills**—Feed mills supply medicated feeds and are licensed by the Food and Drug Administration (FDA). As part of that program, they are routinely and randomly inspected, including observation of all records and the premises. Inspectors are looking for any product that should not be in the mill because it is a banned substance or not labeled for the animals being fed by the mill. Processing of feeds also requires temperature control. Care is taken to flush the mixers after each use in order to avoid the
carry-over of any drugs to the next feed being prepared. Ingredients are tested for quality, pathogens, and toxins.

Mills must maintain records for all feed additives purchased and those used. Inventories of feed additives must balance for the FDA inspector during the visit, and use is in accordance with FDA approvals as compiled in the Feed Additive Compendium. The Compendium is regularly updated as changes in approvals are made. All feeds produced must be recorded, including date and time produced, and which truck was used to specific farms and poultry houses on the farm. A feed tag with the name of the feed and the additives included is left at the farm for the farm record on the flock. Warnings for any withdrawal times required are included on the tag. Company records for the flock include the feeds provided, and the mill has all formulas used for each feed on record. Processing of feeds require temperature control. Prescriptions require veterinary approval; therefore, use of a Veterinary Feed Directive drug is permitted only under the professional supervision of a licensed veterinarian.

**Processing plants**– The age of processing varies, but broilers are usually marketed at 6 weeks of age. Before birds are processed, they are usually inspected by the service person so the plant can get an idea of the health and weight of the birds. Samples for testing for pesticides, drugs, and polychlorinated biphenyls (PCBs) are taken at this time. The veterinarian, farmer, service person, and grow-out manager are responsible for ensuring the proper withdrawal time is observed for the feed additives. The final feed given to the flock does not contain any ingredients requiring withdrawal time. All feed is removed from the flock on the day of processing, and water is removed prior to loading of the birds.

At the plant, the Inspector in Charge (IIC), a veterinarian employed by the Food Safety Inspection Service (FSIS), is responsible for the team of inspectors trained by the service. This team is responsible for inspecting every carcass, both inside and out, for pathologic changes and wholesomeness. Carcasses not meeting the proper criteria are condemned, sprayed with inedible dye, and taken out of the plant. Inspectors roam the plant taking samples of the environment and sampling carcasses for *Salmonella*, *E. coli*, and fecal material. Random samples are ordered by the FSIS and taken by the IIC for testing in government labs to check for drugs, pesticides, and PCBs. Before the plant can begin operation, it is inspected for sanitation and maintenance issues by the IIC or inspector with IIC oversight. Records are maintained in every plant. Antemortem inspections are performed by the veterinarian, and the inspectors routinely observe operations in all areas of the plant. If the FSIS inspectors or veterinarians have a concern or observe something they feel should be corrected, they can and do stop the line. Stopping the line means a total halt to all inspections, and several hundred people may be standing idle until the problem is corrected. Regular testing of temperatures and chlorine levels are conducted and recorded. Carcasses are sampled every hour and inspected for processing defects and quality by the inspectors. All records of all inspections, observations, and tests are maintained by the United States Department of Agriculture (USDA) and the plants. Weekly, the IIC and plant managers meet to discuss issues and concerns from each side. District supervisors from the FSIS visit the plant regularly.

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Major integrated companies have a brand name. People know the product and associate the quality with the label. If a company produced an inferior product or one with a recognized quality or food safety issue, it could have serious economic consequences for the company.

**Human health threat of avian influenza**

Global outbreaks of influenza have occurred periodically in the human population. The viruses of the outbreaks in the 20th century were avian in origin and arose through mutational events. In particular, recent evidence of direct bird-to-human transmission has increased global concerns over the pandemic potential of these viruses (De Jong & Hien, 2006).

**The virus**– Influenza viruses are covered by protein and a fatty membrane coating called an envelope. There are two proteins of particular importance in this envelope. One is the hemagglutinin (HA), which helps the virus attach to cells (e.g., cells in the respiratory track) that it then invades. The other is neuraminidase (NA), which allows the virus to leave a cell after multiplying so that it can spread to other cells. A unique characteristic of influenza viruses is their genetic structure: each gene is on a separate piece of genetic material, called RNA; this is distinct from many other viruses, most of which have a single piece of genetic material that contains all of the genes. This unique structure allows “mixing” of influenza viruses, contributing to their high mutation rate, discussed below.

Influenza viruses are classified as types A, B, or C, with the majority characterized as type A. Within the type A classification are subtypes based on the structure (antigenicity) of the HA and NA proteins; thus far 16 HA and 9 NA subtypes have been identified. Influenza viruses are also classified based on their virulence (ability to cause serious disease) in avian hosts and are termed high pathogenic (HP) or low pathogenic (LP) strains to denote their potential to cause severe vs. mild disease signs, respectively, in infected birds.

Antigenicity refers to the ability to stimulate an immune response. The HA and NA envelope proteins are major determinants of the antigenicity of influenza viruses and are the major targets of a host’s immune response. These proteins are given numeric designations (HA1-16, NA1-9). Only 3 HA subtypes (1, 2, and 3) and 2 NA subtypes (1 and 2) have circulated in humans since the beginning of the 20th century (DeJong & Hien, 2006). These methods of classifying virus strains based on the envelope proteins is why strains are referred to in an abbreviated format using the number of the two types of proteins. For example, H5N1 means that the virus has the hemagglutinin protein #5 and the neuraminidase #1 structure. The H5N1 virus is thus antigenically distinct from the common human strains such as H3N2 and H1N1; that is, the immune response we develop to H3N2 will not protect against H5N1 should it become adapted to humans. Birds, and in particular waterfowl, are the natural reservoir of influenza viruses (i.e., where the viruses are perpetuated indefinitely), and harbor all known subtypes of the virus.
Because of the nature of their genetic material, influenza viruses have a relatively high mutation rate compared to many other types of viruses; this is because the enzyme responsible for copying this genetic material during virus replication makes frequent “mistakes.” These mistakes made when the virus replicates lead to minor or “point” mutations in viral genes and thus in the resultant viral proteins. When these changes occur in the genes that produce HA or NA, it is referred to as antigenic drift, with “drift” alluding to the small changes that occur in the protein. These minor changes alter the antigenicity of the virus, leading to a large number of different influenza virus strains. As mentioned above, influenza viruses also have their genes distributed on individual segments. This allows for an additional mechanism of mutation termed reassortment, which refers to the exchange or “mixing” of genome segments between two distinct influenza viruses infecting a single cell. For example, the “swine flu” of 1976 arose from mixing of swine and human influenza viruses. Reassortment between avian and mammalian influenza viruses may allow for rapid and significant changes in the virus, including its ability to cause disease and the severity of that disease. These so-called “new viruses” can spread rapidly, as no one will have pre-existing immunity because of vaccination or past infection.

Pathogenesis of influenza virus—Influenza viruses are transmitted by aerosol and direct contact (virus shedding is discussed in the section on epidemiology). The virus enters through the mouth and/or nose and attaches to the cells lining the respiratory track by using sialic acid (SA) residues. Human influenza viruses use $\alpha$-2,6 SA linkage, while avian viruses use $\alpha$-2,3 SA linkage. This is believed to be one barrier to transmission from birds to humans. However, the cells lining the human lower respiratory tract have both linkages (Peiris et al, 2007). Following attachment of the virus to the cell, it enters the cells by fusing its envelope with the cellular membrane wall. This process requires that the HA protein be essentially cut into two pieces by an enzyme present in animal respiratory and gastrointestinal tracts. The requirement for this enzyme limits the ability of the virus to infect cells only within these body systems. However, certain mutations in the HA may allow this process to occur more easily and by a number of different enzymes found in many different tissues; this allows replication in tissues outside of the respiratory and GI tracts, a characteristic of the highly pathogenic influenza strains described below.

After the virus enters the cell, viral replication occurs. Assembly of new virions (individual virus particles) occurs, and the mature viruses bud through the cellular membrane. This is the stage of replication in which the neuraminidase protein in the envelope is important. It allows the virus to leave the cell and be released to infect new cells.

Viral replication within a cell leads to its death. Virus factors that increase the ability of the virus to replicate, or its “infectivity” affect the virulence of the virus. Influenza viruses are classified based on pathogenicity, with HP strains leading to severe disease and death in infected animals. Most avian influenzas do not cause obvious disease or cause only mild disease, referred to as LP strains. Infection of poultry with HP strains
shows up as decreased egg production, respiratory disease, edema and hemorrhages, diarrhea, neurological signs, and death (De Jong & Hien, 2006). Currently, HP strains are restricted to the H5 and H7 subtypes, but HP strains are believed to arise from LP strains by mutation or transformation of the virus as described previously. This occurs primarily in domestic poultry. While it probably also occurs in wild birds, documented outbreaks are rare (Gauthier-Clerc et al, 2007). The outbreaks in domestic poultry generally remain localized geographically, though a few have been more widespread, leading to significant economic losses (Gauthier-Clerc, 2007).

**Epidemiology of influenza virus**—As stated above, the reservoir of influenza virus is birds, particularly aquatic species like ducks and geese. In wild birds, the viruses rarely cause disease, a consequence of a long co-evolution, allowing the viruses to remain in their hosts without destroying them (Gauthier-Clerc, 2007). The viruses replicate in the gastrointestinal tract, are shed in feces, and will contaminate the water where the birds live. In lake water, the virus may remain viable for several days at 22°C, (~76°F) and over a month at freezing temperature (Alexander, 2007). Fecal-oral transmission is the most common mode of spread to new avian hosts. However, among domestic poultry, respiratory transmission is also important (Alexander, 2007).

Surveillance studies done on wild birds in North America and Europe have revealed a high prevalence rate of infection with influenza viruses of low virulence for poultry (Van Reeth, 2007). Some of these, such as ducks, geese, terns, and gulls, have the potential to spread the virus within and between continents via migration. Infected wild birds may also introduce the virus into domestic poultry, especially those in open areas (Alexander, 2007). Once in domestic flocks, spread can occur through contaminated food and water, and movement of contaminated equipment and personnel (Alexander, 2007; Van Reeth, 2007).

From the reservoir of aquatic birds, viruses may also be transmitted to mammals, causing transitory infections and outbreaks. Through adaptation by mutation or genetic reassortment, some of these viruses may become adapted to different mammalian species, including humans, and could cause epidemics or epizootics in the new host (DeJong & Hien, 2006).

Receptors for both avian and mammalian influenza viruses are present on the cells lining the respiratory track of swine. Because of this, swine are considered to be the “mixing pot” for influenza viruses, potentially allowing production of new virus strains with genetic elements from viruses of birds and mammals (Periris et al, 2007). In fact, most swine isolates are reassortants with mixtures of human, avian, and swine virus genes (Van Reeth, 2007).

Direct transmission of avian influenza to other mammalian species, including humans, is uncommon. Various viral properties are believed to be responsible for this barrier to interspecies spread. However, reassortment has led to several influenza pandemics, including those of 1957 and 1968 (Peiris et al, 2007). Direct spread from avian reservoirs has also occurred, with the 1918 pandemic (H1N1; “Spanish Flu”) being the most notable
example (Peiris et al, 2007). In addition, direct transmission leading to disease in humans has occurred with several other subtypes, including H7N7, H9N2, H7N3, and H5N1 (Peiris et al, 2007).

**Non-H5N1 avian influenza in humans**– As stated above, several subtypes of avian influenza virus have been known to infect and cause disease in humans. H7N7 has been associated with conjunctivitis in humans, and during a poultry outbreak in the Netherlands in 2003, infection with a flu-like illness occurred in a number of exposed persons (Peiris et al, 2007). The highest infection rate was in veterinarians and those involved with culling of the poultry. An outbreak of H7N3 in Canadian poultry led to infection with conjunctivitis in two people. The H7 subtypes appear to have a predilection for the cells of the tissues around the eye (conjunctival epithelia) in humans (Peiris et al, 2007). H9N2 has repeatedly infected humans in Asia, causing a mild flu-like illness. In all of these incidents, human-to-human spread has been nonexistent or minimal (Peiris et al, 2007).

**Highly pathogenic avian influenza (HPAI) H5N1 in birds**– In recent years, there has been an increase in the frequency of HPAI outbreaks and numbers of birds affected (Alexander, 2007). This is speculated to be due to a number of factors, including increased awareness of the possibility of infection, improved diagnostic tests, changes in poultry production, and perhaps changes in wild bird movements (Alexander, 2007). The emergence of HPAI H5N1 in 1996 and its global spread has been unprecedented. It was first detected in geese in Guangdong Province of China. By 1997, an outbreak in both domestic and wild birds in Hong Kong led to infection of 18 people, 6 of whom died (Peiris et al, 2007). Since 2000, a series of reassortants have emerged in terrestrial poultry, but by 2003, a dominant genotype (Z) emerged in southern China (Peiris et al, 2007). Despite this, significant genetic and antigenic variability occurs among H5N1 isolates. Unusually, some of the H5N1 isolates caused severe disease in ducks and other aquatic birds. In May 2005, an outbreak occurred in the Qinghai Lake region of western China in migratory waterfowl, the first sustained outbreak in wild birds that has been documented (Peiris et al, 2007). Since then, the virus has been found in wild birds and domestic fowl in Europe, the Middle East, Africa, and Asia. By July 2006, it had occurred in 54 countries, led to death or culling of over 600 million birds, and had infected humans and other species, causing disease, and in some cases, death. The virus is now endemic in poultry in southeast Asia (Chen et al, 2007).

**Human infection with H5N1**– From the first occurrence of H5N1 in humans, it was apparent that infection with this virus led to severe disease with a high mortality rate. Most cases manifest as typical but severe influenza, with fever, cough, and pneumonia (DeJong & Hien, 2006). A significant proportion also experienced gastrointestinal illness, including diarrhea and vomiting. Complications have included acute respiratory distress, renal failure, and multi-organ failure. Involvement of the central nervous system has been implicated in a minority of cases. Tissue destruction leading to disease may result not only directly from the virus replicating, but also from the immune response of the person against the virus (DeJong & Hien, 2006). Increased levels of certain components of inflammation are believed to contribute to the severity of the disease with H5N1. The
The apparent increased virulence of H5N1, its ability to infect humans, and its widespread geographic distribution in both domestic and wild birds have raised concerns over its potential to initiate a pandemic (a worldwide epidemic). Two of the three requirements for a human pandemic have been met: 1) the emergence of an antigenically novel strain, and 2) transmission of the virus to humans, leading to disease (DeJong & Hien, 2006). An H5N1 isolate that is easily transmissible person-to-person could lead to a global outbreak in people. Since H5N1 would be a “new” virus in humans, no one would be immune to the virus, either from previous infections or vaccination. Thus, all people would be susceptible to infection. Whether a human-adapted strain arises through minor mutations in an avian virus or via reassortment with human or other mammalian influenza (eg swine), the consequences could be significant.

Spread of H5N1– Early discovery of H5N1 in poultry in one country has allowed eradication by aggressive measures, including culling of exposed flocks (Peiris et al, 2007). Once it is widespread, it becomes more difficult to eliminate; reasons contributing to this difficulty include high prevalence of backyard flocks, mixing of chickens and ducks, asymptomatic shedding in ducks, live poultry markets, and wildlife trade (Peiris et al, 2007). Live poultry markets in particular serve as mechanisms for amplification and spread of the virus. In addition, in ducks, the virus appears to lose virulence for ducks while retaining virulence for chickens; as the virus replicates in ducks, it undergoes antigenic change and may be shed for 2-3 weeks. Thus, ducks may serve as important sources of infection for other domestic fowl. Pet birds, poultry products, and fighting birds may also spread the virus (Peiris et al, 2007).

Infection of humans first occurred in the Hong Kong outbreak of 1997; the source of exposure was live poultry markets (Peiris et al, 2007). Most cases of human infections have been from handling of diseased poultry, including slaughter, preparation for consumption and consumption of raw products, and close contact with live poultry (Hayden & Croisier, 2005). Indirect exposure via a contaminated environment has also led to infection of humans in some cases. Despite this evidence, many people exposed to large doses of the virus in their work or home environment do not become infected; thus, transmission to humans appears to be inefficient and may involve as yet unknown host susceptibility factors (Peiris et al, 2007). Transmission to humans from infected poultry has been low in H5N1 outbreaks in Cambodia, for example, despite high exposure rates (Vong et al, 2006). Exposure from live animal markets has been identified as a risk in urban China, but even in these situations, the risk was low (Yu et al, 2007).

As per the authors, the spread of H5N1 in Africa was due primarily to movement of poultry and wild birds in trade, while movement in Europe was primarily via migratory birds (Kilpatrick et al, 2006). Introduction of H5N1 into the United States is most likely
to occur via trade in poultry and poultry products, as well as trade in wild birds rather than spread via migratory birds (Kilpatrick et al, 2006). However, spread of H5N1 into northeastern Siberia would increase the risk of spread to North America through migration. Additionally, if this virus strain was introduced into the United States, migratory birds could contribute to the dispersal of the virus (Rappole & Hubalek, 2006).

Factors that may impact spread of H5N1 in the United States— Influenza infection in wild birds manifests as sick birds and die-offs; thus it is unlikely that its introduction via wild bird movements would go unnoticed by wildlife officials (Rappole & Hubalek, 2006). Additionally, most domestic poultry are kept isolated from wild birds through total confinement, which would also minimize the risk of exposure of commercial domestic poultry from wild birds. However, mixing of wild birds with captive birds at zoologic institutions is common; thus, ill birds at these facilities should be screened for the virus.

Movement of poultry or poultry products within the United States is unlikely to be an important means of spread given the existing regulations (Rappole & Hubalek, 2006). However, movements of birds and bird products have been the sole means of virus movement between geographically distant locales such as between continents (Gauthier-Clerc et al, 2007). In fact, illegal import of birds or bird products seems to be the most likely mode of entry into the United States (Rappole & Hubalek, 2006). Control of legal and illegal imports should be a focus of prevention.

If H5N1 were introduced into domestic animals, whether poultry alone or with swine, workers in contact with these animals could be at significant risk. In a report described by Gilchrist et al (2007), farmers, veterinarians, and meat processors were all at increased risk for exposure to influenza. A study by Myers et al (2007) investigating seroprevalence of avian influenza infection among US veterinarians found that their risk was significant. Measures to address this risk, including education, hygiene, and vaccination (including for seasonal influenza, the common influenza viruses experienced annually in human populations) of these groups will be important.

In animal populations, CAFOs could facilitate rapid spread of the agent (Gilchrist et al, 2007). There is also concern that increasing numbers of swine operations adjacent to poultry facilities could contribute to emergence of pandemic influenza (Gilchrist et al, 2007). The intense and prolonged exposure workers at these facilities experience may provide an opportunity for mixing of human and animal viruses, either through zoonotic transmission or vice versa (Gray et al, 2007). Thus, these workers could serve as an important bridge from the animal populations to the human community. Agricultural workers should be a priority population for training, surveillance, and immunization (Gray et al, 2007).

If the H5N1– or other avian influenza virus to which the human population is immunologically naïve– becomes adapted to humans allowing efficient person-to-person transmission, a pandemic will be likely. A recent model– based on analysis of the 1918-1919 influenza pandemic– estimates that in the United States, one third of transmissions
will occur in the household, one third in workplaces and schools, and one third in the general community (Bartlett, 2006). Thus, social distancing would be of paramount importance to control the spread (Larson, 2007). During a pandemic, health care workers also would be at increased risk. In the recent SARS outbreak, health care workers constituted 20% of the cases (Bartlett, 2006). Nosocomial (hospital acquired) transmission of H5N1 occurred in health care workers in Hong Kong in 1997 and Vietnam in 2005 (Hayden & Croisier, 2005). Appropriate measures to protect at-risk personnel will also be vital. Guidelines designed by the World Health Organization and CDC should be in place in all health care facilities, and include the recommendation of the use of personal protective equipment in all suspected cases of avian influenza (Sandrock & Kelly, 2007).

Even if adaptation to humans does not occur, introduction of this virus to US poultry could be devastating economically. Biosecurity measures at the farm level will be required to minimize the risk from avian influenza. Bioexclusion and biocontainment will create a “firewall” against infection of poultry flocks (Capua & Marangon, 2006). Enhanced surveillance and diagnostic capabilities as well as planning for a rapid response if introduction occurs will be critical (Peiris et al, 2007). Low pathogenic strains of H5 and H7 subtypes should be included in the surveillance programs due to their potential to become highly pathogenic. This measure has been adopted by the European Union (Pittman et al, 2007). In addition, a complete understanding of the epidemiology of the virus will allow identification of “points of intervention,” where a break in transmission may be most easily interrupted (Peiris et al, 2007). For example, control measures at some live markets in Asia have been instituted, including “day of rest” where the market is closed to facilitate interruption of transmission. Continued surveillance and biosecurity will allow rapid and effective response, but questions remain as practices change.

**Avian influenza, globally and in the United States**

Avian influenza, also called H5N1, was first recognized in southeast China in geese in 1996, but the virus is thought to have been circulating in duck and geese flocks in that area for some time. The disease first gained international recognition when Hong Kong experienced an outbreak in 1997 during which 18 humans contracted the disease and six died. Since 2003, the disease has spread in domestic poultry and/or wild birds to, first, East and Southeast Asia, then to Mongolia, southern Russia, and the Middle East, and then to Europe, Africa and South Asia (Jutzi & Domenech, 2006).

**Effect on US poultry industry**– Avian influenza has not reached the western hemisphere as of this writing (2007). Although this is encouraging news, the fact that the disease is widespread in other parts of the world and is endemic in at least one country makes H5N1 a very real threat to the US poultry industry.

If one wild bird with HPAI H5N1 were to be identified in the United States, the entire export market could be lost. If a flock became infected with HPAI H5N1, the export market definitely would be lost. Countries have imposed strict trade restrictions in the past whenever an H5 or H7 avian influenza-positive poultry flock has been found, and
this virus, highly pathogenic H5N1, is much more significant in terms of the disease and the public perception.

While there are government programs to assist with control of the disease, the losses resulting from a positive case would be tremendous. One such program for control of H5N2 avian influenza in 1983-84 that involved layer operations in Pennsylvania resulted in $63 million in direct costs, with 17 million birds destroyed, and $350 million in increased cost to the consumer (Perez & Slemons, 2004). A similar control campaign conducted for exotic Newcastle disease in five Western states affected mostly backyard poultry and layer operations instead of large poultry flocks in 2002-2003, but it cost $175 million with 4.5 million birds destroyed (USAPHIS, 2005b).

If the first positive case of HPAI H5N1 were diagnosed very early in the disease outbreak and eliminated immediately, losses could be decreased, but surrounding flocks would be destroyed, movement controls would be implemented, markets would be lost, increased surveillance would result, and expenses for these and other necessary reactions to the positive case would be enormous. In addition, it would take several years to regain the export market. All related losses could be financially crippling to the industry.

**Status of H5N1 global spread**— The 44 countries reporting H5N1 in domestic poultry from 2003-2007 are listed below (World Organisation for Animal Health, 2007). A review of the control program for selected countries follows the list.

Afghanistan, Albania, Azerbaijan, Bangladesh, Burkina Faso, Cambodia, Cameroon, China, Cote d’Ivoire, Czech Republic, Denmark, Djibouti, Egypt, France, Germany, Ghana, Hungary, India, Indonesia, Iraq, Israel, Japan, Jordan, Kazakhstan, Korea, Kuwait, Laos, Malaysia, Myanmar, Niger, Nigeria, Pakistan, Palestinian Autonomous Territories, Romania, Russia, Serbia and Montenegro, Sudan, Sweden, Thailand, Togo, Turkey, Ukraine, United Kingdom, Vietnam.

The following is a review of the reactions to H5N1 in a few of the countries that have experienced significant disease challenge from the virus.

**Hong Kong (China)**

Hong Kong adopted a series of control and preventative measures beginning in 1998, which includes vaccination, regulation of local farms, import control, segregation policy, market rest days, hygiene requirements for markets, and surveillance, making the Hong Kong avian influenza control program the most comprehensive avian influenza H5N1 control program to date (Yeoh, 2004).

- **Vaccination:** All birds offered for sale in the markets must have been vaccinated. Regulation of local farms—All farms must be bird-proof and monitored. Sentinel birds, birds that are susceptible to avian influenza and are used as biological monitors to detect if and when the virus enters the flock, are placed in each batch of vaccinated poultry, and the antibody level of vaccinated birds is monitored. Each batch is inspected and tested prior to marketing.
• **Imports:** All farms must be registered, and each consignment of imported birds must be accompanied by a health certificate. Dead/sick birds and antibody levels of imported chickens are monitored, and random screening for infection occurs.

• **Segregation:** Waterfowl are not allowed in retail markets and must be centrally-slaughtered. Waterfowl offal must be separately and individually packed. Live quail must be segregated from live chickens from the farm through retail, and no live quail are sold in retail outlets.

• **Rest days for markets:** Wholesale markets must have four rest days per month and retail outlets must have two. All poultry must be slaughtered in the markets, and the premises must be cleaned and disinfected.

• **Hygiene requirements for markets:** All cages, trucks and litter trays must be cleaned and disinfected everyday. If one dead bird with H5 is found, all birds must be immediately slaughtered and the outlet cleaned and disinfected.

• **Surveillance:** Poultry at all levels are targeted: farms, imports, wholesale market, and retail outlets.

These measures were extreme, but with the density of the human population and number of human deaths in Hong Kong, the extensive, continued marketing of live birds in the city, and the ongoing threat from the outbreaks in mainland China and wild bird cases, the expenses for the program can be justified. Hong Kong has experienced several outbreaks since 1997 and, through the ongoing surveillance program for markets and wild birds, several wild birds in the area have been found to be infected with the virus.

**Indonesia**

H5N1 was first reported there in 2004. Given the large poultry population, the density of the human population, and the intensive live bird marketing system requiring tremendous numbers of birds to be moved on a daily basis, spread of the virus and human cases were inevitable. The disease is considered endemic with all but two provinces positive. Complicating control efforts are the lack of an ability to enforce control measures and competing and significant demands on the few resources available. Demands include those of natural disasters, such as earthquakes and volcanoes; and diseases, such as brucellosis and anthrax in animals and tuberculosis, AIDS, and dengue fever in humans.

To consider the difficulty of the H5N1 control situation in Indonesia, ponder only this one important aspect of disease control: effective movement control can have significant positive impact on disease control efforts. However, just preventing smuggling of birds, where virtually every backyard has poultry and the nation consists of over 13,000 islands, is a daunting task.

**Vietnam**

HPAI was first reported in January 2004 and, subsequently, the majority of cases were found in the Mekong River Delta in the south and the Red River area in the north. These two locations are the sites of intensive duck farming, where domestic ducks are free-ranging and move from rice paddy to rice paddy to feed. This type of farming is a traditional way of life in the area.
From the initial finding through 2005, over 45 million birds were culled resulting in a 0.5 percent decrease in GDP for Vietnam in 2004 (Vietnam, 2007).

Vietnam reacted to the disease challenge with aggressive culling, widespread community awareness campaigns, strong political commitment, and an intensive vaccination program, where hundreds of millions of ducks and chickens were vaccinated. In major cities, live bird markets were closed, and domestic birds of all types were eliminated. These actions and others resulted in significant control of the disease, but outbreaks and human deaths have continued. Vietnam has a renewed commitment to vaccination, culling, and surveillance, but new animal disease challenges, Porcine Respiratory and Reproductive Syndrome (PRRS) and Foot and Mouth Disease, are decreasing the focus on avian influenza.

**Thailand**

Before avian influenza hit Thailand, this country was the fourth largest exporter of poultry meat in the world. Although some of the market has been regained through the export of cooked product, at one point 70% of the export market was lost.

Commercial poultry flocks were hardest hit with the infection and, with an eye to future export marketing of poultry products, the country decided to cull and compensate rather than vaccinate. In 2004, 62 million birds were killed by the disease or were destroyed to prevent virus replication and spread, and $132 million was paid in compensation (referenced in Tiensin et al, 2005). By 2004, losses amounted to $631 million and had an estimated effect on the national gross domestic product of 0.39%. Sporadically, cases have surfaced, but most have been near border areas, and all poultry were rapidly depopulated before the disease could spread. Thailand maintains a widespread surveillance program.

**Dairy cows and the US dairy industry**

**Dairy cow production life cycle**

The function of a dairy cow is to produce milk. Cows do not produce milk before giving birth. Consequently, conception followed by nine months of gestation is the first step in the dairy cow production cycle.

Young cows are referred to as “heifers”. They begin to have normal estrus cycles (which means they have reached sexual maturity) when they reach 43% of their adult weight, or at about 12 months of age. Heifers usually have their first calf between 21 and 30 months of age. After the calves are born, they suckle the mother for a day or two so that the calf can consume the early immune-rich milk (called colostrums), and then the calves are reared on bottles, and the heifer enters the milking parlor. After 50-60 days of milking, the heifer is bred again. She is “dried off”, that is, milking is stopped at about 7 months months of gestation, and then after calving, once again she goes through the cycle of moving into the milking parlor. Cows need to give birth (this is called “freshening”)
every year in order to continue producing milk. Cows are always given some time off (or “drying”) between milking cycles.

Dairy cows produce between 65 and 75 pounds of milk per day. The larger the dairy, the greater the per cow production. (see Fig. 5). Cows during the second lactation tend to produce more milk than during the first lactation. Cows may continue to produce for 7-10 years. Cows are removed from the milking chain when they no longer produce adequate milk or if they fail to conceive. This process is referred to as “culling” and these older dairy cows are usually sent to the processing plant where they are slaughtered and their meat becomes hamburger. Because a dairy cow is designed to produce milk and not meat, their muscle does not have the same desirable qualities as beef cows and so dairy cows do not become steak, but rather hamburger.

Dairy cows give birth once per year. The female calves are raised to become replacement animals for the dairy herd. In very good herds, some of the male calves may be reared to become replacement bulls, but most male dairy calves are reared for a few months and slaughtered for veal.

**Unique aspects of the dairy cow as a production animal**

**Feeding**– Unlike poultry and swine, cattle are ruminants, which means they have a large fermentation vat for a stomach and can consume feedstuffs that are high in cellulose and gain good nutrition from these. So, cows can eat grasses, which are often referred to as “forage”. Much of a dairy cow’s diet consists of grasses such as hay, and often waste products from other industries, such as citrus pulp or cotton seed. As the character of the forage changes, the additional feed given to the dairy cow must be modified to ensure a balanced diet. Many if not most dairy cattle receive some form of additional rations, that can include high energy grain and some non-protein nitrogen that helps them to maintain their milk production.
**Structural demographics**

As with many other animal industries, the US dairy industry is undergoing rapid change and is constantly adapting to an ever-changing environment (See Fig. 6). Most notable have been the continued consolidation and dramatic improvements in production. In 1950, the national dairy herd consisted of almost 22 million cows on 3.6 million farms, with 6 cows per farm yielding an average of 14.5 lbs of milk per day, requiring a land mass of 21.4 million acres (estimated acreage to balance phosphorus). In 2000, dairy farm numbers had dropped to 105 thousand with 88 cows per farm. By 2005, the national dairy herd was 9 million cows yielding an average of 53.5 lbs of milk per day – a 3.7 fold increase in production since 1950 – and required a land mass of 9.3 million acres. In 2006, approximately 49.5% of US milk is produced from herds with 500 or more cows (DSI, 2007), and in 2004, the US dairy industry was yielding 15.6% of the world’s milk output. In addition to the decreases in cow numbers, the national heifer replacement herd has also decreased due to need to maintain fewer cows in the national herd as well as the decreases in age at first calving over time. Today, more milk is produced on fewer farms, from fewer cows, and is handled and marketed by fewer dairy cooperatives.

Improvements in raw milk quality and declining transportation costs have reduced the advantage of local milk production over time and allowed the industry to move to specific regions (west) with a more favorable balance of conditions to grow crops and house cows. The Pacific and mountain regions have increased in shares of milk production so that in 2007, the top ten dairy states in order of cow numbers are: California, Wisconsin, New York, Pennsylvania, Idaho, Minnesota, New Mexico, Michigan, Texas, and Washington (USDA, NASS Data).
With these shifts, new housing systems evolved as well as the style of “dairying,” which refers to the management of cows that are in herds of more than 200. These large operations are called large CAFOs when a herd consists of at least 700 mature cows and medium CAFOs when mature cow numbers range from 200 to 699. Despite the increases in herd size, individual or family ownership dominates all regions of the dairy industry and, if partnerships (primarily family members) are included, is over 90% (Blayney, 2002).

**Consumer trends**
American consumption of dairy products has also changed over time. In 1975, 27.9 billion pounds of milk were used in cheese production, while in 2004, 88.3 billion were used. Cheese represents the largest single use of milk (43% of the 2004 production) and is one of the most important products shaping the dairy industry. Average annual cheese consumption in the US nearly tripled between 1970 and 2004, from 11.3 pounds per person to 31.25 pounds. Fluid milk accounted for 25% of sales in 2006 and is expected to decline as competition from other beverages increases and as the US demographic shifts to an older population (DSI, 2007). At the same time, more fast-food establishments are providing single-servings of milk and flavored milk options. For instance, between 2000 and 2007, these bottled milk offerings went from appearing in 0 to 50,000 fast-food restaurants in the United States (Dairy Management Inc.).

There is also an increasing focus on the marketing of natural/organic milk, which is creating confusion about what is in milk, how is it produced, and the human health

Figure 6. Structural changes in the US dairy industry since 1950 (USDA data).
benefits. The labeling of products as “free of antibiotics” or “free of bST” (bovine somatotropin) implies that other products contain them, which is not true, as milk from all sources is routinely tested. This issue of “process attributes” was mentioned in the introduction. In addition, there is consumer shift toward lower fat fluid milk products, which has caused a shift in breeds of dairy cattle, from smaller Jerseys that have a high milk-fat content, to larger Holsteins, with a lower milk-fat content.

![Milk Price in (83,84 dollars)](image)

Figure 7 shows that society is spending less per 100 lbs of milk than previous generations, when the prices are adjusted for inflation (US$ 83/84). To maintain income, producers have expanded herd size and adopted technologies and management practices that result in efficient production.

**Technologies employed in US dairy industries**

**General**—The history of the US dairy industry is a history of the adoption of technologies. The transfer from horse power to tractor power, as well as feed harvesting methodologies and concepts in feed storage had a great effect on the dairy industry. Forages formerly stored as hay in expensive buildings are now stored in trench silos as haylage (plastic-wrapped hay with a higher moisture content), which greatly improves the harvest of nutrients from the field as well as storage life. In concert with these changes, our understanding of ruminant nutrition has greatly improved and been applied in the field through the use of nutritional software programs that facilitate production and health through good nutrition (Ferguson et al, 1987). By better understanding ruminant nutrition as well as the availability of quality forages, greater amounts of forages are included in diets of high producing cows than was the practice 10 years ago. Milking parlors have undergone continual evolution with industry testing, with a variety of configurations. Today, robotic milking machines are becomes more common and the industry is approaching capacity flow of 100 cows per hour per worker. Improved milking technologies have allowed producers to do three milkings per day, increasing yield per cow by about 15%.
Artificial insemination removed dangerous bulls from the farm environment and provided a more efficient method to select desirable traits. The Dairy Herd Improvement Association farm computer record systems (DC305, PCDart) and radio frequency identification (RFID) technology allow producers to monitor production, reproduction, health, and treatment events on an individual animal basis. Furthermore, these record systems allow management better oversight of the operation than ever before.

Impact of dairying

Local impact—The dairy industry is an important part of the national economy as well as the local economy. A dairy operation requires considerable infrastructural support and thus has been concentrated in selected regions of the United States. The location of these concentrations is determined by a number of factors, including existing resources, access to water, ability to grow quality forage, and proximity to markets, to list a few. Each supporting infrastructural group (feed dealer, milk hauler, veterinarian, equipment dealer) requires different geographically defined concentrations of animals to be successful. In Pennsylvania, a state with a solid concentration of dairy cows, the local impact of a dairy cow is estimated at $13,737 per cow per year and creates one job in the dairy production chain for every nine cows (Center for Dairy Excellence, 2006).

Environmental impact—The modern dairy cow is fed a combination of forages and cereal grains that maximize the rumen’s (stomach location where feed is fermented) efficiency as much as possible. As forage quality increases, greater amounts can be fed to replace cereal grains. Nutrients that are not captured in milk, body tissue, or incorporated in crop production (via manure applications) are returned to the environment (Tamminga, 1992). These losses can be reduced by improving the management and application of manure for cropping (Dou et al., 2001; Dou, 2002), improving the quality of feed, improving the formulation of rations by minimizing nutrient excesses, and increasing the level of production relative to animal maintenance (Tamminga, 1992). At the industry level, losses can be reduced by reducing total cow numbers.

Diseases and conditions of dairy cattle and potential animal health impacts

Disease and production in the dairy industry—Dairymen and animal/veterinary scientists have worked hard to identify ways to reduce stress on the dairy cow, improve health, and ultimately enhance production. Well balanced rations, comfortable housing, good ventilation, cooling, and stocking density, access to clean water, head gates, quality milking management, and responsive health care reduces stress and the likelihood of disease and increases production.

Disease conditions have always been a challenge to all animal production systems (intensive and non-intensive). Disease erodes profit by affecting culling, reproductive efficiency, milk production, and milk quality, and thus it is in the best interest of management to prevent their occurrence—simply stated, sick cows do not milk or reproduce well. (Beaudeau et al., 1993; Fourichon, 1999; Grohn et al., 1998). Prevention

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7 DairyComp305 (DC305) and PCDart are computer software programs used to manage dairy herds.
is much more economically attractive to producers than allowing conditions to develop and then having to treat the animals (Dijkhuizen et al, 1997; Galligan, 1999).

Correlated observations (production and disease) have been assumed to be causal by some. Trends (correlations) observed at the population level are assumed to be causal at the individual level (Erb, 1987). Often, ways in which these associations are made have been greatly influenced by management decisions, definitions and culling strategies. For example, a high producing cow is going to be given many opportunities to get pregnant (bred many times), while a poor producing cow will get fewer breeding opportunities to get pregnant before she is culled for low production. A strong negative correlation will be observed between high milk production and conception, which is really based on a sound management decisions to cull low producing cows and not necessarily due to production effects on fertility. Similarly, low producing cows with mastitis will be culled, while high producing cows will be maintained longer in the herd and treated– again yielding a correlation between production and mastitis. The sick cow presented to the veterinarian is often the high producing cow (i.e., valuable animal), while the sick, low producing cow is often cared for by on-farm management or culled. Veterinary records will therefore show a correlation between production and sick cows because that is the population they are exposed to.

**Epidemiological reviews**– While this issue of production and disease is complicated, it has been investigated in the dairy model several times over the last three decades. Erb (1987) reviewed 15 large-scale, epidemiological studies that investigated the role of production as a causative factor of disease. Approximately 100,383 lactations were accumulated in the 15 studies. The author concluded that cows that produced more milk than herd mates were not at increased risk of any disorder other than milk fever. Milk fever is one of the most preventable diseases by proper dry cow management– hence, its occurrence is a strong indicator of poor management (Kronfeld & Ramberg, 1970).

A larger and more recent review consisting of 647,936 cows (Ingvartsen et al, 2003) reviewed 11 epidemiological and 14 genetic studies and found little evidence that high yielding cows have increased risk of dystocia, retained placenta, metritis, or left displaced abomasums. Results for milk fever (periparturient paresis) were inconsistent. In contrast to Erb’s review (1987), an association of mastitis and production was observed (mastitis is discussed below).

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
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<tbody>
<tr>
<td>Vet-assisted dystocia</td>
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<td>6</td>
</tr>
<tr>
<td>Retained placenta</td>
<td>1</td>
<td>8</td>
</tr>
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<td>Metritis</td>
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<td>Cystic ovary</td>
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<td>5</td>
<td>7</td>
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<tr>
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</tr>
<tr>
<td>Mastitis</td>
<td>4</td>
<td>7</td>
</tr>
</tbody>
</table>

The table of the combined reviews (Table 3) shows that the relationship between milk yield and these diseases and conditions is inconclusive. Given the number of cows studied, there is not a strong relationship as is suggested in the term “production diseases.” Most of the diseases are strongly influenced by management practices that ultimately influence their occurrence/severity on a herd (Dohoo, 1983).

NAHMS disease incidence reports—The NAHMS, sponsored by the USDA, randomly selects herds to participate in collection of data and thus did not rely on convenience sampling. Below are data from the NAHMS 1996 and 2002 reports on disease incidence. In general there has not been a substantial change in the diseases monitored. Furthermore, large herds (>200 cows) tended to have similar or lower incident rates than smaller herds (<100 cows).

<table>
<thead>
<tr>
<th>NAHMS 1996</th>
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<td>Lameness</td>
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<td>12.7</td>
<td>10.8</td>
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<tr>
<td>Respiratory problems</td>
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<td>2.6</td>
<td>2.5</td>
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<tr>
<td>% open at 150 d</td>
<td>11.7</td>
<td>11.6</td>
<td>11.3</td>
<td>11.6</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.8</td>
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<td>2</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>Milk fever</td>
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<tr>
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<tr>
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<tr>
<td>% open at 150 d</td>
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<tr>
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<tr>
<td>Milk fever</td>
<td>7.6</td>
<td>5.3</td>
<td>2.9</td>
<td>5.2</td>
<td></td>
</tr>
<tr>
<td>Displaced abomasum</td>
<td>3.8</td>
<td>4.3</td>
<td>2.4</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>Retained placenta</td>
<td>9.2</td>
<td>8.5</td>
<td>6</td>
<td>7.8</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1.1</td>
<td>1.1</td>
<td>0.2</td>
<td>0.8</td>
<td></td>
</tr>
</tbody>
</table>

Mastitis—Clinical and subclinical mastitis is an important disease condition to the dairy industry. Subclinical mastitis is measured by the presence of cells in the milk. This is measured by a simple test called “somatic cell count” or SCC, which indicative of inflammation and is strongly correlated with clinical mastitis. All large dairy herds are enrolled in the Dairy Herd Improvement Association (DHIA), which implements regular testing of SCC in the milk. The national average for the SCC tests has fallen regularly over the last few years, indicating that the occurrence of subclinical mastitis is decreasing even as herd size is increasing (see Fig. 8).
Figure 8. Average somatic cell counts of milk from Dairy Herd Improvement herds during 2006 (Miller et al, 2007).

Lowering of SCC to qualify as Grade A milk was an important impetus for improved mastitis control. Furthermore, the trends for the increasing percentage of herds that tested above the thresholds of 600,000, 500,000 and 400,000 cells/ml no longer show statistically significant increases as in the past.

To ensure that chemical residues in dairy products do not enter the food chain, the US Pasteurized Milk Ordinance requires that milk tankers be tested for antibiotics. In fiscal year 1996, only 0.104% of the 3.4 million loads had violations (USFDA, 1997). In 2003, this percentage was reduced to 0.053% of 3.6 million loads, signifying a further improvement in milk quality (USFDA, 2004).

**Johne’s disease**– The possible role of *Mycobacterium avium*, subspecies paratuberculosis (*Map*) to Crohn’s disease in humans as well as the economic losses on infected premises (Benedictus et al, 1987; Jones, 1990; Ott et al, 1999; Collins, 1997), has motivated the dairy industry to look for effective methods to reduce its prevalence on farms. The majority of losses associated with Johne’s disease are due to premature culling of infected animals. The use of diagnostic tests to identify infected animals is limited by test sensitivity and specificity, prevalence of the agent on particular premises, and the extended age of the animal at the time of diagnosis. Prevalence can be reduced by improved calf hygiene and separation of calves at birth from adult animals (Groenendaal, 2003; Groenendaal et al, 2002). Large herds, because of their size, often rear heifers in facilities separated from the adult cow as a management practice for many issues, and it helps in the control of Johne’s disease.

**Other diseases**– The dairy industry has made substantial progress in the prevention of diseases in dairy cattle over the last 50 years. The occurrence and impact on production of most diseases in dairy cows are highly influenced by the management practices.
applied to the unit. Decreases in milk fever (by understanding nutritional prevention strategies), clinical respiratory diseases in mature cows (improved ventilation, vaccination programs), calf mortality (calf hutches and colostrums management), contagious mastitis (milking practices and vaccines), clinical parasitism (reduced pasture exposure, control programs, housing management), blackleg, plant toxicities, grass tetany, tuberculosis (national program), brucellosis (national program), and hardware disease have occurred through improved knowledge of the factors that influence animal health and disease. Despite dramatic increases in production, other diseases have remained relatively constant, challenging the hypothesis that high production “causes” disease. Much of this success is attributable to the focus on preventative strategies (often described as herd health and/or production medicine) that are multi-dimensional based on the recognition of the multi-factorial nature of almost all diseases in dairy cattle (LeBlanc et al, 2006). Preventive health care through improved management, nutrition, and health care services is more economically attractive than “reactive” health care.

**Bovine Spongiform Encephalopathy: Human and animal health risks**

Bovine Spongiform Encephalopathy, widely known as “mad cow disease,” is a chronic, degenerative disease affecting the central nervous system of cattle. Worldwide, there have been more than 190,000 cases in cattle since the disease was first recognized in 1986, of which over 186,000 have been in the United Kingdom. In addition to the officially reported and confirmed cases, it is estimated that as many as 3.5 million animals were infected and may have entered the food and feed chains without being detected (Donnelly et al, 2002). BSE has also been reported in most countries of Europe, as well as in Canada, Israel, Japan and the United States, and it should be noted that the absence of reported cases in a country may indicate a lack of effective surveillance more than an absence of disease.

BSE is a member of the family of diseases known as the Transmissible Spongiform Encephalopathies (TSEs), which affect both animals and humans. The animal diseases also include scrapie of sheep and goats, Chronic Wasting Disease (CWD) of deer and elk, Feline Spongiform Encephalopathy (FSE), and Transmissible Mink Encephalopathy (TME). Recently atypical variant of both BSE (Casalone et al, 2004; Biacabe et al, 2004) and scrapie (Benestad et al, 2003) have been identified. Human TSEs include Creutzfeldt-Jakob Disease (CJD) together with its variant form (vCJD) due to BSE infection; kuru, which is limited to Papua New Guinea and is now virtually extinct; Fatal Familial Insomnia (FFI), and the Gerstmann-Sträussler-Scheinker Syndrome (GSS). All TSEs share many common characteristics, including:

- incubation periods ranging from years to decades;
- illnesses of weeks to months, with invariable progression to death after the onset of clinical disease;
- accumulation in the brain (and other tissues) of fibrillar amyloid protein aggregates;
- pathological changes confined to the central nervous system (CNS);
- the absence of any detectable agent-specific immune response;
- transmissibility by either natural or experimental means.
Although these features define the fundamental biologic identity of the TSEs, some important differences occur in pathogenesis, routes of natural transmission, and distribution of infectivity in tissues that must be taken into account for diagnosis, prevention and control of each TSE affecting the different species.

**Characteristics of the BSE agent**– The clinical, pathological, and molecular genetic features of the TSEs, have led to speculation on the nature of the etiologic agent and the pathogenic mechanisms of the disease. There is still debate regarding the nature of the TSE agent and three primary theories have been proposed:

1) The prion theory– The agent is composed exclusively of a host-coded normal cellular protein (PrP\(^c\)) that becomes partially protease resistant (PrP\(^\text{res}\)). In this theory there are no non-host components of the agent (ie, no DNA or RNA) (Prusiner, 1982; Bolton & Bendheim, 1988);

2) The virus theory– The virus would have to have unusual biochemical and biophysical characteristics in order to explain the remarkable physicochemical properties (Rohwer, 1984a, 1984b; Czub et al, 1988; Manuelidis et al, 1988; Manuelidis et al, 2007);

3) The virino theory– The agent consists of a host-derived protein coat, with PrP being one of the candidates for this protective protein, and a small non-coding regulatory nucleic acid (Dickinson & Outram, 1979; Kimberlin, 1982).

All of the proposed theories have some degree of validity. Studies that have provided evidence that prion protein is the agent have increased support for this theory. However, the prion or protein only theory is still debated by the mainstream TSE research community. This is largely due to the lack of correlation between infectivity and PrP\(^\text{res}\) detection. Several studies have identified fairly high levels of infectivity in certain tissues devoid of PrP\(^\text{res}\). Some researchers argue that this challenges the prion theory in that there is infection, and in some cases, disease without prions (Jeffrey et al, 2006). Those supporting the prion hypothesis counter that either: 1) the diagnostic techniques are not sensitive enough; 2) another protein in addition to prion protein is needed; OR 3) there may be protease sensitive forms of PrP that are infectious (Nazor et al, 2005).

Regardless whether the prion (PrP\(^\text{res}\)) is the etiologic agent, the partially protease resistant form of the prion protein is a marker of infection. There are currently a number of tests which may be used to detect the presence of the PrP\(^\text{res}\) (ie, immunohistochemistry, Western blot analysis, ELISA, etc.). It must be pointed out that a growing number of studies caution against assuming that animals that do not become clinically ill or tissues that do not have detectable PrP\(^\text{res}\) / PrP\(^d\) (disease) are not infected. It is unknown if PrP\(^d\) is present but not detectable, or whether infectivity may be associated with molecules of structures other than PrP (Race et al, 2001, Race et al, 2002; Jeffrey et al, 2006; Barron et al, 2007). These findings are important to consider when assessing the efficiency of surveillance systems, the tissue distribution of infectivity and routes of transmission.
**Atypical BSE**—For almost the entire two decades that BSE has been known, it was thought that there was only one “strain” that infected cattle and caused disease in some other species such as humans (Bruce et al., 1997; Hill et al., 1997; Casalone et al., 2004). We now know that there are other manifestations of prion diseases in cattle which have been termed atypical BSE. However, there remain many unknowns regarding atypical BSE. One of the most important of the unknowns is the significance of atypical BSE in regard to human and animal health.

Previous research in mice had suggested the existence of a number of scrapie strains. Historically, research involving the differentiation of TSE strains was based on biological typing using panels of inbred mice inoculated with homogenates of infected tissues. If the mice developed a TSE, it was characterized by length of incubation and lesion pattern in the brain (Bruce et al. 1994). More recently it has been determined that the human and animal variations may be biochemically differentiated on the basis of molecular mass of \( \text{PrP}^{\text{res}} \) and the degree of glycosylation (Collinge et al., 1996).

In 2004, cases of a bovine prion disease molecularly different than already documented as classical BSE were described by scientists in both Italy (Casalone et al., 2004) and France (Biacabe et al., 2004). In both countries the cattle were over 8 years of age. The Italian cases (11 and 15 years of age) named bovine amyloidotic spongiform encephalopathy (BASE) were characterized by an unglycosylated protein band with a lower molecular mass (thus named L cases) and the predominance of the monoglycosylated band. In addition, immunohistochemical detection of \( \text{PrP}^{\text{res}} \) in these cases found greater deposits in the cerebral cortex and thalamus regions of the brain versus the brain stem. The French cases found a higher molecular mass associated with the unglycosylated protein band and were called H cases (see Fig. 9). The different “strains” are now called atypical BSE.

![Figure 9. Comparison of Western Blot patterns from classical BSE and L and H atypical BSE (Reprinted from Brown et al, 2006). M.W.=molecular weight](image)

Since Casalone and Biacabe reported, additional cases of atypical BSE have been found in other countries. H cases have been detected in Canada, France, Germany, Japan, the Netherlands, Poland, Sweden, Switzerland, the United Kingdom, and the United States. L cases have been diagnosed in Belgium, Denmark, France, Germany, Italy, Japan and Poland (Brown et al., 2006). The L cases in Belgium and Japan had additional differences (Yamakawa et al., 2003; De Bosschere et al., 2004). Two important points must be emphasized regarding the atypical BSE cases. Information regarding lesion pattern and
PrP distribution is very limited, as most cases were detected by the large scale surveillance programs that required collection of only the brain stem. In addition, if countries were using certain tests, some cases of atypical BSE may have been misdiagnosed or missed. For example, if a country relied solely on immunohistochemistry to confirm positive ELISA screening test cases and did not use Western blotting at all, the banding pattern differences would go unnoticed.

When atypical cases were first reported, there was some speculation that these may merely be protein accumulation disorders associated with old age. It has now been shown that both the L and H types of atypical BSE are at least experimentally transmissible. Homogenates from L cases have been transmitted to a special strain of mice, *Cynomolgus* monkeys, and one breed of cattle (Buschmann et al, 2006; Holznagella et al, 2006). H cases have also been transmitted to special strains of mice (Béringue et al, 2006). The incubation times for atypical L cases of BSE were shorter in one strain of mice than classical BSE inoculated into the same strain of mice, and the H cases had longer incubations.

Several theories exist for the origin of atypical BSE, including a variation or mutation of the classical BSE strain, a different route of exposure or exposure at an older age, a strain of scrapie transmitted to cattle, and sporadic or spontaneous occurrence of BSE. In 2007, there is no evidence to conclude that any of the theories are correct.

As previously stated, most of the characteristics of atypical BSE have not been defined. In addition to the origin, the risk to other cattle by means of natural transmission and the risk to humans and other animal species such as chickens and pigs are still unknown, as is the distribution of infectivity throughout the body of a cow. There is little information on clinical manifestation, if it occurs at all, in most natural cases. Documented L cases have been diagnosed from samples taken from older “healthy” cattle presented for routine slaughter. Thus the characterization of BSE below is, for the most part, based on what has been documented about classical BSE.

While additional surveillance and research is being conducted, it is important for policy makers to consider the implications of atypical BSE. They may need to rethink what populations are appropriate targets. It would probably be unwise to prematurely lessen or discontinue the current BSE protection measures.

**Stability of the infectious agent**– The agent of BSE shares with other TSE agents the property of unusual resistance to destruction. None of the standard disinfection methods is effective, including irradiation or exposure to various chemical disinfectants. Even harsher conditions that are capable of inactivating all other known pathogens (including bacterial spores), such as heating under pressure at 121°C, exposure to dry heat at 600°C, or immersion in 0.1 N NaOH or 0.5% bleach cannot assure complete inactivation (Brown et al, 2004; Brown et al, 1986; Brown et al, 1982; Taylor, 2000; Taylor et al, 1999). The only procedures known to ensure “sterility” are exposure to dry heat at 1000°C (Brown et al, 2004), immersion in either 1 N NaOH or fresh undiluted bleach (Brown et al, 1986), and steam heating under pressure at 132°C (Brown et al, 1982). The preferred method is
a sequential exposure to both physical and chemical inactivation treatments (Taguchi et al, 1991; Taylor, 2004; WHO 1999).

**Feed-borne and food-borne outbreaks—Cattle**

BSE probably arose sometime in the 1970’s or early 1980’s and, although the species of origin of BSE is unknown, there is ample epidemiologic evidence to indicate that once cattle were infected, the epidemic was perpetuated by the feeding of TSE-contaminated meat and bone meal (MBM) to cattle (Wilesmith et al, 1988; Wilesmith et al, 1992). The disease was then spread to other countries by the exportation of contaminated feed and/or cattle incubating BSE.

It was initially thought that BSE was the result of an increase in the amount of scrapie infectivity entering the animal feed system coincident with a change in the UK rendering process. This hypothesis has the merit of explaining both the timing and geographic location of the epidemic. However, additional information has emerged that has challenged this assumption; specifically, the BSE strain is not identical to any known scrapie strain (Bruce et al, 1997), and at least thus far, the disease produced in cattle that are experimentally infected with scrapie does not resemble naturally occurring BSE (Cutlip et al, 2001; Konold et al, 2006). Although the origin of BSE may never be identified with certainty, current evidence is consistent with the following hypotheses. The origin may have been sheep or goats with an uncharacterized scrapie strain or a strain that was modified in the course of its adaptation to cattle (Horn et al, 2001). Cattle may have developed TSE as a consequence of a gene mutation (Horn et al, 2001; UKMAFF, 2000). Other species such as wild ungulates (eg, deer and elk) infected with TSE entered the feed system (Colchester & Colchester, 2005; Horn et al, 2001).

Prior to the BSE epidemic, ruminant tissues from slaughter houses were rendered, and the solid matter incorporated into feeds that were fed to cattle. As a consequence of recycled ruminant tissue having caused the BSE epidemic, changes in feeding practices led to a precipitous decline in BSE cases in cattle worldwide. For example, there were approximately 1,000 new BSE cases in cattle reported each week in the United Kingdom during 1992-93, whereas there were fewer than 200 confirmed cases during the entire year in 2006 (UK Department for Environment, food and Rural Affairs, 2007). Cases of BSE that continued to emerge after the 1988 feed ban in the United Kingdom (and after the initial feed bans in the European Union) likely were due to cross-feeding and cross-contamination on farms (Doherr et al 2002; Hoinville et al, 1994; Hoinville et al, 1995; Stevenson et al, 2000). Cross-feeding is the practice of feeding meal from rendering intended for poultry, pigs or pet food, which legally can contained ruminant MBM, to cattle on the same farm, usually due to simple human error or negligence.

Rendering may reduce but does not eliminate infectivity (Schreuder et al, 1998; Taylor et al, 1995b; Taylor et al, 1997). Given that BSE can be orally transmitted to cattle with just 1 mg of infected tissue (UK Department for Environment, Food and Rural Affairs, 2005), a very low degree of contamination would be sufficient to recycle the disease. This continues to be true in countries that do not have dedicated lines and equipment to
manufacture and process feed for ruminants and non-ruminants. The continuance of BSE cases due to cross-contamination and cross-feeding of ruminant MBM has resulted in extended feed bans that have prohibited all mammalian or animal MBM to any animals used for human food.

All evidence indicates that BSE does not spread horizontally among cattle. However, the question of maternal transmission between an infected cow and her calf remains unanswered. While it appears that this risk is small to non-existent, the possibility has not been entirely eliminated (Donnelly, 1998; Hoinville et al, 1995; Wilesmith & Ryan, 1997; Wilesmith et al, 1997).

**Human**

Human infection with BSE results in a variant form of CJD (vCJD) that was first recognized in the United Kingdom in 1996, approximately 10 years after the BSE epidemic began (Will et al, 1996). As of November 2007, the number of cases had increased to 166, with 23 additional cases in France, four cases in Ireland, two cases each in the Netherlands and Portugal and a few cases found in or traced to several other European countries and Japan. Humans most likely became infected with the agent that causes BSE through the consumption of beef products contaminated by CNS tissue from cattle, such as mechanically separated meat (MSM) that was pressed and extruded and often contained spinal cord and adjacent nerve tissues in addition to muscle tissue (Ward et al, 2006).

The period of maximum exposure to BSE in the United Kingdom occurred in the mid-to-late 1980s before the ban on high-risk tissues was instituted, and the delay in the peak occurrence of vCJD clearly delineates an average incubation period of about 12 to 15 years, although it is likely that additional cases with longer incubation periods will continue to occur. The delay in the appearance of cases outside the United Kingdom reflects a delay in exposure to BSE in other countries as a result of exports of contaminated beef products and cattle from the United Kingdom. All of the apparent “food borne” cases have thus far been homozygous at codon 129 of the “prion” gene; hence, there is a possibility that heterozygous cases may have a significantly longer incubation period than the already affected homozygotes, and may form a second wave of cases that has not yet begun.

In four instances, patients with orally acquired disease have transmitted infection via blood transfusions, causing concern in the blood donor/recipient communities (Llewelyn et al, 2004; Peden et al, 2004; UKHPA, 2006). Most countries have programs of blood donor deferrals of individuals with specified lengths of residence in the United Kingdom (and in some cases, other European countries), or who have received blood or blood products from individuals in the United Kingdom.

**Characteristics of the disease–Cattle**

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8 [http://www.cjd.ed.ac.uk/vcjdworld.htm](http://www.cjd.ed.ac.uk/vcjdworld.htm)
Affected animals develop a progressive degeneration of the nervous system. They may display changes in temperament, abnormalities of posture and movement, and changes in sensation, including signs of apprehension, nervousness or aggression, incoordination, especially hind-limb ataxia, tremor and difficulty in rising, and a heightened response to stimuli such as sound and touch. In addition, many animals have decreased milk production and loss of body weight despite continued appetite. Only a small proportion of affected cattle exhibit what would be considered typical "mad cow" signs. Many suspects have several, but not all, of the signs described above if they are closely observed.

BSE can be mistaken for other conditions or go unnoticed due to subtlety of the signs. Neurological, metabolic, or other kinds of disease that affect coordination and gait often predispose an animal to injuries such as broken limbs or soft tissue damage. If the animal then becomes recumbent because of a broken leg or torn ligament, the injury may be the prominent or the sole presenting sign, and without a complete diagnostic work up and history of disease progression, the true underlying BSE cause of the non-ambulatory condition may be overlooked. Even more troubling is the occurrence of a significant number of cases in older recumbent cows in the absence of any preceding abnormalities.

It is thought that an animal usually becomes infected within the first year of life. The average incubation period of natural BSE is estimated to range from 2 to 8 years. Following the onset of clinical signs, the animal's condition gradually deteriorates until the animal becomes recumbent, dies, or is destroyed. The clinical progression of BSE may last from 2 weeks to 6 months. Most cases in the United Kingdom occurred in dairy cows between 3 and 6 years of age (Wilesmith & Ryan, 1992), with the youngest confirmed case being 20 months of age and the oldest over 22 years of age (UK Department for Environment, Food and Rural Affairs, 2007).

**Humans**

BSE infection of humans (vCJD) has certain clinical and neuro-pathological features that set it apart from other forms of CJD (Brown et al, 2001). The most distinctive feature is the young age at onset of illness, with many adolescents afflicted, but only occasionally adults older than 50 years of age. This contrasts with the peak occurrence between 50 and 70 years of age in patients with sporadic CJD. The clinical presentation is usually characterized by some form of psychiatric disturbance and complains of sensory symptoms, particularly limb pain. As the illness progresses, however, the clinical distinction between the sporadic and variant forms of illness becomes progressively blurred. The combination of psychiatric and sensory symptoms in an adolescent or young adult is sufficient to raise a suspicion of vCJD in patients who reside or have resided in countries in which has BSE occurred. The average duration of illness is 14 months, or about twice as long as that of sporadic CJD.

Thus far clinical vCJD seems to occur in predisposed individuals with a homozygous methionine-coding genotype at polymorphic codon 129 of the prion protein gene. However, alternative genotypes could conceivably have longer incubation periods and only begin to appear in future cases, as suggested by the asymptomatic (pre- or sub-clinical) infection in a heterozygous recipient of blood from a patient with vCJD.
**Bodily distribution of infectivity**– The CNS and its associated tissues (eg, retinal and ganglionic tissues) invariably contain high levels of infectivity, usually in the range of $10^4$-$10^6$ mean lethal doses per gram of tissue (LD$_{50}$/g). The detection of BSE infectivity in the bovine lymphoreticular system has been extremely limited (tonsil, lymphoid tissue of the third eyelid, and distal ileum) (Wells et al, 1998; Wells et al, 2005) in comparison to other species with TSEs (Hadlow et al, 1982). The peripheral tissues are estimated to have significantly lower levels of infectivity.

Despite the very limited detection of peripheral infectivity in earlier studies, increasing evidence indicates that the pathogenesis of BSE might not be entirely different from TSEs in other species at the point of clinical disease, in that there is wider peripheral involvement than previously documented. The studies indicate that there is a migration of the agent via the sympathetic nervous system to the brain and spinal cord. The agent replicates to high levels in the CNS and then spreads centrifugally from the spinal cord down through the spinal neurons to the junction of the nerves and muscle and possibly into the muscle cells themselves (Espinosa et al, 2007; Hoffmann et al, 2007; Buschmann & Groschup, 2005; Iwamaru et al, 2005; Iwata et al, 2006; Masujin et al, 2007). The research does indicate that the levels of infectivity (and PrP$^{bse}$ presence) are very low. All of the cattle found to have infectivity and PrP$^{bse}$ in peripheral nerves tested positive in the brain and thus were near or at end-stage disease (Espinosa et al, 2007; Buschmann & Groschup, 2005; Iwamaru et al, 2005; Iwata et al, 2006; Masujin et al, 2007)

The public health significance of this is that the current SRM bans do not prohibit these peripheral nervous system tissues from being included in food for humans. In countries that test “normal” adult cattle at slaughter, those animals found to be positive in the brain are prohibited for human consumption, thus eliminating much of the peripheral risk. There are, however, countries that have BSE or have a high BSE risk that do not test older cattle slaughtered for human consumption.

Milk has not been shown to harbor infectivity (Middleton & Barlow, 1993; Taylor et al, 1995a).

**Governmental regulatory measures**– Bovine products and byproducts are widely used for both food and pharmaceuticals, and hence require the highest level of safety. Because of the hardy nature of the BSE agent and its high potential for cross-contamination, the most effective approach to protect bovine products and bovine-derived materials from contamination by BSE is to ensure that infected animals or carcasses never enter processing plants. As there are presently no diagnostic tools sensitive enough for detection of the disease during its long preclinical incubation, governments must rely on measures to prevent exposure through feed to insure only non exposed cattle are processed. In a country in which BSE has been identified in cattle, or in which there has been substantial exposure, specific measures must also be taken to protect human health.

**Protection of animal health**
Countries should conduct a risk assessment to evaluate possible exposures from both external and internal sources of BSE and for potential recycling of the agent within the cattle production system. A country with no known exposure to BSE can best protect its national herd by prohibiting the importation of ruminant MBM, including MBM from other species if there is any possibility of cross-contamination from BSE, and by prohibiting the importation of cattle from countries with BSE or with high risk factors for BSE. Imported live cattle pose a risk if they are eventually slaughtered, rendered, and incorporated into MBM.

Given that the primary, if not sole, route of BSE transmission is through the feeding of contaminated MBM to cattle, countries with any risk factors need to implement feed controls. The level of restriction is usually dependent upon the amount of contamination thought to be in the system. There are three main factors that can increase the stability of a national feed production system:

(i) Feed bans – These regulations can range from the basic prohibition of feeding ruminant MBM back to ruminants, to prohibiting most animal proteins from being fed to all animals used for food production including fish.

(ii) SRM bans – This ban requires that high infectivity tissues such as bovine brain and spinal cord be removed from both the food and feed chain and be destroyed. The intent of this control is to remove the primary source of infectivity from the entire system to prevent the possibility of cross-contamination.

(iii) Regulation of rendering – Although no rendering process can completely remove all detectable infectivity, some are more effective than others. The best procedure studied to date requires a 20-minute cooking exposure at 133°C under 3 bars of pressure (Schreuder et al, 1998).

Experience in countries that have expended considerable effort to eliminate BSE has underlined the need for an extremely high level of compliance with feed controls in order to remove the agent from the system and prevent new infections in cattle. There can be no complacency.

Protection of Human Health
Standard cooking temperatures do not inactivate the BSE agent and there is no screening test to guarantee that an infected animal would not enter a processing plant. Therefore, the primary public health protection measure is to remove SRMs from the food supply and to mandate procedures to prevent the possibility of cross-contamination between SRMs and edible tissue. The basic list of SRMs includes brain, spinal cord, trigeminal ganglia, dorsal root ganglia, eye, skull, vertebral column, small intestine, and tonsil. In the past, some countries have also included additional tissues that are known to be infectious in scrapie, even though they have not been shown to be infectious in BSE-affected cattle.

Processing can increase the BSE risk in edible products via cross-contamination, especially considering that TSE agents tend to adhere to surfaces and are unusually
durable. Standard measures that are used in slaughter plants to reduce the level of microbial contamination (eg, dipping in 180˚ F water) do not inactivate the BSE agent. The time, temperature, and chemical treatments that would reduce levels of the TSE agent are extremely caustic and would corrode food processing equipment and adversely affect food quality. However, certain less onerous practices can at least reduce the risk of cross-contamination, including the use of dedicated equipment (eg, knives, hooks, steels, etc.) for SRM removal. If used for SRM removal, such equipment should not be used on edible tissues. Color coding of such equipment increases awareness and reduces the opportunity for misuse. Another protective procedure is the removal of SRMs from the slaughter floor and prior to processing. This prevents contamination of the area where fabrication occurs and the edible product that could be contaminated, and also provides an opportunity for quality and safety checks to assure that the SRMs have been removed prior to further processing. Employee training on proper removal of SRMs and the significance of the procedure is also important.

Although testing will not guarantee identification of all infected animals, many countries have used testing at slaughter to reduce the amount of infectivity in the system by eliminating the carcasses of animals that test positive. In addition, carcasses that may have been contaminated by close association with the positive carcass can also be eliminated.

The tenacious nature of the agent makes the complete elimination of risk in countries with BSE extremely difficult. Hence, it is imperative for the government and the industry to reduce the avenues for contamination of food or pharmaceutical products by having multiple effective safeguards in place.

Methods of detection—
Postmortem
Historically, the diagnosis of BSE relied on the occurrence of clinical signs of the disease confirmed by post-mortem histopathological examination of brain tissue (Wells et al, 1987). A diagnosis could also be made by electron microscopy detection of fibrils in denatured brain extracts, called scrapie-associated fibrils (SAF) because they were first observed in the brains of scrapie-infected sheep.

In the 1990s, the development of tests to detect the pathognomonic PrP$^{\text{TSE}}$ greatly enhanced the diagnostic capabilities for BSE and other TSEs, because of their improved sensitivity and the fact that they could be used on frozen or partially autolyzed tissue. Two types of tests for the detection of PrP$^{\text{TSE}}$ have been internationally approved for the diagnosis of BSE: immunohistochemistry and Western blots. In addition, a number of rapid immunoassays have been developed and approved by governments for use as screening tests, with positive results subjected to confirmatory Western blots, immunohistochemistry or both. There are no reliable tests for BSE that can be performed on live animals.

BSE in the United States and Canada— Three cows with BSE have been identified in the United States through a testing program initiated in 1990 that targeted cattle with
neurologic symptoms, were recumbent (‘downers’), or died for unexplained reasons. The first case was detected in December 2003 and had been imported several years before from Canada. Another was detected in November 2004 and confirmed in June 2005, and the third was found in March 2006. The latter two were born and raised in the United States, and thus infected in this country. The two indigenous cases of BSE in the United States demonstrated characteristics consistent with the H type of atypical BSE. Using surveillance data, the US Department of Agriculture estimated that the prevalence of BSE in the United States was less than one case per million cattle given an adult cattle population of 42 million head (USAPHIS, 2006).

Canada has identified 10 domestic cases in addition to the one found in Washington state. Five of these were identified in 2006 and one in 2007. Of the ten cases identified by the Canadian Food Inspection Agency (CFIA, 2007), five were born after the 1997 feed ban and one as recently as 2002. Both the United States and Canada have enacted regulations to remove the high risk tissues from food processed for human consumption. In addition, CFIA has recently implemented a regulation to remove these SRMs from all animal feed as well.

Conclusions– Modifications of feed production and practices have resulted in a steady decline in cases of BSE around the world (World Organisation for Animal Health, 2007). Likewise, precautionary measures to exclude high-risk cattle and SRMs from all cattle entering the human food chain have reduced the number of new cases of vCJD. While this is an extremely positive trend, governments and industry cannot become complacent about measures to minimize animal and human risk from this family of diseases. There are several important issues about BSE, vCJD, and other TSEs that need to be monitored during the next several years.

- Secondary cases of human-to-human transmission of vCJD through blood transfusion. The costs associated with a loss of blood donation sources, leukodepletion of the blood supply, and the extreme restrictions on the use of surgical equipment are significant. The extent to which infection from blood-borne sources may be incubating in the population of the United Kingdom and other countries with vCJD is unknown, and there is at present no validated screening test or filtration method to eliminate infected blood. Recent evidence suggests that no genotype is completely resistant to infection, and a carrier state possibly exists (Bishop et al, 2006; Ironside et al, 2006). Given the broader public health implications from human-to-human transmissions, it is imperative for countries to prevent primary food-borne transmission.

- Countries where BSE may be present but not detected. Many countries have imported vast amounts of MBM from countries with BSE-infected cattle, some of which do not have adequate surveillance programs and have not implemented policies to prevent contamination of animal feed and human...
food chains. These countries may still serve as a source of the disease for other parts of the world.

- **Potential peripheral involvement.** Despite the very limited detection of peripheral infectivity in earlier studies, there is increasing evidence that indicates that the pathogenesis of BSE might not be entirely different from TSEs in other species at the point of clinical disease, in that there is wider peripheral involvement than previously documented. Research indicates that the levels of infectivity (and PrP$^{bse}$ presence) are very low. All of the cattle found to have infectivity and PrP$^{bse}$ in peripheral nerves tested positive in the brain, thus were near or at end-stage disease (Espinosa et al, 2007; Buschmann et al, 2005; Iwamaru et al, 2005; Iwata et al, 2006; Masujin et al, 2007). The public health significance to this is that the current SRM bans do not prohibit these tissues from being included in food for humans. In countries that test “normal” adult cattle at slaughter, those animals found to be positive in the brain are prohibited for human consumption, thus eliminating the peripheral risk as well. There are, however, countries that have BSE or have a high BSE risk that do not test older cattle slaughtered for human consumption.

- **The emergence of new strains or species adaptation of existing strains.** The origin of BSE has not been identified with certainty, and its emergence should be a warning to us that TSEs may occur in other species and have unpredictable characteristics that will provide new challenges.

Finally, it is important that regulatory policies be modified in accord with advances in experimental and epidemiologic knowledge to minimize adverse consequences to both human and animal health. In particular, the development of preclinical diagnostic tests may vastly improve the precision of proactive measures to minimize risk to human and animal health.

**The US Beef Industry**

**Beef Production Life Cycle**

The beef production lifecycle can be divided into multiple phases of production, and each provides unique contributions to the overall end product (Fig. 10). Cattle breeding operations (cow-calf farms) produce the annual supply of calves for the industry. These herds consist of female (cows) and male (bulls) adult cattle, and their offspring (calves). The breeding herd typically has a calving season of 60 to 120 days when all calves are born, and they are weaned at 5 to 9 months of age. Most cow-calf herds in the United States calve in the spring (February, March, and April) and wean the calves the subsequent fall (USAPHIS, 1997a). There are also regional differences in calving season, and some producers maintain a calving season in the fall (September, October, and December) while weaning and marketing their calves the subsequent spring.
After weaning, calves may go through a growing phase prior to entering a feeding system (feedlot, feedyard). The growing phase, which is often referred to as “stocker” or “backgrounder” phase, often uses available feed resources to achieve a moderate growth rate for 60 to 180 days. Stocker operations tend to be seasonal based on growing patterns of predominant forage species in the geographic region. Alternatively, some cattle move directly from the cow-calf farm to the feeding operation. High-energy rations (grain and other concentrates) are the primary source of nutrition for cattle in feedlots. Calves are fed this high-energy food for 100 to 250 days, depending on weight at arrival, feeding conditions, and the desired end-point. The production system results in two major industry components (cow-calf and feeding) with the overall goals of producing quality beef in an economically efficient manner. Cow-calf farms focus on efficient reproduction and calf growth until weaning, and feedlots target efficient calf growth and end product traits. Final product traits are the characteristics of the carcass that indicate efficiency (red meat yield; lean to fat ratio) and have been associated with consumer acceptability (intramuscular fat or marbling).

![Cow-Calf Production System](image)

**Grower / Feedlot Production**

Figure 10. Beef production life cycle.

**Biological life**– Beef cattle have an average gestation length of 285 days. After birth, calves typically live in a pasture with their mothers (called dams) until 5 to 9 months of
age when they are weaned. Females kept for replacement in the breeding herd (called heifers) will reach puberty (be capable of conceiving and maintaining pregnancy) at 65% of their mature body weight or 12-14 months of age. Replacement heifers are managed to have their first calf between 24 and 36 months of age. The production year for the mature cow can be divided into four phases: 1. calving to breeding (the immediate post-calving period, characterized by heavy lactation), 2. breeding to calf weaning (lactation and early gestation), 3. weaning to late-gestation (non-lactating), and 4. the pre-calving period (late gestation). The goal is for each cow to calve annually and remain productive until 9 to 10 years of age. Cows may be culled at any time for either biological (disease, failure to reproduce) or production (calf growth rate until weaning) reasons. Cow-calf producers cull approximately 10 to 15% of their herd annually. After weaning, calves will be grown until they reach harvest size between 900 and 1,400 pounds, depending on breed and feeding program. At this time, they are usually 16-20 months of age. Stocker cattle gain between 0.75 and 2.5 pounds per head per day while using available feedstuffs. Feedlot cattle will gain between 2.5 and 4.5 pounds per head per day while using 5 to 8 pounds of feed (dry matter) for each pound of gain.

Unique aspects of beef cattle as production animals–Feeding
Cattle have a relatively unique digestive system among food production animals and have the ability to use forage for a primary source of nutrition. Consequently, cows can graze and sustain body weight on rangeland unsuitable for growing crops or other agricultural enterprises. The stocking rate (number of cows placed per acre) varies by region of the country from one cow per acre to one cow on more than 50 acres in more arid regions. Stocking density is largely controlled by the amount of rainfall and native forage base. In many parts of the country, cows graze for a large portion of the year. In the winter or dry season, rations for mature cows may be supplemented with stored forages (hay), by-products from other industries (soybean hulls, cottonseed hulls, distillers grains), or a small amount of grain.

Calves are fed a high energy ration, usually grains, during the feeding and growing phase. Grains provide an energy-dense source of nutrition and facilitate efficient growth, allowing calves to reach harvest weight with fewer pounds of feed and less time relative to a forage-based ration. Commercial feedlots closely monitor ration delivery to match the nutrients provided to the requirements of the cattle.

Production response
Production in the beef cow-calf operation is measured by reproductive efficiency and calf growth rate until weaning. Reproductive efficiency is gauged through the annual herd pregnancy rate and the percentage of calves weaned per cow exposed to the bull. Monitoring the number of calves weaned for each cow also provides insight into the health management of cows and calves during the pre-weaning phase. Another measure, the average calf weaning weight, evaluates calf growth during the pre-weaning phase.

Beef cattle feeding operations measure the production response through growth efficiency and final carcass traits. Growth efficiency is evaluated by average daily gain
and feed to gain conversion rates. Final carcass quality can be judged by carcass traits including hot carcass weight, quality grade (degree of marbling or intra-muscular fat), and yield grade (relative carcass composition of lean beef to fat).

**Food safety**
Several pathogens including *E. coli* O157:H7 and *Salmonella* are potential food safety concerns and warrant attention in the beef industry. Although it is impossible to entirely eliminate consumer risk from microbial pathogens, the industry has implemented research-based programs to mitigate risk of contracting food borne illness from beef products. The use of hazard analysis and critical control points (HACCP) during the pre- and post-harvest processes help assure final safety of the product (Smith et al, 1997).

Recent events (the identification of BSE in the United States in 2003) have caused some researchers to question the consumer response to perceived food safety issues. Prominent food safety events create significant, immediate responses in consumer demands for US meat. However, Piggott and Marsh (2004) found that the average demand response to food safety concerns is relatively small when compared to the impact of price on consumer demand.

**Structural demographics of the US beef industry**—The beef cattle industry is the least integrated of all the animal agriculture sectors. Unlike poultry and swine operations especially, in beef cattle rearing, there are no overarching mega-companies that are monitoring the production of their cattle. Most operations are relatively small in comparison to the other sector, and also quite widely dispersed throughout the U.S.

Cow-calf farms represent the largest number of beef producers and are located throughout the country. Forage type and water availability influence the cattle population density in regions of the country. Cow-calf operations are concentrated in the southern and northern plains states (North Dakota, South Dakota, Nebraska, Kansas, Oklahoma, and Texas) in addition to selected states in the midwest (Missouri, Iowa) (Short, 2001). Although these states represent the majority of operations, cow-calf ranches can be found in every state. The national mean herd size is 40 head, and herds greater than 100 head represent 50% of the cattle, but only 9% of the beef producers (Fig. 11) (USDA, 2004). The cattle population in the US is genetically diverse, with more than 100 breeds or combinations that descend from two species, *Bos taurus* and *Bos indicus* (Feuz & Umberger, 2003). The sale of weaned calves (5 to 10 months of age) is the primary source of income for most cow-calf farms.
The current cattle feeding industry in the United States has evolved from small finishing lots to larger enterprises marketing thousands of head annually. Although feedlots with less than 1,000 head comprise the majority of producers, they represent a small percentage of the fed cattle. Feeding operations with greater than 1,000 head capacity market 80-90 percent of the fed cattle in the United States (USDA, 2004). In addition to large operations, many feedlots are geographically concentrated in the plains states, with the largest three cattle feeding states—Texas, Nebraska, and Kansas—marketing 60% of the fed cattle in 2002 (Mintert, 2003).

Finished cattle leaving the feedlot are traditionally sold to the packer (meat processor) based on a final live or carcass weight. The packer (purchaser) typically procures pens of cattle using a price determined in large part by the estimated weight of the animals. The formation of vertical integration and cooperative alliances in the beef industry provide systems to compensate participants for high quality cattle. Cooperative arrangements between segments of the production chain offer several benefits, including increased communication of product performance, and the number of organizations using some form of vertical industry coordination has grown dramatically in the last 10 years (Schroeder & Kovanda, 2003).

Value-based marketing of fed cattle assigns worth to individual animals based on carcass characteristics, including maturity, marbling, yield, and weight. Several of these traits influence consumer acceptability and perceived palatability of the beef (Platter et al, 2003a). This marketing mechanism shifts industry focus from undifferentiated commodities to identification of products with specific traits and may influence beef demand by generating a product that aligns with end-product user desires (Fausti et al, 1998). Final product attributes evaluated by a value-based system are influenced by genetics and management at each stage of production.
The beef industry is influenced by economic factors, and cattle prices tend to adhere to seasonal and long-term trends. Seasonal price patterns are relatively consistent and associated with the number of animals available as inputs for each segment of the production chain. Most cow-calf herds in the country calve in the spring, then wean and sell their calves in the fall. Most spring-born calves are harvested the next summer, and the large seasonal supply results in the annual low for fed cattle prices.

Long-term temporal fluctuations in inventory and demand are referred to as the cattle cycle, and the subsequent price swings greatly affect potential income for each producer. The cattle cycle is the period of time from the lowest US inventory of cattle to the next lowest inventory. The length of time between cattle cycle peaks is based on biological restrictions of cattle production (Feuz and Umberger, 2003). Cattle cycles have averaged 10 years in length throughout the last century (Anderson et al, 1996).

**Consumer trends**—Beef is a major source of protein in the United States, and changes in consumer consumption impact the demand for the product. From 1982 to 1998, beef consumption fell by nearly 10 pounds per capita, and the demand for beef is highly responsive to changes in consumer disposable income (Schroeder et al, 2000). In 2005, the average beef consumption in the United States was 67 pounds per person per year, making beef the second-most consumed meat behind chicken (Davis and Lin, 2005a). (Fig. 12)

![Figure 12. United States per capita consumption of beef in selected years (Davis & Lin, 2005a).](image)

Beef consumption varies by income type, with low-income consumers eating over 4 pounds more per capita per year than middle or high-income consumers (Davis and Lin, 2005a). This trend emphasizes the importance of maintaining efficient production leading to affordable prices for the consumer.

**Technologies employed on US beef industries**—New technologies in genetic improvements, pharmaceutical products, animal management, and feedstuff production decrease necessary inputs while maintaining or improving output from the beef system.
The national beef cow herd greatly increased production efficiency between 1975 and 1996: in 1975, 47.7 million beef cows produced 23.7 billion pounds of beef, and in 1996, 35.2 million beef cows produced 25.4 billion pounds of beef (Marsh, 2001). Figure 13 indicates the difference in gross beef production and number of head in the United States. The increase in production efficiency has been coupled with a decrease in price as the consumer cost per pound has decreased by 26% over the last 50 years after adjusting for inflation (Elam & Preston, 2004).

![Figure 13. Domestic beef production and January 1 total cattle inventory (USERS, 2006).](image)

Growth promotants
Pharmaceutical technologies in the beef industry allow animals to grow more efficiently and produce more pounds of product while consuming fewer resources. Ionophores (e.g., monensin) are feed additives that modify volatile fatty acid production in the bovine digestive tract, allowing more efficient processing and gain of nutritional value from forage and grain sources. Ionophores are commonly used in beef feeding settings, with over 96% of all feeding operations in the United States employing this technology (USAPHIS, 2000b). Research indicates that ionophores increase the rate of gain and improve feed efficiency compared to using the same ration without the feed additive (Anderson and Horn, 1987; Delfino et al., 1988; Potter et al., 1986).

Growth promoting implants are also commonly used in the beef industry. According to the NAHMS 1999 Feedlot Survey, over 97% of all cattle received at least one growth promoting implant during the feeding phase (USAPHIS, 2000b). The FDA reports, “Consumers are not at risk from eating food from animals treated with these compounds because the amount of added hormone is negligible compared to the amount normally
found in the edible tissues of untreated animals and that are naturally produced by the consumer’s own body” (USFDA, 2002). Implants increase the average rate of gain, feed efficiency, and final carcass weights of calves relative to negative controls (Bruns et al, 2005; McPhee et al, 2006; Perry et al, 1991). Recent work has shown that the lifetime implanting protocol (number and type of implants) impacts beef quality, palatability, and production characteristics. Platter et al (2003b) illustrated that cattle implanted multiple times had decreased marbling (intra-muscular fat) and tenderness relative to non-implanted cattle. In similar work, multiple implants were shown to increase skeletal maturity, resulting in a higher percentage of lean tissue (lower marbling score) and subsequent decreased product tenderness (Scheffler et al, 2003). The result of applying a planned implanting program is the ability to feed cattle more efficiently without detrimental effects on beef tenderness or consumer acceptability (Barham et al, 2003).

Overall, the technologies of genetic improvement, pharmaceutical products, animal and nutritional management have drastically improved the efficiency of the beef production system in the United States. Cattle can be raised without using these technologies, but greater resources are required to reach the same level of production. Recent research estimated that due to differences in carcass weight and feed efficiency, producers that manage cattle for a forage-fed, non-implanted beef market need a 16% higher level of income to remain competitive with producers that finish cattle conventionally (Berthiaume et al, 2006).

Local impact of the beef industry–

The importance of the beef industry to the local economy varies by region of the country. Beef operations provide significant sources of farm income and create the opportunity for jobs in the rural United States. Cows are able to graze land that is otherwise unsuitable for growing other crops, thereby providing a source of income in these regions. Cow-calf production represents a relatively large percentage (35-41%) of total value of farm production for operations in the plains and western states (Short, 2001).

Potential human health impact of E. coli O157:H7

*Escherichia coli* O157:H7 is a major public health concern in North America and other parts of the world. The feces of animals, particularly cattle, are considered the primary source of these bacteria, and major routes of human infection include consumption of food and water contaminated with feces, and to a lesser extent, contact with live animals. Human infections are often asymptomatic or result in uncomplicated diarrhea, but may progress to bloody diarrhea, kidney disease, and death. There are many serotypes of enterohemorrhagic *E. coli* that cause outbreaks and sporadic disease, but O157:H7 is considered the most important serotype in North America. Other bacteria such as *Campylobacter* and *Salmonella* cause disease more frequently, but concern with *E. coli* O157:H7 is often focused on potential complications, particularly kidney failure in young children.

In 1999, it was estimated that *E. coli* O157:H7 infections result in approximately 73,000 illnesses, leading to over 2,000 hospitalizations and 60 deaths each year in the United States (Mead et al, 1999). However from 1982 to 2002, there were a total of 350 reported
outbreaks of *E. coli* O157:H7, comprising 8,598 cases, 1,493 hospitalizations, and 40 deaths (Rangel et al, 2005). Ground beef was the most frequently reported source of the outbreaks; yet produce-associated outbreaks are becoming increasingly common (Rangel et al, 2005). Costs associated with *E. coli* O157:H7-related illnesses in the United States were estimated at $405 million annually, including $370 million for deaths, $30 million for medical care, and $5 million for lost productivity (Frenzen et al, 2005). In addition, *E. coli* O157:H7 has cost the beef industry an estimated $2.67 billion in the past 10 years (NCBA).

*Escherichia coli* O157:H7 was first recognized as a pathogen over 25 years ago following outbreaks associated with undercooked hamburgers at a US fast-food restaurant chain (Riley et al, 1983; Wells et al, 1983). A 1993 outbreak that resulted in over 700 illnesses and led to the recall of more than 250,000 hamburgers led to significant changes in the fast-food and beef industries, as well as major shifts in US regulatory, surveillance, and research initiatives (Rangel et al, 2005; Koohmaraie et al, 2007). The fact that there have been no fast-food/hamburger-associated outbreaks since 1995 is largely attributed to industry-driven efforts (Rangel et al, 2005; Koohmaraie et al, 2007). The beef industry and the US government have invested millions of dollars in *E. coli* O157:H7 research, and the industry has made considerable changes in the processing environment in order to reduce beef contamination and improve beef safety (Rangel et al, 2005; Koohmaraie et al, 2007). Although procedures and interventions aimed at reducing *E. coli* O157:H7 contamination at cattle harvest and post-harvest are effective, reducing *E. coli* O157:H7 in/on live cattle (pre-harvest) has proven to be extremely difficult (Loneragan & Brashears, 2005; Koohmaraie et al, 2007).

**O157:H7 and cattle—** *Escherichia coli* O157:H7 has been recovered from the feces of many wild and domestic animal species; yet cattle are considered the major reservoir of these bacteria (Renter & Sargeant, 2002). Because cattle feces are often implicated as the source of *E. coli* O157:H7 in human infections, there has been considerable research on *E. coli* O157:H7 in cattle so control might begin at the farm level. However, the complexity of the ecology and epidemiology of *E. coli* O157:H7 within cattle production environments has led to major challenges in developing effective interventions (Renter & Sargeant, 2002; Loneragan & Brashears, 2005).

Cattle can shed high concentrations of *E. coli* O157:H7 in their feces with no affect on their health or production efficiency. These bacteria are extremely widespread in US cattle, and it is believed that *E. coli* O157:H7 may be recovered from essentially all herds with adequate sampling (Renter & Sargeant, 2002). Studies of cattle in the early 1990s found that a small percentage of cattle, usually less than 5%, were positive for *E. coli* O157:H7 at any one time (Renter & Sargeant, 2002). Recent estimates of fecal prevalence have been much higher, but some, if not all of the increase is attributed to improved detection methods (Renter & Sargeant, 2002). These detection methods were used in more recent studies where fecal prevalence in feedlot cattle were 10% (Sargeant et al, 2004), 23% (Smith et al, 2001) and 28% (Elder et al, 2000). Prevalence estimates from the NAHMS were 11% in 1999 compared to 1.6% in 1994, but laboratory methods and sampling seasons differed (USAPHIS, 2001).
Animal, herd, environment and production factors can affect the prevalence of *E. coli* O157:H7 in cattle. Although *E. coli* O157:H7 can be recovered from essentially all production systems, the percentage of cattle in a pen or farm shedding *E. coli* O157:H7 in their feces can vary tremendously over time and between groups. For example, the fecal prevalence can range from ≤ 10% to ≥ 80% within pens in the same feedlot or on the same day, and similar variability also has been seen with cattle hide samples (Sargeant et al, 2004; Khaitsa et al, 2003; Renter et al, in press). Variability in pre-harvest prevalence may indicate an opportunity for identifying factors that may be modified to reduce levels of *E. coli* O157:H7 prior to slaughter. However, the interrelatedness of factors associated with *E. coli* O157:H7 have limited the ability of researchers to identify specific factors that can be modified to reduce public health risk (Renter & Sargeant, 2002; Loneragan & Brashears, 2005).

A higher prevalence of *E. coli* O157:H7 in cattle during summer months and with warmer temperatures is well described. Similar seasonal patterns have been reported in feedlots, dairies and abattoirs, as well as for human cases of *E. coli* O157:H7 and prevalence in raw meat (Renter & Sargeant, 2002). Although seasonal increases in human cases may be associated with a corresponding increase in cattle prevalence, the effect also may be related to human behaviors associated with food preparation and consumption patterns that vary seasonally (Rasmussen & Casey, 2001). Seasonal changes also may be related to bacterial multiplication in food production, processing, and preparation environments. Season seems consistently associated with *E. coli* O157:H7 in studies of cattle; yet prevalence varies even within season. Environmental factors in cattle production systems such as temperature, humidity, wind, day length, pen floor and water tank conditions, and other factors may vary by season, but cattle populations and production practices also can change seasonally. Many of these factors have been associated with *E. coli* O157:H7 but none have been identified as determinants that can be modified directly to reduce *E. coli* O157:H7 in cattle (Renter & Sargeant, 2002).

**Pastured and confined cattle production systems**– It is difficult to directly compare the results from disparate studies of *E. coli* O157:H7 in different cattle production systems due to differences in research procedures and other factors that may affect such comparisons. Many studies of pastured beef cattle differ from studies of feedlot cattle in several ways that may affect *E. coli* O157:H7 prevalence, such as the age and weaning status of the animals studied, the animals’ feed composition, and the season of the study. However, similar prevalence estimates of *E. coli* O157:H7 are reported for feedlot/confined beef cattle, dairy cattle, and range/pastured beef cattle in the United States (Renter & Sargeant, 2002). Few studies have directly assessed whether differences in the production system impact *E. coli* O157:H7 shedding in cattle.

A recent review of beef cattle research showed that prevalence of *E. coli* O157:H7 in feces ranged from 0.3 to 19.7% in feedlots and from 0.7 to 27.3% for pastured cattle (Hussein, 2007). The author suggests that there is a high potential for infection and re-infection of cattle with *E. coli* O157:H7 during grazing of dense vegetation on pasture,
but that this effect may be less on open ranges where cattle are more dispersed when the edible vegetation is sparse. In an Australian study, researchers recovered potentially virulent *E. coli* from 48% of pasture-based productions systems, yet only from approximately 18% of feedlot and dairy cattle properties (Hornitzky et al, 2002). Another Australian study found no difference in concentrations of *E. coli* O157:H7 in feces of grass-fed versus feedlot cattle and determined that the levels of *E. coli* O157:H7 in feces at slaughter were not affected by the production system (Fegan et al, 2004).

One US study that directly compared confined and pastured beef cattle found that the prevalence of *E. coli* O157:H7 was much higher in weaned beef calves than cow-calf and dairy cattle, but within age-groups there was no difference in prevalence for pasture versus confined cattle (Renter et al, 2004). The prevalence of *E. coli* O157:H7 in cattle feces is known to vary by age, with higher estimates generally reported for young weaned cattle (Renter & Sargeant, 2002). Diet, immune status, and management factors related to specific age groups could explain age-related differences in *E. coli* O157:H7 prevalence (Meyer-Broseta et al, 2001). Although reasons for differences between age-groups are not entirely clear, it is apparent that a comparison of *E. coli* O157:H7 prevalence between disparate studies of cattle in different types of production systems could be biased if the ages of studied cattle differ.

In a study of beef cattle in Scotland, there was no evidence that fecal shedding of *E. coli* serotypes was affected by a change from a pastured to a confined production setting despite the fact that cattle diets also changed (Pearce et al, 2004). Because *E. coli* O157:H7 colonizes the gastrointestinal tract of cattle, the type of diet that cattle consume and dietary changes can affect the microbial ecosystem and fecal prevalence of *E. coli* O157:H7. A major misconception is that *E. coli* O157:H7 is only found in feces of cattle fed grain diets. In actuality, cattle fed grass, hay and other fibrous forage can have *E. coli* O157:H7 in their feces, as can many other grazing animals, including deer, sheep, goats, and bison (Renter & Sargeant, 2002).

Many studies have examined relationships between cattle diets and *E. coli* O157:H7 prevalence, particularly with regard to feeding forage versus grain. Still, results are conflicting, and researchers do not agree whether forage or grain feeding is more likely to result in higher levels of *E. coli* O157:H7 (Callaway et al, 2003; Nagaraja et al, 2007). Feedlot cattle are typically fed high-grain diets to meet energy demands for high levels of productivity, and some researchers believe these diets may contribute to increased levels of *E. coli* O157:H7 in feces. However, several studies have shown that *E. coli* O157:H7 is shed in feces for a longer duration in cattle or sheep consuming forage diets than those fed grain diets (Nagaraja et al, 2007). Other studies indicate no difference or a reduced shedding in cattle fed forage-based diet compared to cattle fed grain-based diets (Nagaraja et al, 2007). In a highly publicized 1998 paper, Diez-Gonzalez et al showed that the growth of acid resistant, generic *E. coli* was promoted by grain-feeding and speculated that hay feeding may reduce shedding of acid resistant *E. coli* such as *E. coli* O157:H7 (O157:H7 was not directly evaluated in the study). A later study discounted the hypothesis by demonstrating that acid resistance of *E. coli* O157:H7 in feces was similar between grain-fed and hay-fed animals (Hovde et al, 1999). Again, several subsequent
studies have shown conflicting results, but it is definitely apparent that diet composition and changes can affect the shedding of *E. coli* O157:H7 in cattle. The reasons for the influence of diet on *E. coli* O157:H7 in cattle are now believed to be quite complex, but some researchers believe that dietary interventions may offer an opportunity to reduce *E. coli* O157:H7 in cattle (Callaway et al, 2003; Nagaraja et al, 2007).

**Cattle: interventions**– Although in-plant (post-harvest) interventions have improved beef safety, the pre-harvest reduction of *E. coli* O157:H7 in cattle has proven to be much more difficult (Loneragan & Brashears, 2005; Koohmaraie et al, 2007). Reducing *E. coli* O157:H7 in live cattle would likely reduce the occurrence of post-harvest intervention failure and improve beef safety (Loneragan & Brashears, 2005), as well as potentially improve public health through reduction of other cattle-related exposures to *E. coli* O157:H7 (discussed below). Loneragan and Brashears (2005) suggest two broad categories for potential pre-harvest mitigation of *E. coli* O157:H7: 1) the modification of management factors in production environments based on the epidemiology of *E. coli* O157:H7 in these settings; and 2) the development and implementation of specific technologies that are targeted toward reducing *E. coli* O157:H7. The former has proven to be ineffective thus far, largely due to the complex epidemiology, as discussed above. The latter approach has led to research on several potential interventions and has shown some considerable promise for reducing *E. coli* O157:H7 in cattle (Loneragan & Brashears, 2005; Sargeant et al, 2007a).

Several intervention strategies such as antimicrobials, bacteriophages, fed microbiotics or probiotics, and targeted feed additives have potential and are currently being developed and evaluated. In addition, multiple vaccine technologies for *E. coli* O157:H7 in cattle have been developed and are being intensively assessed. However, a recent systematic review of pre-harvest interventions found evidence of efficacy for just two interventions: 1) feeding cattle a specific microbial combination (*L. acidophilus* and *P. freudenreichii*); and 2) administering sodium chlorate in cattle feed or water (Sargeant et al, 2007a). Neither the direct-fed microbial nor the sodium chlorate eliminates *E. coli* O157:H7 from cattle, but both have been shown to reduce fecal shedding (Loneragan & Brashears, 2005; Sargeant et al, 2007a). Currently, only the direct-fed microbial is available and implemented in the beef industry (Loneragan & Brashears, 2005). Interestingly, interventions for which evidence of efficacy exists have been adequately evaluated only for confined cattle production systems, and thus their efficacy in other production systems is unknown. In addition, the implementation of these interventions, which rely on delivery through feed and/or water, could prove to be logistically unfeasible in some pasture-based production systems.

**Other public health risks**– Although *E. coli* O157:H7 is primarily recognized as a foodborne pathogen, outbreaks and sporadic infections also result from water-borne, animal-to-person, and person-to-person transmission. In US outbreaks reported between 1982 and 2002, the transmission route was food-borne 52% of the time, while 21% were unknown, 14% person-to-person, 9% water-borne, and 3% from animal contact (Rangel et al, 2005). Most of the food-borne outbreaks were due to ground beef (41%) or produce (21%). The majority (80%) of the person-to-person outbreaks was in child
daycare centers, and most (70%) occurred in the summer (Rangel et al, 2005). Outbreaks due to contaminated drinking water were much larger than any other type of outbreak (Rangel et al, 2005). One of the largest North American outbreaks of *E. coli* O157:H7 was due to a contaminated water supply in Walkerton, Ontario. Manure from a small cattle farm was the source of contamination; yet heavy rain falls, poor well structures, inadequate water surveillance, and several other ecological and social factors contributed to the outbreak (Ali, 2004).

Although few US outbreaks were associated with animal contact, contact with cattle or cattle environments could lead to exposure to *E. coli* O157:H7. Outbreaks in the United States have occurred from exposures at farms, petting zoos, county fairs, a barn dance and a camp (Rangel et al, 2005). Recreational or occupational visits to farm environments were associated with sporadic *E. coli* O157:H7 infections in England, but the increased risk was seen in people not routinely exposed to farms rather than the farmers (O’Brien et al, 2001).

Some research indicates that people occupationally exposed to cattle have an increased risk of acquiring *E. coli* O157:H7 infection (Silvestro et al, 2004). However, the isolation of *E. coli* O157:H7 from asymptomatic individuals may not be disease-related and may indicate developed immunity and/or exposure to less virulent strains (Silvestro et al, 2004). Variability among different *E. coli* O157:H7 strains may explain why human infections are relatively rare, despite the low infectious dose of *E. coli* O157:H7 and the potentially high prevalence in cattle and other species with which some humans have frequent contact (Baker et al, 2007). Although some data indicate cattle exposure is associated with human disease (Locking et al, 2001), no data suggest that differences in cattle production systems affect the human health risk associated with direct or indirect contact with cattle.

**Conclusions**—Cattle are considered the main reservoir for *E. coli* O157:H7, and these bacteria have major effects on public health. The widespread presence of *E. coli* O157:H7 in cattle feces may represent a public health risk through fecal contamination of food and water or by direct transmission to people. There are effective interventions to reduce *E. coli* O157:H7 in beef; however, progress in reducing these bacteria in live cattle has been more difficult. Many factors may affect the prevalence of *E. coli* O157:H7 in cattle, but there are no data to suggest that differences in production systems impact public health risks. Dietary effects and the effectiveness of intervention strategies could impact the public health risks associated with raising cattle in pasture versus confined settings, but there is insufficient evidence to indicate that either production system would be advantageous in terms of public health.

**Bovine respiratory disease complex in feedlot cattle**

More feedlot cattle develop bovine respiratory disease complex (BRDC) than all other disease conditions combined (Smith, 1998). This disease complex is also known as shipping fever because the vast majority of disease events occur soon after arrival at (i.e., shipment to) the feedlot (Schunicht et al, 2003; Kelly, 1981). Not only is BRDC the
leading cause of morbidity, it is also the leading cause of mortality in feedlots (Loneragan et al, 2001).

Respiratory disease of cattle is truly a disease complex because there are many and varied pathogeneses that lead to the underlying lesion (Griffin, 1996), i.e., bacterial bronchopneumonia. In this regard, BRDC is best defined using the classical disease triad that describes a complex interaction of pathogens, host, and environment. While this may add complexity to the understanding of BRDC, it also provides additional opportunities for control, some of which can be effectively implemented in modern cattle feeding systems.

Because BRDC is the primary animal-health event affecting the feedlot industry and since it can have substantial impact on economic returns, considerable time and effort is invested into its prevention, control, and treatment (USAPHIS, 2000a; 2000b; 2000c). Substantial progress has occurred in these efforts; however, for additional meaningful reductions in BRDC burden, a systems approach to the entire beef industry is needed in which novel mechanisms for control in an integrated beef-industry concept can be developed.

**Factors involved in bovine respiratory disease complex**— Bovine respiratory disease complex results from the classical disease triad involving a complex interaction of pathogens, host susceptibility, and environment. The latter usually takes the form of various stressors that increase an animal’s susceptibility to infection and subsequent disease. While a combination of factors is required to give rise to BRDC, the underlying lesion is bacterial bronchopneumonia, and as such, bacteria are a necessary cause but not a sufficient cause.

**Pathogens**

*Bacteria:* A variety of bacteria have been implicated in the pathogenesis of BRDC, but those believed to have the most significant role are *Mannheimia haemolytica* (formerly *Pasteurella haemolytica*) (Martin et al, 1989; Booker et al, 1999), *Pasteurella multocida* (Griffin, 1996), and *Histophilus somni* (formerly *Histophilus somnus*) (Guichon et al, 1996; Booker et al, 1997). Just as importantly, however, these bacteria are frequently recovered from the upper respiratory tract or tonsillar tissue of healthy cattle. As such, their role in the pathogenesis of BRDC may be opportunistic. *Mycoplasma* species, particularly *M. bovis*, are being increasingly implicated as a pathogen (primary or secondary) in BRDC (Gagea et al, 2006; Shahriar et al, 2002). Although its role is not entirely clear, it does seem likely that in certain situations, this genera is associated with significant morbidity in feedlot animals.

It is not uncommon to isolate other bacteria from tissue samples recovered from dead animals. The role of these other bacteria in the pathogenesis of disease is probably negligible, and they are likely secondary invaders of damaged or necrotic lung tissue.

*Viruses:* Bovine herpes virus type 1 (McKercher & Moulton, 1957), bovine viral diarrhea virus (Booker et al, 1999; Fulton et al, 2002), bovine respiratory syncytial virus
(Bingham et al, 2000; Martin & Bohac, 1986), and parainfluenza virus type 3 (Martin & Bohac, 1986) are the viruses most commonly implicated in BRDC. Other viruses have also been implicated, such as bovine corona virus (Martin et al, 1999; O’Connor et al, 2001), but their contribution to BRDC pathogenesis in real-world settings is not entirely certain.

Environmental factors or stressors
Stressors are an important component in the multifactorial etiology of BRDC in feedlot cattle. Such factors include transportation, commingling, climactic variations, animal handling, passage through auction markets, and recent weaning (O’Connor et al, 2005; Alexander et al, 1989; Cusack et al, 2007; Frank et al, 1996; Frank & Smith, 1983). Many of these stressors are also associated with exposure of naïve animals to different strains of pathogens, and consequently, it is frequently difficult to separate the effect of stressors from pathogen exposure.

Host factors
Host susceptibility (or inversely, resistance) is in part age dependent and affected by exposure to various stressors and certain pathogens. As animals grow toward adulthood, their immune systems generally become more competent and able to deal with the challenges of stress and pathogens. There are some viruses, however, that can lower resistance to other infections such as infection with bovine viral diarrhea virus, which is believed to be immunosuppressive (Welsh et al, 1995; Ellis et al, 1988).

Specific ages are not always known for animals entering US feedlots. However, animal weight may be a reasonable proxy for physiological and chronological age. In other words, given constant confounding variables, heavier animals are, on average, older than lighter animals. As weight (and ergo age) decreases, risk of death increases (Fig. 14) (Loneragan, 2004). This occurs in a similar manner for both steers and heifers, even though in one report, heifers were associated with an increased risk of death compared to steers (Loneragan et al, 2001). The investigators did not, however, control for arrival weight, and the observed differential risk between the sexes was likely due to heifers being placed at a lighter weight than steers.
Classical pathogenesis– Rarely does BRDC result from an uncomplicated infection with a single pathogen (Yates, 1982; Yates et al, 1983; Autio et al, 2007). Rather, BRDC is a classic example of a condition that results from a complex, multifactorial etiology. Viral agents and stressors decrease an animal’s innate and acquired pulmonary defense mechanisms (Yates, 1982), thereby facilitating multiplication of bacteria in the lower respiratory tract. Bacterial bronchopneumonia may ensue, and its clinical manifestations are a function of the dynamic host-pathogen interaction.

Frequently, bacterial and viral agents interact to increase the likelihood of disease. For example, disease associated with experimental challenge with bovine herpesvirus type 1, bovine respiratory syncytial virus, and M. haemolytica were more severe in animals with concurrent BVDV infections (Brodersen & Kelling, 1998; Potgieter et al, 1984; Turk et al, 1985; Kelling et al, 1995).

Epidemiology of BRDC– Few national estimates of the burden of this disease complex are readily available. The most recent estimate, from data collected as part of the National Animal Health Monitoring System’s Feedlot ’99 study indicated that 14.4% of cattle entering feedlots are treated for BRDC (USAPHIS, 2000b). There are, however, a wide variety of other published cohort-level estimates where treatment rates varied from 0% to 95%. It is difficult, however, to compare treatment rates among studies because it is often unclear what diagnostic criteria were used to define an event of BRDC; in other words, what some may consider a case of BRDC, others may not. Consequently, the methods used to calculate the numerator and denominator are not always certain. Furthermore, since there are many unique cohort-level determinants of disease (i.e.,

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**Figure 14.** Percentage of placements that died prior to reaching a desirable harvest weight by arrival weight and by sex (Loneragan, 2004).
pathogen-host susceptibility-stressor combinations), the ability to infer to wider populations is limited. Regardless of the challenges in estimating the burden of BRDC nationally, the majority of studies indicate that it is reasonable to assume that a typical burden of BRDC is between 10% and 25%, depending on arrival weight.

Most BRDC events are clinically manifested soon after arrival at the feedlot (Fig. 15) (Schunicht et al, 2003; Kelly, 1984). This is largely because stressors and exposure to respiratory pathogens are temporally associated with the movement of cattle from ranches of origin (including likely passage through auction markets) to the feedlot, and subsequent introduction into the feedlot environment. Hence, BRDC is commonly referred to as *shipping fever* because of its temporal proximity to shipment. Of initial treatments for respiratory disease, 67% and 86% occurred within the first 28 and 56 days on feed, respectively, in one report (Loneragan, 2001).

![Figure 15. Frequency of initial treatment for bovine respiratory disease complex (BRDC) among approximately 20,000 cattle housed in multiple pens across multiple feedlots. Overall risk of initial treatment for BRDC was 5.7% (Loneragan, 2001).](image)

In many respects, BRDC may be somewhat paradoxically considered to result from contagious and non-contagious determinants. For example, there are data that indicate that the presence of pathogen shedders may increase BRDC risk (Loneragan et al, 2005) and, to follow this line of logic, that improving immunity against certain pathogens may reduce risk of treatment for BRDC (Schunicht et al, 2003). However, these events (presence of pathogens or increasing immunity) explain only a small proportion of the number of animals separated from the group for BRDC treatment. In the former field study (Loneragan et al, 2005), exposure to an animal persistently infected with bovine viral diarrhea virus accounted for approximately 17% of respiratory disease events,
whereas in the latter clinical trial (Schunicht et al, 2003), failure to vaccinate with a modified live virus containing four of the commonly implicated respiratory viral pathogens (compared to vaccination with only one viral pathogens) accounted for only 13% of disease events. The majority of BRDC events, therefore, are likely due to factors not directly attributable to the transmission of pathogens between animals.

Seroepidemiological studies suggest that most animals are exposed to a variety of respiratory pathogens within a short period of time after arrival (Booker et al, 1999). When one considers the disease triad and that pathogen transmission likely accounts for relatively few disease events, host susceptibility to a particular pathogen load and the effect that stressors have on susceptibility appear to account for the majority of BRDC events. Not only does this provide a mechanistic approach to better understanding BRDC epidemics in feedlots, it, more importantly, elucidates various opportunities for meaningful control of BRDC in cohorts of animals.

Stressors causally associated with BRDC are not temporally restricted to the feedlot setting. In many respects, practices on the ranch of origin and the marketing system through which they are sold appear to be critical, if not primary, determinants of risk of this disease complex. Commingled, sale-barn derived calves were approximately 3 times more likely to develop disease than single-source calves (i.e., calves from a single farm or ranch) (O’Connor et al, 2001); similar observations have been observed by other investigators (Martin et al, 1981; Ribble et al, 1995). Other predictors of BRDC that are frequently associated with marketing of cattle to feedlots include weaning, castration, and dehorning.

Moreover, it is possible that the likelihood of successfully adapting to the feedlot environment is at least in part determined well before weaning and subsequent marketing. Some evidence indicates that management to improve transfer of passive immunity from dam to calf during the first 24 hours of life will impact risk of BRDC in the feedlot (Wittum & Perino, 1995). At 24 hours of age, calves with lower plasma protein, an indirect measure of passive immunity transferred through consumption of sufficient quantities of quality colostrum, were more likely to develop BRDC in feedlots than calves with higher levels of plasma protein.

Because weight at feedlot arrival is clearly (and inversely) associated with adverse animal health outcomes in feedlots, the price of corn is also a factor that cannot be ignored (Fig. 16). Factors that influence weight at arrival will have significant impacts on animal health. One factor frequently overlooked is the unit cost of inputs required to return a unit cost of gain (typically described as cost of gain and reported as dollars per 100 lbs or cents per pound). When the primary energy ingredient in feedlot rations, typically corn, is relatively inexpensive, then the cost of gain favors gains in feedlots over gains on grass. If, conversely, feedlot rations increase in cost, then there are economic advantages to weight gain on grass. Therefore, in times of historically low corn prices, there are economical pressures on ranchers, stockers, and feedlot managers to place lighter animals in feedlots and vice versa. In other words, the price of corn can have an indirect influence on the level of BRDC events in a cohort of animals.
While critical determinants of BRDC occur prior to arrival at the feedlot, there are indeed controllable and uncontrollable stressors imparted at the feedlot level, including animal handling at arrival (e.g., processing) (Martin et al., 1981), weather (and its fluctuations) (Alexander et al., 1989; Cusack et al., 2007), time to fill a pen (Alexander et al., 1989), level of stress associated with arrival and eventual passage to the home pen of the animals, diet and adaptation to it, commingling, and introduction to a novel environment. Modification of controllable factors at feedlots is also warranted for the successful control of BRDC.

To better understand the epidemiology of BRDC in feedlots and how best to reduce its burden, it must be recognized that misclassification of disease status occurs (Table 5). Some animals with bacterial bronchopneumonia do not display clinical signs to a sufficient degree to be detected by trained feedlot personnel. Additionally, some animals identified as suffering from BRDC may not actually have a pneumonic condition but are likely displaying non-specific clinical signs associated with another, non-respiratory condition such as a digestive disturbance or viremia.

Table 5. Misclassification of bovine respiratory disease complex status. Lesions were evaluated at harvest via gross examination of lungs.

<table>
<thead>
<tr>
<th>Study</th>
<th>Cattle</th>
<th>Overall BRDC treatment rate</th>
<th>Displayed clinical signs of BRDC; administered therapeutic intervention</th>
<th>Never displayed clinical signs of BRDC; not treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wittum et al, 1996</td>
<td>469</td>
<td>35%*</td>
<td>78%</td>
<td>68%</td>
</tr>
<tr>
<td>Thomson, unpublished</td>
<td>1,690</td>
<td>26%**</td>
<td>62%</td>
<td>43%</td>
</tr>
<tr>
<td>Gardner et al, 1999</td>
<td>204</td>
<td>50%**</td>
<td>74%</td>
<td>58%</td>
</tr>
</tbody>
</table>

* cohort followed from birth through the feeding process
** morbidity in the feedlot only

The reason for misclassification based on gross evaluation of lung lesions is not entirely clear. Some possible reasons are:

- Some animals developed BRDC prior to entry in the feedlot (hence, never identified as sick at the feedlot level but with gross evidence of lesions).
- Animals treated for BRDC successfully resolved the lesions to the extent they were not visible during gross examination.
- Some cattle sufficiently tolerate BRDC without displaying signs sufficient to be identified as sick, but they have identifiable lesions at harvest.

Regardless of the underlying causes of the apparent misclassification of disease status, animals with lung lesions generally have poorer performance characteristics than those with no evidence of lung lesions. In one study for instance, cattle with lesions gained 0.17 lbs less per day than animals without lesions (Wittum et al., 1996). In other studies,
cattle with gross evidence of bronchopneumonia had carcasses that weighed 33 lbs less\(^\text{10}\) and had lower marbling scores (Gardner et al, 1999) than animals with no evidence of lesions.

Consequently, BRDC imparts substantial economic challenges for all segments of the cattle industry, but the largest burden occurs at the feedlot level of the industry. Owners and caretakers of cattle, therefore, have significant economic as well as moral and ethical obligations to provide for the well-being of the animals in their care. In other words, there are substantial financial disincentives for feedlots to provide anything less than acceptable animal welfare standards.

**Efforts to reduce burden of BRDC**—A wide variety of efficacious vaccines (against viral and bacterial pathogens) are available to feedlot managers. Based on available data, essentially all feedlots vaccinate their cattle against the major pathogens implicated as causal in the pathogenesis of BRDC (USAPHIS 2000a; 2000b; 2000c). These vaccines are generally administered within 3 days of arrival (but mostly within 24 hours of arrival). Depending on the protocols established by the consultant veterinarian, some cohorts might be revaccinated in the event of a significant disease challenge or at the time of reimplantation approximately 50 to 80 days after arrival. However, there are few, if any, available data that support revaccination.

While control of BRDC-causing pathogens is an important component of health management in feedlots, it will have a relatively small effect compared to modifying other factors. Some critical determinants of BRDC occur prior to arrival at the feedlot and largely depend on the manner by which the cow-calf producer decides to manage and market calves. These decisions are largely uncontrollable at the feedlot level. Consequently, feedlots and their consultant veterinarians have developed protocols that they believe provide optimal control and treatment of BRDC.

Early identification and administration of an effective antimicrobial drug is the most effective predictor for a successful resolution of BRDC. To accomplish this task, feedlots employ pen-riders trained by veterinary consultants to effectively identify animals requiring treatment, then move them to an animal handling facility in a timely, low-stress manner. Most feedlots have their pen-riders evaluate all their cattle at least once a day (USAPHIS 2000a; 2000b; 2000c). In certain situations, eg, for cohorts of cattle believed to be at high risk of developing BRDC, pen-riders may evaluate the animals more than once a day.

An important determinant of a successful outcome is selection of an efficacious antimicrobial drug. A variety of efficacious, long-acting injectable products have been developed and approved for use (Booker et al, 1997; Jim et al, 1999; Schunicht et al, 2002a; Schunicht et al, 2007). Each product has its own set of characteristics so that veterinarians can prescribe and develop customized protocols that best fit the particular circumstances.

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\(^\text{10}\) Thomson DU. Unpublished data, Kansas State University, 2007.
management of the feedlot. The advent of long-acting injectable antimicrobials has provided distinct animal-welfare and management advantages (Schunicht et al, 2007; Booker et al, 2006). Animals no longer need to be handled on a daily basis to complete an antimicrobial regimen. This reduces stress and risk of injury for the animal and labor needs.

Identification and prompt treatment of sick animals is a foundation of animal health management in feedlots. As described in Table 5, however, there is a population of animals that, for whatever reason, develop bacterial bronchopneumonia but do so without displaying sufficient clinical manifestations to facilitate visual identification. These animals gain weight more slowly, and they represent an opportunity to improve both animal welfare and economic returns. Feedlots and their veterinary consultants have developed control regimens that effectively target these animals.

These control regimens are based on two premises: 1) that feedlot personnel can, with some degree of predictability, identify cohorts of animals at high risk of developing BRDC; and 2) they can administer an efficacious, long-acting antimicrobial prior to the expected peak of BRDC events to reduce the epidemic and its impact (e.g., rate of weight gain) within the cohort. Since most BRDC events occur soon after arrival, blanket administration of an injectable antimicrobial to a high-risk cohort at feedlot is convenient and frequently practiced; it is referred to as metaphylaxis or mass-treatment. A plethora of studies are available that show BRDC can be effectively controlled in this manner (Booker et al, 2006; Schunicht et al, 2002b; Step et al, 2007; Galyean et al, 1995; Frank et al, 2002; Morck et al, 1993; Rooney et al, 2005). Veterinary consultants now have a variety of long-acting antimicrobial drugs that are approved for this use (i.e., control of BRDC in high-risk cattle).

Continued availability and development of new antimicrobial drugs that are effective for the treatment and/or control of BRDC in feedlot cattle improves the ability of feedlot personnel along with their consulting veterinarians to effectively care for the welfare of animals in their care. Targeted metaphylactic use of approved injectable antimicrobial drugs also appears to benefit those animals that do not display clinical signs to a sufficient level to be visually identified as sick.

Recently, there have been increasing efforts to control BRDC by modifying those determinants that occur prior to arrival at the feedlot. These include the use of preconditioning or backgrounding programs whereby vaccines are administered, calves are weaned, castrated, etc., and potentially introduced to a feeding-type environment for a certain period of time prior to arrival at the feedlot. There is some evidence that these practices significantly reduce the morbidity of BRDC once the calves arrive at the feedlot (Macartney et al, 2003b). Moreover, it appears that calves preconditioned and marketed as such receive a premium over conventionally marketed calves (Macartney et al, 2003a). It is hopeful, therefore, that as these data are disseminated and more integration and coordination occurs between feedlots and the sectors identified previously, meaningful control of BRDC determinants will continue to expand.
Conclusions—Respiratory disease in cattle is truly a multi-etiological complex that presents challenges to all segments of the cattle industry, both large and small. Bovine respiratory disease complex is by no means unique to the US production system but can and frequently does result in significant morbidity within cattle herds worldwide. While the majority of the disease events and control efforts occur at the feedlot sector in the United States, much of the disease observed is attributable to the traditional methods by which cattle are marketed; these methods have not varied greatly for many decades and predate modern cattle feeding.

Many cow-calf producers enjoy the camaraderie and price discovery provided by the auction market system. Furthermore, many operations simply do not have sufficient resources to overwinter calves on range. Consequently, selling calves through the auction market system remains a way of life as well as a necessity for many producers, the result of which is that calves are exposed to a variety of stressors, such as commingling, that may increase their susceptibility to BRDC and other diseases. Recently, there has been a gradual trend away from traditional auction-market systems to virtual auctions whereby buyers can bid on cattle while still on the ranch via real-time broadcasting. This reduces commingling and provides more single-source groups.

Preconditioning programs are effective in controlling BRDC, but they add direct input costs for the cow-calf producer with no guarantee of a return in a commodity market. Consequently, producers who precondition calves need to differentiate their product from commodity, and this is becoming increasingly common through alliances and pharmaceutical/biologic company-sponsored programs.

At present, most control is implemented at the feedlot level. Feedlots invest considerably in prevention, control, and treatment of BRDC. It is likely that effective measures can reduce expected morbidity in high-risk cohorts by 50% or more. Additional substantive control, however, will likely require modification of determinants that occur prior to arrival at the feedlot. Ultimately, as the cattle industry becomes more integrated either through ownership, alliances, or other coordination, the opportunity for meaningful control of BRDC will increase.

The US Swine Industry

Swine production life cycle

Biological life—A piglet’s life starts with conception, followed by 114 days of gestation. Upon birth, female swine, called gilts, reproductively start to cycle when they are 5 or 6 month old. The gilts are typically bred for the first time when they are 7 or 8 months old. The average sow (sow is the term for an adult female pig) will produce about 3.5 litters of piglets during her lifetime. The piglets are usually weaned by 35 days old (range 17-11

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35 days) and then slaughtered at about 180 days. Slaughter hogs usually weigh about 260 pounds (Plain & Lawrence, 2003).

**Unique aspects of swine as a production animal**

**Feeding**– Feed costs represent an estimated 60-70% of total production costs (USAPHIS, 1996). Unlike beef and dairy cattle, a large component of swine feed ingredients must come from grains, particularly corn. Other grains, such as oats, barley, sorghum, and rye, may also serve as components in swine rations. Since grain can be shipped into the facility, it is less critical that the swine facility be located close to the grain production area. This is in contrast to many dairy and beef operations since they are typically located in or near forage production areas because of the challenges of shipping forages of low density and high volume over long distances. According to the NAHMS (USAPHIS, 1996), larger swine operations (greater than 10,000 animals) were less likely to mix swine diets on-site than smaller operations. The components of swine diets are adjusted as the pig progresses through the grower and finisher phases of production and often by gender through split-sex feeding.

**Production response**– The production response of swine is observed by measuring litter characteristics (number, weight, litter mortality), weight gains, feed efficiency, days on feed, morbidity, and mortality. These measured production responses are also used as an indicator of immediate health issues.

**Structural demographics of the swine industry in the United States**

Similar to the poultry and dairy industries, the US swine industry has also undergone significant demographic changes in the past 10 years. Most notably, the swine industry has decreased the number of swine operations while increasing the average herd size at operations since the 1990s. According to US Census of Agriculture data, the number of sites reporting data in 1992 was 191,347, and the average herd size at each site was 301. In contrast, 2002 data showed that only 78,895 sites were included in the census, and these sites averaged 766 animals per herd. According to National Agricultural Statistics Service (NASS) data, the number of US swine sites in 2003 (73,600 sites) was only 43.7% of the 168,450 sites reported in 1995 (USDA).

Swine production has also moved into other regions of the United States not previously extensively involved in swine production. Some states in the western, southwestern and mountain regions have significantly increased their swine production as shown by NASS 2000 data. Colorado, Oklahoma, Texas, Utah, and Wyoming all reported significant increases in inventory for the 2000 census (USDA). Other states with marked increases in swine inventory included Minnesota, Mississippi, and North Carolina. The top five swine states in order of swine numbers are Iowa, North Carolina, Minnesota, Illinois, and Indiana (USDA).

With the shift from smaller to larger swine herd sizes, the number of CAFOs has greatly increased. Large CAFOs include operations with at least 2,500 swine each weighing 55 pounds or more or at least 10,000 swine each weighing less than 55 pounds. Medium CAFOs are operations with 750 to 2,499 swine each weighing 55 pounds or more or
3,000 to 9,999 swine each weighing less than 55 pounds. Despite the increases in swine herd size, most hog operations are still small. Data obtained from NASS and Iowa State University show that of the 77,260 swine operations in 2000, 54,512 of them marketed less than 1,000 hogs annually (Plain & Lawrence, 2003).

**Consumer trends**

American consumption of pork products ranks third in meat consumption behind beef and poultry. Pork consumption has declined approximately 10% between 1960 and 2003. Approximately 62% of the pork currently consumed in the United States is processed and includes such products as bacon, sausage, hot dogs, and lunch meats, while fresh pork products, such as pork chops or steaks, represent about 38% of US pork consumption. Processed pork products have the advantage of specific steps during processing (eg, cooking/smoking of hot dogs, pickling/salting of bacon and hams) that reduce the likelihood of consumers being exposed to potential pathogens. The preference for processed pork products is not surprising in today’s fast-paced lifestyle, and consumers may prefer its convenience when compared to fresh pork products. Most pork is consumed at home, not in restaurants or other facilities away from home, so attention to consumer education on proper food handing to prevent cross contamination is critical. Highest consumption of pork occurs in the midwest states, followed by the south, northeast, and the western United States (Davis & Lin, 2005b).

**Diseases and conditions of swine and potential animal health impacts**

Disease discussion is divided into categories based on the pig’s lifecycle: farrowing, pre-weaning piglets, piglet nursery phase, breeding age females, and grower/finisher phase. Data from NAHMS national swine surveys (USAPHIS, 2005a) are used.

**Farrowing**—The rate of stillbirths and mummies (8.41% in 1990, 7.53% in 2000) per litter at farrowing has remained similar between 1990 and 2000. Estimated 1990 pre-weaning deaths per litter and 2000 deaths per litter have remained at about 12%. In terms of number of piglets weaned per litter, total litter productivity has increased slightly from 8.37 pigs in 1990 to 8.77 in 2000.

**Pre-weaning piglets**—Despite the use of farrowing stalls, piglet mortality due to being laid on by an adult still ranks as the top producer-identified cause of death among piglets. According to NAHMS (USAPHIS, 2000) data, approximately 51% of deaths among piglets was attributed by producers to being laid on. Starvation (18.6%) and scours (diarrhea) (11.0%) rank second and third among producer-identified causes of piglet death. Scours-related piglet deaths have significantly decreased between 1990 and 2000, from 23.9% to only 11.0%. The increase in intensive animal production methods and management practices may have contributed to this decrease.

**Nursery phase**—During the piglet nursery phase, producers identified respiratory disease as the reason for almost 29% of deaths. Other known (but not reported by producers) problems accounted for 24.5% of piglet deaths during the nursery phase. Unknown causes of death, 20.7%, also figure significantly into mortality rates. Starvation (13.3%) and scours (12.6%) are also important causes identified by producers in nursery piglet
Deaths. Diseases of significance reported by sites with nursery-age pigs included mycoplasma pneumonia (19.6%), colibacillosis (24.0%), *S. suis* infection (31.6%), *S. hyicus* (25.3%), roundworms (18.0%), and PRRS (17.5%). The diagnosis of PRRS (11.6%), *Salmonella* (4.5%), and *Actinobacillus pleuropneumoniae* or Haemophilus, commonly known as APP (3.8%), are the most common nursery pig diseases identified on swine sites by veterinarians or laboratories. *Haemophilus parasuis* (Glasser’s disease) is also commonly diagnosed by veterinarians or laboratories.

Antimicrobials are commonly used to treat respiratory disease in nursery age pigs. The protocol most commonly reported by sites was to administer antibiotics to all pigs in a room with clinically affected animals. So, any animals that share air space with ill pigs are treated with antimicrobials. The next most commonly used strategy (16.0%) was to treat only pigs identified with clinical signs of respiratory disease. Twelve percent of the sites did not treat any pigs for the most recent occurrence of respiratory disease outbreak in nursery-age pigs in the previous 2 years. For most sites (75.3%), the site owner was the primary decision maker for antibiotic selection. Veterinarians were more likely to be the primary decision maker on medium and large sites compared to small sites. Antimicrobials were also used by 82.7% of reporting sites to promote growth in nursery-age pigs.

**Breeding age females**—The culling rate of sows has decreased from 43.5% in 1990 to 37.7% in 2000. Many sows are culled because of advanced age, reproductive failure, or lameness. Among breeding females, PRRS (21.4%) and roundworms (40.8%) are the two most frequently reported diseases. Mycoplasma pneumonia (14.2%), swine influenza virus H1N1 (traditional swine flu, 11.2%), gastric ulcers (10.7%), and swine influenza virus H3N2 (new swine flu, 5.3%) are also important reported causes of disease.

Vaccination against common swine diseases is commonly used in swine health management programs. Particular emphasis is placed on the breeding female herd since they generally maintain a presence on the site longer than market hogs. The control of PRRS is a priority for many swine producers. Most, 53.5%, of breeding females reside on sites that use PRRS vaccines. Of the breeding-age females that received PRRS vaccine, most (80.6%) were vaccinated upon their entry into the breeding herd. Most, 55.5%, of these sites also vaccinated females again for PRRS while they were in the breeding herd. Growers also reported the use of measures to control or prevent PRRS in their herds by using only PRRS-negative boars or semen (33.3%), maintaining a closed herd for replacement females (25.4%), and obtaining replacement females from PRRS-negative sources (23.9%). In addition, an estimated 39.7% of breeding females receive mycoplasma vaccines. Of the sites that reported the use of mycoplasma vaccines, 74.6% vaccinated gilts before they became a part of the breeding herd. Many, 31.0%, breeding females reside on sites that report vaccinating for both types of swine influenza virus. Of the breeding-age females that received swine influenza virus H1N1 vaccine, most (71.4%) were vaccinated upon their entry into the breeding herd. Of those that received swine influenza virus H3N2, 75% were vaccinated upon their entry into the breeding herd.
Antibiotics are typically used to treat breeding females with disease conditions. Most sites, 61.3%, reported using antibiotics to treat disease conditions. The owner of the swine operation is typically in charge of antibiotic selection, and 45.9% of sites reported that the owner was primarily responsible for choice of antibiotics. Veterinarians were more likely to be the primary decision maker on medium and large sites compared to small sites. The majority, 58.7%, of sites that reported the use of antibiotics also maintained treatment records. The type of drug used, date of administration, and the individual animal ID were commonly recorded if producers kept treatment records.

**Grower/finisher phase**— Similar to the nursery pig phase, PRRS (10.3%), *Salmonella* (5.1%), and APP (4.8%) are common diseases identified in grower/finisher pigs on swine sites by veterinarians or laboratories. More large sites experienced outbreaks of respiratory disease when compared to smaller swine operations. Only 7.2% of larger swine operations reported no respiratory disease outbreaks, significantly less than the 29.3% of smaller operations reporting no respiratory disease outbreaks. Overall, only 25.8% of grower/finisher operations reported no problems with clinical respiratory disease. Thus, respiratory disease is an important disease problem in this swine production phase. Most sites reporting respiratory disease estimated the onset of clinical signs at around 15 weeks of age.

Since respiratory illnesses are significant in the grower/finisher phase, many producers employ measures to control or prevent causes of disease. Most, 66.6%, producers report using some type of preventive measure designed to control or prevent mycoplasma in their weaned pigs. Of these sites, 38.6% of them reported vaccinating pigs weighing 70 pounds or less for mycoplasma. Many producers (47.6%) reported the use of antibiotics to control disease by treating pigs demonstrating clinical signs of respiratory disease. Some farms (24.0%) used an “all-in, all-out” system so that animals stayed together, thus reducing the chance of introducing respiratory disease with the addition of new pigs.

Only 5.2% of participating sites reported the use of a PRRS vaccine in their weaned market pigs. Although vaccination was not commonly used, 37.2% of sites reported using other strategies to manage or prevent PRRS in their weaned pigs. Limiting the source of weaned pigs was used by 25.5% of reporting sites to control PRRS. Nursery depopulation (15.5%), obtaining pigs from stable PRRS positive herds (11.4%), or obtaining pigs from PRRS negative herds (10.4%) were also more common measures used to combat PRRS.

A vaccination to control influenza was more commonly used by sites when compared to vaccination for PRRS. Of the sites that participated in the NAHMS study, 10.5% reported using a swine influenza vaccine in their weaned market pigs. Most sites vaccinated their pigs between 7 and 10 weeks of age. Other measures to prevent disease were not reported.

Antimicrobials may be used to treat or prevent respiratory disease during the grower/finisher phase. Most (39.5%) sites that reported using antimicrobials treated all pigs that shared air space with pigs showing clinical signs or respiratory disease. Some
(27.1%) sites treated only pigs showing signs of respiratory disease. Over six percent of
the sites did not treat any pigs for the most recent occurrence of respiratory disease
outbreak in grower-finisher pigs in the previous 2 years. Larger sites were more likely to
use antibiotics. More than 90% of sites with at least 2,000 pigs used antibiotics to treat
disease while only 65.4% of smaller operations used antibiotics. Most (63.6%) of
reporting sites used treatment records for animals receiving antibiotics. At a minimum,
sites that used treatment records recorded dates of administration and type of
antimicrobial used. Similar to other swine production phases, the operation’s owner was
typically in charge of choosing antibiotics for use on the site, and veterinarians were
increasingly used on the medium and large sites compared to the small sites. A
substantial percentage (88.5%) of sites reported using antimicrobials in feed for disease
treatment or disease prevention, but most commonly to promote growth. Since parasites
may plague some grower/finisher operations, 15.6% of sites reported using injectable
parasite treatments, 6.2% used a water treatment method to administer a dewormer, and
39.7% of sites added a dewormer to the pig ration.

Trichinella, a nematode parasite that infects muscle, may be passed to humans from
consumption of infected undercooked pork. Effective tests are available to detect
trichinella infection in hogs both pre- and post-harvest (Smith & Lechman, 2003), and the
prevalence is very low in the United States. Cysticercosis is a rare parasitic infection
caused by _Taenia solium_, the pork tapeworm. In a NAHMS report describing a summary
of slaughter condemnation rates from 1990 to 2000, no carcasses were reported to be
condemned for trichinella infection, and only an average of 1.3 carcasses were
condemned for cysticercosis infection per year. Antibiotic residues have also decreased
markedly. According to NAHMS (2000), only 5 carcasses from federally inspected
slaughter plants were condemned between 1996 and 2000. When contrasted with the 111
carcasses condemned for antibiotic residues between 1990 and 1995, the improvement is
significant.

_Potential human health risk of Salmonella enterica serotype Typhimurium DT104_
Food safety concerns pertinent to the hog industry often relate to _Salmonella_, parasite
infections, and antibiotic residues. According to an NAHMS fact sheet (USAPHIS,
1997b) that detailed results of a _Salmonella_ prevalence study, only 38.2% of the sampled
farms with finishing hogs had samples that were positive when tested for _Salmonella_. Of
this 38.2% of _Salmonella_-positive farms, the level of bacterial shedding in finishing hogs
was low, an estimated 6%. In another study (Duffy et al, 2000), 9.6% of uncooked or
unprocessed samples obtained from retail stores were contaminated with _Salmonella_.
Although proper handling and cooking will prevent the consumer from becoming
infected, food safety is of primary importance to the swine industry, and studies to
identify means to reduce _Salmonella_ are being conducted by scientists.

In the United States, _Salmonella_ species are the leading cause of hospitalizations and
deaths due to known foodborne bacterial infections, with an estimated 1,400,000,
infections resulting in 16,000 hospitalizations and nearly 600 deaths annually (Mead,
1999). _Salmonella_ species live in the intestines of mammals, birds, and reptiles and are
shed into the environment in the feces of infected hosts. The organism can survive for extended periods of time in water, soil, and food (Angulo et al, 2000).

**Multiple drug resistance**
Of increasing concern is a multi-drug resistant strain of *Salmonella enterica* serotype Typhimurium defined by phage typing as definitive type 104 (DT104) (Rabatsky-Ehr et al, 2004). Multiple drug resistant (MDR) DT104 is characterized by its chromosomally encoded antimicrobial-resistance pattern to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline, abbreviated as R-type ACSSuT (Rabatsky-Ehr et al, 2004; Besser et al, 2000). In the United Kingdom, MDR *Salmonella enterica* serotype Typhimurium DT104 was first detected in humans in 1984 and in cattle in 1988 (Akkina et al, 1999). The number of reported human isolates of *S. Typhimurium* with MDR continued to increase in the United Kingdom, with 81% of isolates collected in 1996 (Threlfall et al, 1997). In the United States, R-type ACSSuT isolates reported to the NARMS increased from <1% in 1980 to 34% in 1996 (Glynn et al, 1998). In that same year, the United States experienced its first MDR DT104 outbreak among seven elementary school children in Nebraska, likely linked to contaminated milk (USCDC, 1997). Even though the prevalence of DT104 has decreased in the United States since the late 1990s, in 2004, *Salmonella enterica* serotype. Typhimurium was still the most common serotype reported to the NARMS, accounting for 23.3% of non-Typhi *Salmonella* isolates (USCDC, 2004; Rabatsky-Ehr et al, 2004). Since its first isolation in the United Kingdom, MDR DT104 has caused numerous infections and outbreaks in food animals and humans worldwide, involving several countries in Europe, Africa, Southeast Asia, the Caribbean, as well as the United States, and Canada (Threlfall, 2000).

MDR DT104 has subsequently been isolated from poultry, sheep, pigs (Swartz, 2002), cats, horses, goats, emus, dogs, elk, mice, coyotes, ground squirrels, raccoons, chipmunks, and several species of birds (Besser et al, 1997). Other possible sources of nontyphoidal *Salmonella* include water, reptiles (Swartz, 2002), and vegetables that have been contaminated with infected animal manure (Inami et al, 2001).

The emergence of antimicrobial resistance patterns in zoonotic bacteria, as is seen with MDR DT104, is a significant human and animal public health concern with potentially severe and adverse health effects and possible life-threatening consequences (Hohmann, 2001). The concern is further supported by reports that link human MDR DT104 infections to foods of animal origin, including pigs, cattle, and poultry, and associated increases in morbidity and mortality in humans infected with MDR *Salmonella* Typhimurium (Helms et al, 2002; Varma et al, 2005). Person-to-person transmission of *Salmonella* is infrequent (Swartz, 2002). Rather, most human salmonellosis cases result from eating contaminated foods of animal origin, as food-producing animals are reservoirs for nontyphoidal *Salmonella* (Angulo et al, 2000).

**Origins and transmission**
Human salmonellosis outbreaks have repeatedly been traced back to food products of animal origin, including pork, in many parts of the world (Pontello et al, 1998; Mølbak et al, 1999; Maguire et al, 1993). Over the last few decades, animal husbandry practices in
the United States have become more industrialized, and CAFOs are more common (Cole et al, 2000). The significant amount of waste material from swine CAFOs is a huge reservoir of potentially harmful organisms, MDR DT104 included, that, in addition to contaminating pigs, can accidentally enter the food chain and cause serious human health problems (Cole et al, 2000; Gebreyes et al, 2004; Gebreyes and Altier, 2002; Hohmann, 2001). Furthermore, Cole et al (2000) specifically identifies emerging antimicrobial resistance as a hazard of swine CAFOs.

*S. Typhimurium DT104* is the most common type of *Salmonella* isolated from pigs in the United Kingdom (Delsol et al, 2004). However, pork is more frequently implicated in *Salmonella* outbreaks in Scandinavian countries and Germany, where it is often consumed raw or lightly cooked (Davies, 2001). This supports the concept that thoroughly cooking pork significantly reduces the risk of exposure (Altekruse et al, 1997). Studies in Denmark implicate swine herds as important sources for human DT104 outbreaks (Molbak et al, 1999; Baggesen and Aarestrup, 1998). Molbak’s (1999) Denmark study describes a human outbreak of salmonellosis caused by MDR and quinolone-resistant DT104 linked to Danish swine herds. Human patient samples and pork samples collected from a slaughterhouse were positive for *Salmonella* with the same penta-resistant drug phenotype, identified as MDR DT104. Eleven of 25 patients were hospitalized and 2 died. Two of the patients probably acquired the infection by occupational transmission. One patient worked at the incriminated slaughterhouse and the second, a nurse, was exposed in the hospital ward while treating another DT104-infected individual. One patient acquired the DT104 infection in the hospital, where she shared a room with another positive patient. Nineteen patients reported eating pork products, including meatballs, tenderloin, and other pork products. Molbak et al (1999) clearly document the spread of DT104 from swine slaughterhouses to humans, and through their surveillance system were able to mitigate the spread of DT104 (Molbak et al, 1999).

Gebreyes and Altier (2002) describe resistance patterns and genetic characterization of MDR *Salmonella* Typhimurium strains cultured from commercial swine operations in the United States. Commonly identified were two penta-resistant patterns, one of which is the pattern usually exhibited by DT104, the other by DT193, both of which represent important public health implications. A majority of the DT104 isolates were of serovar Typhimurium variant Copenhagen, a variant adapted to the swine host. Based on their results, the investigators suggest that variant Copenhagen is common among pigs and is associated with phage type DT104. Additionally, they identified that the DT193 antimicrobial resistance pattern is encoded on plasmids, which can easily be transferred within the Genus *Salmonella* and to organisms other than *Salmonella* (Altier, 2004). The risk of antimicrobial gene transfer, in addition to the high prevalence of DT104, poses a significant threat not only through foodborne salmonellosis attributed to pork consumption, but also through the horizontal transfer of resistance determinants to commensal or resident organisms of the human digestive tract or other pathogens of importance to human health (Gebreyes & Altier, 2002). The investigators demonstrate that commercially raised pigs can represent a reservoir for *Salmonella*, harboring genes resistant to multiple antimicrobial agents, and they conclude that contaminated pork
products present a substantial risk for the acquisition of strains with this type of antimicrobial resistance pattern by humans. They suggest transfer of resistance genes may also create new patterns of resistance and new types of resistant organisms, which might represent a threat to human health (Gebreyes & Altier, 2002).

Though Gebreyes et al (2004) recognize there is limited information on the potential role of commercial swine production in dissemination of MDR Salmonella in the United States, their recent research continues to support the theory that pigs raised in commercial production systems pose a human health risk by serving as reservoirs of MDR Salmonella. In the study, DT104 was the most common isolate (34% prevalence) among eight phage types identified from 24 farms of two commercial swine production systems. In addition to DT104, another common multi-drug resistance pattern was identified (R-type AKSSuT DT193). Together, these two penta-resistant phage types constituted two-thirds of the serotype Typhimurium isolates in his study (Gebreyes et al, 2004).

In addition to CAFOs, smaller family farms with Salmonella-infected animals can pose a risk for transmission (Wall et al, 1995). While most human cases of salmonellosis are foodborne, close contact with infected farm animals, including pigs, is a risk factor for S. Typhimurium DT104 infections (Besser et al, 2000; Hendriksen et al, 2004; Wall et al, 1995). Hendriksen et al (2004) report a case of a Dutch child who was culture positive for DT104A (a subtype of DT104) that was identical to isolates collected from a diseased pig and calf with which the young boy had contact. This case report suggests an epidemiologic link between the sick child and the sick farm animals because all three strains appeared to be phenotypically and genotypically identical based on antimicrobial-drug susceptibility testing and pulse field gel electrophoresis (PFGE) patterns.

Perron et al (2007) suggest infected pigs not showing clinical signs may be an unexpectedly larger reservoir of DT104 than previously considered. Much of the understanding of DT104 is a result of outbreak investigations and studies of clinical isolates with few studies of isolates from “non-clinical” pigs (Perron et al, 2007). Healthy pigs may often be infected with Salmonella without showing any signs of disease. Therefore, many farmers and others working with pigs are unaware that the pigs are infected (Swanenburg et al, 2001). Furthermore, an important aspect of Salmonella Typhimurium DT104 population structure and ecology is neglected when considering disease or outbreak isolates only. Following a cross-sectional study of the Canadian swine industry, Perron et al (2007) report the genetic and phenotypic diversity among asymptomatic porcine S. Typhimurium DT104 isolates and note a high proportion of MDR DT104 among apparently healthy pigs. This highlights the importance of healthy pigs as reservoirs of Salmonella DT104 and potential reservoirs of antimicrobial resistance, knowledge critical for developing effective control strategies (Perron et al, 2007).

**Control measures**– A study of slaughter pigs in the Netherlands identified Salmonella, including DT104, in 47% of the sampled pigs where carcass samples were taken from the liver, tongue, rectal contents, mesenteric lymph nodes, tonsils, and serum (Swanenburg et al, 2001). Salmonella prevalence in pigs differ depending on the type of sample.
collected, therefore, collecting more than one sample per pig increases the chance of detecting a *Salmonella* sp. positive pig (Swanenburg et al, 2001).

Botteldoorn et al (2003) and Swanenburg et al (2001) report pigs can become *Salmonella* contaminated during and after slaughter by cross contamination from the slaughterhouse environment. The major contamination sources of pig carcasses are pig- (feces, pharynx, and stomach) and environment-related (contact surfaces and handling by workers) (Borch et al, 1996). Contaminated lymph nodes and intestines can be one of the main sources of carcass contamination during the evisceration process (Botteldoorn et al, 2003). Swanenburg et al (2001) notes that resident lairage *Salmonella* can be an environmental source of cross contamination for pigs entering the slaughterhouse. Swanenburg et al (2001) identify resident *Salmonella* in addition to the carcass splitter as critical control points during slaughter, and note control measures such as cleaning and frequent disinfection should be taken to avoid cross contamination. Though *Salmonella* are brought into the slaughterhouse by delivered pigs, slaughter hygiene should be kept at very high standards to minimize cross contamination (Swanenburg et al, 2001).

Another critical point for controlling carcass contamination is to reduce the prevalence of *Salmonella* carriers delivered to the slaughterhouse (Creus et al, 2007). Carrier animals can become active fecal shedders of *Salmonella* due to stress associated with transport and lairage, and may contribute to the spread of infection to other animals (Hurd et al, 2001). Stresses encountered during production, including noise, smells, high stocking densities, temperature changes, and general environmental changes, may induce carriers to shed *Salmonella* at a higher rate and increase the susceptibility of *Salmonella*-free pigs to infection (Lo Fo Wong et al, 2002; Mulder, 1995). Consequently, transportation stress can significantly increase the number of pigs excreting *Salmonella* upon arrival at the slaughter plant (Berends et al, 1996). Cross-contamination of DT104 strains between herds could also result from animal trade, passive and active transfer due to human interactions, or from insect or rodent movements and activity (Perron et al, 2007). Reduction of *Salmonella* in pork and pork products should include monitoring and intervention not only at the farm level (Mousing et al, 1997), but at all levels of production (Lo Fo Wong et al, 2002).

Creus et al (2007) evaluated the effects of acidified feed on *Salmonella* prevalence in pigs. Investigators report that the addition of lactic and formic acid in pig feed during their fattening period results in a statistically significant reduction in *Salmonella* prevalence in finishing pigs. However, measures of hygiene and management cannot be overlooked in controlling *Salmonella* contamination throughout the pork production chain (Creus et al, 2007).

Van der wolf et al (2001) studied the effects of acidified drinking water on *Salmonella* infections in swine finishing herds as a *Salmonella* control strategy at the herd level. Investigators found that at a dose of 0.2%, the addition of organic acids to drinking water of finishing pigs reduced the number of *Salmonella*-positive finishers compared to the control groups. However, this approach has potential logistical complications and
disadvantages that include ensuring proper water concentration, equipment failure, and considerable financial costs (Van der wolf et al, 2001).

**In cattle**—Unlike swine, adult cattle and calves in both dairy and beef herds tend to show clinical manifestations of infections of MDR *Salmonella* DT104 with signs of pyrexia, lethargy, decreased milk production, anorexia, dehydration, increased salivation, and diarrhea progressing to dysentery (Davies, 2001; Evans & Davies, 1996). Cattle can shed the organism for up to 18 months after an outbreak (Akkina et al, 1999; Poppe et al, 1998). There is a higher risk of cattle infection associated with herd size, the introduction of animals from sale barns, lack of clean calving facilities, increases in production or environmental stress, recent calving, contact with infected wildlife or humans, and contact with contaminated water sources (Davies, 2001). Cattle can transmit *Salmonella* DT104 to humans directly by feces or indirectly through fomites (Wall et al, 1995) or raw animal products, particularly ground beef, milk, and cheese (Dechet et al, 2006, Villar et al, 1999). Claims have been made that beef and dairy products accounted for 10% of reported food-borne *Salmonella* outbreaks where a source was identified (Olsen et al, 2000).

Farm owners, employees, members of farm families, and veterinarians are at increased risk of infection with *Salmonella* DT104 due to direct fecal-oral contamination or direct contact with infected calves. Direct transmission can result from inadequate hand washing, soiled clothes or shoes, or farming equipment, all of which can be contaminated by infected cows (Poppe et al, 1998).

Ground beef is also a potential source of transmission of *Salmonella* DT104. In 2003-2004, a cluster of *Salmonella* DT104 outbreaks associated with commercial ground beef was documented in the northeastern United States. The long duration of this outbreak suggested that contamination was most likely localized to the centralized processing of contaminated cattle or the contamination of the processing facility. Because some cattle have sub-clinical infections and go undetected through the meat processing facilities, contamination of ground beef is a risk factor for human infection (Dechet et al, 2006).

A 1998 study conducted in Washington, DC, surveyed ground chicken, ground beef, ground turkey, and ground pork. Investigators found that 20% of meat purchased in grocery stores was contaminated with *Salmonella*, and 82% of the strains were MDR, including *Salmonella* DT104 strains (White et al, 2001). In 2002, national surveillance by the FDA, USDA, CDC, and NARMS found that 9 of 642 ground beef samples were contaminated with *Salmonella*, and 22% of those isolates were resistant to greater than 9% of the tested antimicrobials. All together, approximately 0.3 % of ground beef purchased from grocery stores in the United States in 2002 was contaminated with MDR *Salmonella* (USFDA).

*Salmonella* DT104 has been documented in raw milk, cheese, and improperly pasteurized milk (Villar et al, 1999; Olsen et al, 2004). A 1997 outbreak in Washington State was linked to unpasteurized Mexican-style soft cheese (queso fresco), during which 20 (91%) case patients were infected with MDR DT104. The contaminated cheese was traced back
to a local dairy farm. *Salmonella* DT104 was isolated from the bulk milk tank and trucker tank samples (Villar et al, 1999). Another outbreak related to raw-milk Mexican-style cheese was reported in 1997 in California, with similar case findings as the previous outbreak mentioned (Cody et al, 1999).

Reports of *Salmonella* outbreaks from pasteurized milk are rare. However, Olsen et al (2004) report on a multi-state *Salmonella* DT104 outbreak associated with pasteurized milk. Environmental contamination of the milk containers, likely caused by unpasteurized milk contaminated with *Salmonella* DT104, caused contamination of the pasteurized milk (Olsen et al, 2004). In April 1984, an outbreak of *Salmonella* Typhimurium in Kentucky was traced back to consumption of milk not completely pasteurized (USCDC, 1984), also highlighting the importance of pasteurization regulations and educating consumers about risks of consuming unpasteurized milk products (Cody et al, 1999; Olsen et al, 2004).

**Control measures**

The availability and use of a rapid test that could detect MDR *Salmonella* DT104 in animals prior to culling would decrease the risk of contaminating raw beef supplies (Dechet et al, 2006). Additionally, the consumption of unpasteurized milk and cheese should be discouraged (Villar et al, 1999). Recommendations to prevent human infections include safely storing and handling food, washing hands, adequately cooking meat, and eating only pasteurized cheese and milk (Poppe et al, 1998).

**In humans**– Contact with infected animals, raw milk, and improperly cooked or handled foods of animal origin are major sources of human infection with *Salmonella* DT104. Clinical signs in humans infected with MDR *Salmonella* DT104 include diarrhea, fever, headache, nausea, vomiting, and abdominal pain, and 25% of human infections will have bloody diarrhea (Poppe et al, 1998). While most infections resulting in acute gastroenteritis do not require antimicrobial therapy, antimicrobial drugs are often prescribed for high risk patients including the very young, elderly, and those that are immunocompromised (Varma et al, 2005, Thielman & Guerrant, 2004). *Salmonella* bacteremia occurs in 2% to 4% of infected patients (Thielman & Guerrant, 2004). In a case study in the United Kingdom, the fatality rate was 3% for *Salmonella* DT104 when compared to 0.1% for other non-typhoid *Salmonella* infections (Akkina et al, 1999). The decision to treat can be difficult, as antibiotic therapy for patients with nontyphoidal salmonellosis may actually prolong, rather than limit, fecal shedding of these organisms (Hohmann, 2001). Another concern regarding treatment of MDR *Salmonella* is the association with higher frequencies of hospitalization and death compared to antimicrobially susceptible *Salmonella* strains (Helms et al, 2002).

Varma et al (2005) analyzed NARMS data for 1996-2001, and reports that rates of hospitalization and bloodstream infections are markedly elevated among patients with MDR *Salmonella* Typhimurium infection compared to patients with pansusceptible infection. Patients with MDR *Salmonella* infection were more likely to have a bloodstream infection, more likely to be hospitalized, and had longer hospital stays than those infected with pansusceptible *Salmonella* (Varma et al, 2005). Bloodstream
infection is a severe complication of salmonellosis, which can potentially lead to sepsis, endocarditis, endarteritis, meningitis, septic metastases, and death (Hohmann, 2001). Therefore, the human and public health consequences of acquiring MDR DT104 may be substantial (Varma et al, 2005).

There is a reported increased incidence of MDR Salmonella DT104 infections in humans and animals in the northwest United States (Akkina et al, 1999). Humans infected with MDR Salmonella DT104 were more likely to live in counties with larger livestock populations (Besser et al, 1997) or in zip code regions of above average cattle farm density, and were more likely to have direct contact with infected livestock (Besser et al, 2000).

Because dissemination of Salmonella DT104 is now seen in companion animals, risks of zoonotic transmission and environmental contamination in a small animal clinical setting cannot be overlooked. Salmonella DT104 was isolated from three outbreaks in small animal hospitals and shelters in the United States in which animals (mostly cats), owners (including children), and employees were infected. Isolates were tested at the CDC and phage typed to DT104. These outbreaks illustrate the risks of nosocomial and zoonotic infections by transmission from companion animals to employees, clients and pet owners and the risk of nosocomial infection within veterinary facilities and animal shelters. Environmental contamination in the hospital is another risk factor and potential source of infection (Wright et al, 2005).

Increasing drug resistance of Salmonella Typhimurium is another concern of humans because it limits treatments. In 2005, it was reported that, in addition to other drugs (mentioned previously), Salmonella are also becoming more resistant to ceftiofur (Alcaine et al, 2005). This is a primary concern because ceftiofur is closely related to ceftriaxone, a third-generation cephalosporin antibiotic used to treat invasive cases of Salmonella in children (Hohmann, 2001). A case study by Fey et al (2000) identified a ceftriaxone-resistant isolate from a child that was indistinguishable from one of the isolates from the family’s cattle, also ceftriaxone-resistant. This is extremely important for treatment of children because fluoroquinolones, another treatment option, are not approved for use in children (Fey et al, 2000). Development of resistant strains of bacteria can result in increased infectivity and virulence of pathogens and reduced effectiveness of appropriate therapy (Cole et al, 2000). Antimicrobial resistance to clinically essential “first-line” drugs is increasing among Salmonella worldwide (Hohmann, 2001). Many researchers suggest this trend is linked directly to the agricultural use of antimicrobial agents (Hohmann, 2001; Angulo et al, 2000; Molbak et al, 1999), and these antimicrobial resistant Salmonella are subsequently transmitted to humans, usually through the food supply (Angulo et al, 2000).

Summary– Salmonella DT104 has a broad host spectrum (Molbak et al, 1999), and transmission of DT104 potentially occurs through a complex route that may include wild animals, farm animals, domestic animals, slaughter houses, processing and distribution networks, retail outlets, and the consumer (USCDC, 1997; Molbak et al, 1999). Efforts are needed to elucidate its distribution in the environment and means by which the human
food chain is contaminated in order to identify targets of prevention (MMWR, 1997). Because of the broad reservoir, DT104 is difficult to control in animal husbandry (Molbak et al, 1999), and the more animals are being kept together (CAFOs), the more difficult is it to prevent the spread of infection (Berends et al, 1996). Control and/or elimination of DT104 will become increasingly more difficult once it becomes endemic in more animal populations. and this will continue to have serious implications for public health, animal health, and trade (Crerar et al, 1999).

In the United States, the estimated annual economic cost, including medical care and loss of productivity due to foodborne Salmonella infections, ranges from $500 million to $2.4 billion (Frenzen et al, 1999). To reduce foodborne salmonellosis and associated costs, continued research to understand not only the pathogenesis (i.e., adhesion, invasion, survival and replication in hosts) of Salmonella but also the epidemiology (host range, environmental and CAFO distribution and dissemination) of Salmonella is needed to design effective measures for prevention, control, and treatment of Salmonella infection and disease (Brumme et al, 2007; Niewold et al, 2007). Niewold et al (2007) concludes that in vitro models are unlikely to give insight into the complex in vivo mechanisms of Salmonella-host interactions, making it a challenge to implement what is found in the laboratory setting into real life scenarios. These differences in in vitro and in vivo testing may limit furthering scientific knowledge about Salmonella DT104.

Even though the prevalence of R-Type ACSSuT among Salmonella Typhimurium decreased significantly from 1996 (33.7%) to 2004 (23.3%), it is still the most common serotype of Salmonella Typhimurium (USCDC, 2004). Continued surveillance for clinical cases and asymptomatic infections, including a uniform method of genotyping isolates, is necessary to identify the extent to which DT104 might be contributing to the incidence of Typhimurium infection in the United States (Glynn et al, 1998). The ability to characterize and subtype S. Typhimurium DT104 isolates is necessary from an epidemiological perspective in order to trace infections in different animal populations and their relationship to human cases (Murphy et al, 2001). Genotyping is becoming an increasingly important epidemiologic tool that aids in identification of sources of infection during outbreak investigations, detection of sources of cross contamination, recognition of particular strains, and monitoring intervention strategies (Gebreyes, 2003). The current “gold standard” method (PFGE) for molecular typing of Salmonella and other foodborne pathogens is used to identify sources of outbreaks (Best et al, 2007). Recent work, however, suggests that another method of assessing outbreaks, the multiple-locus variable number tandem repeat (VNRT), adds a further level of discrimination to PFGE and can provide potential benefits to epidemiological studies by establishing genetic diversity and identifying possible source attribution of outbreaks (Best et al, 2007). Surveillance and typing are also needed to monitor new strains of even long established pathogens such as Typhimurium (Besser et al, 2000).

Danish Salmonella control efforts have been successful in achieving their objective in reducing human salmonellosis (Wegener et al, 2003). Denmark has an active Salmonella surveillance system, targeting points along the farm-to-fork continuum, whereby all major food animals and foods of animal origin are monitored for Salmonella (Hald et al,
Intensive surveillance for *Salmonella* in live animals, including nearly all commercial food-animal producers and slaughterhouses, and of food products is conducted during processing and distribution to wholesalers and retailers (Molbak et al, 1999). Additionally, it is mandatory that laboratories report human infections (Ethelberg et al, 2007). As a result, the annual incidence of *Salmonella* infections in Denmark has shown a downward trend from 96 cases/100,000 in 1997 to 33 cases/100,000 in 2005 (Ethelberg et al, 2007). Reductions in *Salmonella* incidence is largely attributed to control and intervention strategies targeted primarily at pig and poultry production (Ethelberg et al, 2007). Furthermore, Denmark has special regulations for MDR DT104 whereby food products containing MDR DT104 (typically pork, beef, or imported poultry) are not allowed to be sold and must be destroyed or heat treated. Additionally DT104-infected pig or cattle herds are also put under specific regulations (Ethelberg et al, 2007). Danish efforts illustrate that an integrated surveillance and control program can reduce the incidence of foodborne human salmonellosis (Wegener et al, 2003).

Though increasing centralization and industrialization of our food supply has enhanced the distribution of foodborne organisms (Hohmann, 2001), the decrease in prevalence of penta-resistant DT104 in the United States over the last decade (USCDC, 2004) suggests a change in either the epidemiology of the organism and/or growth in commercial food production, despite appropriate and improved control measures (i.e., judicial and prudent use of antimicrobials, change in sanitary conditions on the farm, improved slaughterhouse hygiene, reduction in transport/environmental stress to reduce shedding, decreased cross contamination, etc) in the farm-to-fork continuum.

The production of safe food, from farm to fork is a public health challenge, as there are major gaps in our understanding of the biology and epidemiology of foodborne pathogens. While it is difficult to accept the implausibility of a zero risk for foodborne illness, the food production industry along with federal oversight and legislation must continue to work to reduce the risks of microbial contamination and reduce foodborne illness (Sargeant et al, 2007b).

**Recommendations**

- **Funding to help fill gaps in knowledge**—Recommendations and decisions for modifying livestock production systems to satisfy the need for improving food safety must be based on scientific data that have been objectively collected. Technical report # 3 has identified gaps in our knowledge of the risks and impacts of CAFOs to human and animal health. These data gaps should be the focus of research funding from commodity groups as well as state and federal agencies charged with human and animal health.

- **Enhanced surveillance systems for imported food products**— Imported food products as well as domestically produced foods of animal origin should be included in enhanced, comprehensive surveillance systems. These systems should be based on objectively determined risk and diagnostic tools to improve early detection and response to prevent food safety problems and food-borne illnesses. Diagnostic tools should be sensitive, specific, and continuously evaluated to detect newly emerging variants of microbial agents of food origin.
• **Funding for surveillance systems and diagnostic tools**— Surveillance and early detection are key elements to optimize quality and safety of food and to minimize health impacts to people or animals. This fact is true regardless of the disease agent or the commodity. Scientific process control is a key component, and programs like HACCP have been very effective. Modifying the controllable sections of production may have a greater impact than testing of final products. However, product testing is also important to assess whether the agent, host, or environment has changed. Consequently, resources should be made available through competitive grants to encourage the development of practical but rigorous surveillance systems and rapid diagnostic tools targeted to enhance food safety and quality during production. Once new technologies and processes are identified or developed, resources must be available for their application. Application must also include resources for the training of inspectors and quality control staff of facilities.

• **Animal identification and data management**— Animal identification is an important part of an effective and efficient surveillance and response system. Animal ID must be coupled with an appropriate data management structure that would collect, manage, and use the information collected. Animal ID and management of such data should be encouraged at a national level.

• **Inclusion of externalities**— Because economics continue to be a major driver of livestock production systems, the costs and benefits of externalities incurred locally, regionally, nationally and internationally must be included in calculations. Considering costs and benefits to the producer alone is not adequate.

• **Assessment of livestock production vulnerabilities**— Livestock production systems must be assessed for vulnerabilities beyond the naturally occurring disease agents. The US production of food has been a model for the world, but there are a number of countries currently challenging us with better practices. Our food production systems are also one of our most vulnerable critical infrastructures. The US food production industry must be hardened against and prepared for possible domestic or foreign bioterrorism. Confidence in the safety of our food supply must be maintained and, in some cases, restored.

• **Consistent and accurate process-attribute labeling**— Labeling of animal-origin food products with process attributes (eg, free range, organic, natural, grass-fed, environmentally friendly) must be specifically defined based on detailed verifiable criteria to allow a reliable base for consumer education efforts and consumer decisions. Definitions will sometimes lose their original meaning (eg, grass fed cattle may be those in feedlots that receive hay), which can result in loss of consumer confidence in good products and our food production systems in general.
• **Aquaculture regulations**– Food products produced through aquaculture should be included in any discussion/research/regulation along with the five commodity groups traditionally considered (i.e., layers, broilers, dairy, beef, and swine).

• **Parallel preventive health measures**– As production systems increase the number of animals in the same spaces, preventive health care strategies must be developed in parallel in order to minimize the risks of disease. Consideration and use of the term “production diseases” must be carefully considered and based on scientific data.

• **Biologic and pharmaceutical assessment**– The use of specific biologics and pharmaceutical agents (vaccines, prophylactic medication, and therapy treatments) in food-producing animals is a complicated issue that requires a thorough scientific evaluation before recommendations can be derived on their ecological impacts. Scientific assessment of such ecological impacts requires comprehensive review of the various factors associated with the use of biologics and pharmaceutical agents. Scientific assessment, therefore, must be the basis of regulations.

• **Regulation of biologics and pharmaceuticals in exporting countries**– Approval to export products from food animals to the US requires reviews of the disease status and processing/inspection procedures of the country requesting approval to export. However, neither review nor regulation of the biologics or production methods used with the animals is required for approval prior to export to the US. Standard information on the approved use of biologics and pharmaceutical agents in exporting countries should be required prior to approval for export. Government agencies should maintain the responsibly and authority to inspect and certify animal products in order to maintain high standards and quality of foods of animal origin.
Summary

Food production around the world has changed dramatically over the course of human history. Had our species remained in the hunter-gatherer mode, as we were at the beginning of our collective past, we would have likely surpassed the carrying capacity of the earth many generations ago. Instead, agriculture developed and over millennia has undergone many evolutions, if not revolutions, to keep pace with the burgeoning population. Today, with over 6.3 billion people on earth, it is apparent that we need to continue to maximize efficiency in all aspects of food production and also persist in finding ways to protect human and animal health and wellbeing as well as our natural resources.

Protein remains an essential component of the human diet and much is supplied through animal agriculture. The five main animal production industries in the United States—eggs, poultry, dairy, beef, and swine—all contribute to the continuing demands for necessary protein in our daily diets. These American products have considerable value in the international marketplace, and animal agriculture contributes significantly to the national economy and the global advancement of the efficient use of animal protein. Over time, comparative advantages influenced the development of each of the industries in specific parts of the United States. Proximity to grain, natural forages, inexpensive labor, access to transportation, or suitable climate all predisposed the development of animal industries in certain areas. Then, the additional incentive of economies of scale and efficiency in protein conversion led to large concentrations of animals that we know today as CAFOs.

CAFOs differ significantly between animal commodities. Regardless of the animal species, all CAFOs present both opportunities that must be taken advantage of and challenges that must be met. The opportunities lie in supplying the amount of essential protein in the most efficient, cost-effective, and welfare-conscious manner possible. CAFOs, as business operations, are already engaged in these opportunities. Challenges are similar and daunting and include providing the amount of protein needed in a way that minimizes environmental damage, animal suffering and disease, and human health risks. Many of these challenges are met through regulatory standards and industry initiatives.

This report was written in an attempt to explain the reasons for the development of CAFOs, to provide background on each of the five commodities (referred to in the report as industries), and to address by selected examples some of the major human and animal disease issues associated with the egg, poultry, dairy, beef, and swine industries.
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