BURLEIGH DODDS SERIES IN AGRICULTURAL SCIENCE

Improving gut health in poultry

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Contents

Introduction

This collection summarises current research on the composition and function of the gastrointestinal tract in poultry, the factors that affect its function, and nutritional strategies to optimise poultry nutrition, health and environmental impact. Part 1 begins by summarising advances in sequencing and omics technologies to understand gut function. It then reviews our current understanding of the gut microbiota, the development of the gut microbiome over the life of the bird, and gut function in nutrient processing and immune response.

The second part of the book reviews what we know about factors affecting gut function and health. Chapters cover gastrointestinal diseases, the interaction between pathogens and the gut as well the impact of antibiotics. The final group of chapters discuss current research on the effectiveness of feed additives in optimising gut health, including probiotics, prebiotics, synbiotics, antimicrobials, essential oils and other botanicals as well as cereal grains.

Part 1 Understanding the gastrointestinal tract

Chapter 1 provides an overview of the development of the commercial poultry industry, and the impact of changes in production practices on poultry gut health. Beginning with an introduction to the origins of the broiler chicken, the chapter discusses developments in nutrition, genetic selection, poultry housing and veterinary care. All of these areas have created challenges in optimizing gut health which are explored in the rest of the book.

Chapter 2 summarizes the range of molecular tools used to analyze the gut microbiome in poultry such as T-RFLP, DGGE, and TGGE and clone library sequencing using the Sanger method. The chapter goes on to survey the development of next-generation sequencing techniques such as Roche 454, Illumina, and Ion Torrent. The chapter also discusses third-generation sequencing techniques including Pacbio SMRT sequencing and Oxford nanopore. Finally, the chapter introduces other 'omics' approaches such as metagenomics, metatranscriptomics and metaproteomics which are help advance our understanding of microbiome functions in poultry.

Building on Chapter 2, Chapter 3 summarizes the use of different 'omics' technologies (e.g. genomics, transcriptomics, proteomics, metabolomics) used to identify the response of chicken intestinal cells to various effectors. The chapter begins by introducing the functions, physiology and microbiota of the gastrointestinal tract in chickens. It then explores what omics technologies can tell researchers about gut function, using the example of the chicken intestine.

The chapter concludes with a case study on the proteomic analysis of the mucosal layer of the chicken gut.

Poultry gut microbiota include bacteria, archaea, protozoa, fungi and viruses. Their role in the gastrointestinal tract has a profound effect on the health and productivity of poultry. Chapter 4 outlines what we know about the establishment and development of the gut microbiota, some of the mechanisms by which the microbiota can affect poultry, and the ways that the microbiota can be manipulated to enhance poultry health and productivity. The chapter reviews the manipulation of microbiota for chicken health and productivity, covering the use of microbes to manipulate gut microbiota and also the use of feed additives and antibiotics. The chapter concludes with an overview of future trends in research.

Chapter 5 discusses the *in ovo* development of the chicken gut microbiome and its impact on later gut function. The gut of hatchlings contains both beneficial as well as pathogenic microorganisms derived from external and maternal sources. Research has focused on ways to optimize the enteric development of chicks and to assist in the establishment of intestinal bacteria populations that promote health and provide protection against invading pathogens. The chapter examines competitive exclusion cultures, specifically probiotics, prebiotics, synbiotics, and nutrients. The chapter looks at the prospects for the commercial *in ovo* use of these biologics and looks ahead to future research trends in this area.

In poultry production a tradeoff has traditionally been made between growth and efficiency, on the one hand, and immune potential and disease resistance, on the other. The emerging field of immunometabolism is an opportunity to eliminate this tradeoff and achieve both production efficiency and immune robustness. Chapter 6 provides an overview of metabolism and immunometabolism, including the most important links between metabolic pathways and immune pathways. The chapter discusses the absorption and metabolism of carbohydrates, amino acids and lipids in the poultry gut.

Chapter 6 then discusses metabolism and immune responses within the gut tissue, influenced by the feed and microbiota located in the lumen. It reviews the components of feed that lead to inflammation and how to mitigate this effect. The chapter concludes by looking at examples of how feeding the immune system with pre- and probiotics can both enhance growth and immune response in poultry.

Chapter 7 examines intestinal immunity and microbiota interactions with the immune system. The chapter considers the role of gut microbiota as an epigenetic regulator of gut function as well as the causes of dysregulation of gut functionality. As the chapter points out, the host immune response is important to maintaining microbial balance but can also be the cause of a disrupted microbiota (dysbiosis) which can contribute to disease. The chapter discusses microbiota interactions with the immune system, including microbiota-based metabolites and immunity as well as colonization resistance. It then focuses on dysregulation of gut functionality, looking at the causes of chronic, low grade inflammation, sterile and metabolic inflammation as well as pathobiont expansion, with an emphasis on nutritional strategies to avoid these conditions.

Part 2 Factors that impact the gastrointestinal tract and different types of birds

A comprehensive understanding of how various factors shape the intestinal microbiota in poultry can help develop new dietary and managerial interventions to enhance bird growth, maximize feed utilization efficiency, and lower enteric diseases caused by pathogens. Chapter 8 reviews the current understanding of how different factors (except diet and growth promoters that are covered in other chapters of this book) can affect the intestinal microbiota. These factors include genetics and breeds, hatchery conditions and environment, bedding and litter, climate and geographic regions, gender and diseases. This understanding provides the foundation for developing the nutritional and other management practices needed to optimize gut function.

As antibiotic resistance continues to evolve, finding alternatives to these chemical compounds that increases poultry performance has become imperative. Some of the most promising alternatives that been investigated include: bacteriocins, bacteriophage therapy, plant-derived phytochemicals, competitive exclusion of pathogens, and predatory bacteria. Chapter 9 places the use of antibiotics in poultry production in its historical context to understand the benefits that antibiotics have conferred on animal production to date. The chapter focuses in particular on the potential use of bacteriocins and plant-derived phytochemicals to replace the growth promoting and health benefits of the sub-therapeutic levels of antibiotics.

Gastrointestinal health plays a critical role in ensuring the overall health and productivity of livestock, including poultry. Antimicrobial growth promoters (AGP) have been used to maintain and promote gastrointestinal health. The move to phase out AGP in poultry production threatens to increase the incidence of enteric diseases such as necrotic enteritis. Chapter 10 reviews what we know about important enteric diseases and disorders, highlighting their etiology followed by possible nutritional interventions. These include feed additives such as plant-derived extracts, prebiotics, probiotics and organic acids, as possible alternatives to AGPs for disease control.

Although the majority of the microbiota in the poultry gut are commensal bacteria, pathogens are also present. Commensal and pathogenic microbes interact with each other, either positively or negatively, profoundly affecting host nutrition and incidence of infection. A better understanding of the gut pathogen-microbiota interaction is essential to address the current challenges in poultry production. As Chapter 11 highlights, recent studies using metagenomics have provided new insights into the interactions between the gut pathogens and commensal microbes in poultry. Chapter 11 reviews current understanding of the interaction between gut microbiota and pathogens in poultry. The intestinal pathogens discussed in this chapter include *Escherichia, Salmonella, Clostridium, Campylobacter, Eimeria* and viruses. In each case, the chapter summarizes what we know about these pathogens and their associated diseases, interactions with gut microbiota and what this means for health and nutrition.

Chapter 12 reviews current knowledge about the function and microbial ecology of the layer hen gastrointestinal tract. As the chapter points out, with the introduction of next generation sequencing, a more comprehensive identification of the laying hen gastrointestinal tract microbial population has emerged. This research has shown there are several factors that can influence the composition and function of the layer hen gastrointestinal tract, including age of the bird, diet, and type of feed amendment. Studies have identified the microbial communities in each compartment of the layer hen gastrointestinal tract and their impact on the host. Some compartments such as the ceca harbor a highly complex microbial population of fermentative microorganisms that produce short chain fatty acids. The ceca can also be colonized by foodborne *Salmonella* and some serovars such as *S.* Enteritidis can become invasive, infecting the reproductive tissues. The chapter shows how a variety of feed additives have been used to limit *Salmonella* colonization in laying hens and improve laying hen performance.

Part 3 Feed additives and gut health modulation

Foodborne pathogenic bacteria are all too often found as commensal or transient organisms in the gastrointestinal tract of poultry. Many of these organisms do not reveal themselves through illness in the bird, although some do. This means it is important find ways to apply treatment to all members of a flock, rather than simply treating ‘sick’ birds. After summarizing what we know about the gastrointestinal microbiota of poultry, Chapter 13 reviews alternatives to the use of antibiotics, discussing the use and effectiveness of organic acids, bacteriophages, sodium chlorate, and pro- and prebiotics.

Building on the overview in Chapter 13, the next group of chapters look at key feed additives, starting with Chapter 14 on probiotics. The chapter reviews current research on the safety and efficacy of individual monocultures for prophylactic and/or therapeutic use against *Salmonella* infections in poultry, under both laboratory and field conditions. There is a particular focus on the role of probiotics in preventing inflammation. The chapter discusses key issues and advances in the development of novel, cost-effective, feed-stable direct-fed microbials with potential for widespread application in poultry production. The chapter concludes with a review of the use of direct-fed microbials in commercial poultry diets.

As Chapter 15 highlights, prebiotics have been established as a series of feed compounds that serve as specific substrates for gastrointestinal tract (GIT) bacteria. Such compounds support those GIT bacteria that benefit the host and, in addition, can be antagonistic to foodborne pathogens and prevent their colonization in the GIT. As the chapter shows, prebiotics have been used primarily to prevent establishment of foodborne pathogens but have also received attention regarding their impact on overall GIT health. The chapter reviews the impact of prebiotics on bird health, GIT function, and prevention of foodborne pathogen GIT colonization. There is a particular focus on the impact of prebiotics on avian upper GIT health and optimizing function of the avian caecum.

As previous chapters have highlighted, the drive to ban the use of antibiotics in animal feed due to the current concern over the spread of antibiotic resistance genes makes the development of alternative prophylactics imperative. Chapter 16 reviews the combination of probiotics and prebiotics in synbiotics. It focusses particularly on the use of short chain fatty acids (SCFA) (especially butyrate). The chapter reviews the beneficial effects of SFCA on digestive physiology, blood flow and muscular activity, enterocyte proliferation and mucin production

As Chapter 17 points out, short chain organic acids have been employed as feed additives for a number of years. They have been primarily used for their antimicrobial properties, particularly in limiting *Salmonella* in feed and in the GIT. Short chain organic acids are also produced by indigenous gastrointestinal bacteria during fermentation. These are primarily generated in the cecum which is the site where most GIT microbial fermentation occurs. The chapter reviews current research on poultry GIT responses to short chain organic acids generated by GIT fermentative microorganisms, and how this can be optimized through feed interventions.

Chapter 18 discusses the role of essential oils and botanicals in improving gut function in poultry. The chapter focusses on four major functions of phytobiotics that could potentially contribute to gut health. These relate to digestive conditioning, antimicrobial properties, immunomodulation and gut microbiota modulation The chapter discusses the impact of these functions on performance as well as carcass and egg quality. Finally, the chapter looks ahead to future research trends in this area.

As Chapter 19 points out, cereal grains constitute the greatest proportion of most poultry diets. As dietary components, cereal grains provide most of the dietary energy and help to support the development of the structural and functional integrity of the digestive tract. However, many cereal grains contain one or more deleterious factors which may negatively affect the structural and functional development of the gut. Some of the key factors are carbohydrate in nature but there are non-carbohydrate fractions which function mainly as anti-nutrients. This chapter reviews what we know about the key components of cereal grains, particularly the components that may influence the development of intestinal structure and function. The chapter examines the role of cereal grain components on poultry gut function and the possible mechanisms by which these interactions take place and can be optimized.

Part 1

Understanding the gastrointestinal tract

Chapter 1

Commercial poultry production and gut function: a historical perspective

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1 Introduction

In 2016, it was estimated that the United States poultry industry provided 1 682 269 jobs with a total economic impact of $441.15 billion (NCC, 2016). The US industry also provided $68 billion in wages and $34 billion in government revenue (NCC, 2016). The broiler industry alone was estimated to provide 1 195 745 jobs with $68 billion in wages and contributing $313.12 billion in economic output (NCC, 2016). As of 2017, the US industry produced $42.7 billion in sales from the production of broilers, eggs, and turkeys (USDA, 2018). Broilers alone contributed 71% of annual sales amassing to $30.2 billion in 2017 (USDA, 2018), and in that year 8.91 billion broilers were produced. Thus, the US poultry industry contributes substantially to the economic welfare of this country and will continue to do so as it expands its markets, both domestically and internationally.

Since the beginnings of the modern industry in the early 1900s, the commercial industry has continued to advance and expand substantially. From

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2016 to 2017, the industry grew 10% in sales (USDA, 2018), and this growth will continue because the demand for poultry and poultry products in the United States and around the world continues to rise. In 1960, the total amount of poultry consumed in the United States (chickens and turkeys) was 34.2 pounds (15.5 kg) per capita (NCC, 2019a). In 2018, the per capita consumption of total poultry was 110.0 pounds (49.9 kg), and it is forecasted to be 110.1 pounds (50.21 kg) in 2020 (NCC, 2019a).

The poultry industry will need to continue to grow to meet the demand related to the projected increases in our human population. In 2018, the US population was 326 766 748, but by 2050 it is projected to be 390 million (UN, 2017). Furthermore, the world's population will be 9.6 billion by 2050 (UN, 2017). To meet the rising demand for poultry products, both domestic and internationally, integrators will have to continue to develop and improve sustainable practices that will allow for more and more efficient production. Consumer demands for alternative production practices, however, including the demand for the removal of antibiotic from poultry feeds, have led to a shift in industry response. Some integrators have removed antibiotics from their feeds or they have removed antibiotics completely from the rearing process. Unfortunately, that removal has presented a major challenge to the industry due to increased disease levels, increased mortality, and losses in growth performance related to the resulting changes and imbalances in gut microbiota or 'dysbacteriosis' (Huyghebaert et al., 2011).

Due to the vast impact that the commercial poultry industry has on our human society, as well as its impacts on the economy of the United States, it is important to grasp the beginnings, the advancements, and the issues the industry has had to face in order to become the vertically integrated power house that it is today. The most significant of those advancements revolve around the incorporation of scientific advances made in nutrition, genetics, housing, and veterinary care. Therefore, it is the objective of the current chapter to provide a brief description of the history and development of the commercial poultry industry, and the impact of changes in production practices that are having impacts on poultry gut health.

2 Origins of the broiler chicken

In order to understand the current state of the poultry industry, it is important to understand the history of chicken domestication. The modern chicken, *Gallus gallus domestica*, is believed to have originated from the red jungle fowl of Asia (Sawyer, 1971). The red jungle fowl is one of four species within the jungle fowl genus, *Gallus*. That genus encompasses *Gallus gallus* (red jungle fowl), *Gallus varius* (green jungle fowl), *Gallus sonneratii* (grey jungle fowl), and *Gallus lafayetii* (ceylon jungle fowl) (Al-Nasser et al., 2007). *Gallus gallus*, the red jungle fowl, can still be found in regions of India, China, Java, Malaysia, Indonesia, and the Philippines (Al-Nasser et al., 2007). With the development of human societies, domestication of the red jungle fowl is thought to have occurred primarily due to its use for cultural and entertainment purposes (Crawford, 1990b). The earliest domestication is thought to have started around 5400 BC; however, it is also believed that most of the modern breeds were domesticated and developed primarily between 2500 and 2100 BC in the Harappan culture of the Indus Valley (Crawford, 1990a,b). Today's *Gallus gallus domesticus* is believed to have its origins about 3000 years ago (Crawford, 1990a).

Even before the domestication of the red jungle fowl, poultry had been utilized for both meat and egg production. Although it was not an uncommon occurrence to eat poultry in historic times, poultry was not the primary source of protein for humans. Chickens were used mainly for cockfighting until the mid-1800s when cockfighting was deemed illegal. After that occurred, chickens were sought after for exhibition purposes (Moreng and Avens, 1985; Crawford, 1990b). Even so, the consumption of *Gallus gallus* by humans was considered a luxury, and it generally occurred only at special events.

Domesticated chickens were brought to North America in 1607 by the initial settlers of Jamestown (Sawyer, 1971). The early breeds of domestic fowl were so numerous in the United States that an 'American Standard of Excellence' was created in 1873 to standardize the characteristics and requirements of the various so-called pure breeds of poultry in America (Sawyer, 1971). By the nineteenth century, chickens were an essential part of American agriculture, and by the onset of the twentieth century, chickens were commonly found on almost all farms. During the early twentieth century, chickens were mainly kept for their ability to produce eggs and the birds were used as a source of protein only on rare occasions (Sawyer, 1971).

It was not until 1923 that chickens were raised solely for meat consumption. In that year, Cecile Steele of Ocean View, Delaware, was mistakenly delivered 500 chicks instead of the 50 she had ordered (Williams, 1998). She decided to raise the extra birds as small broilers, and subsequently sold 387 chickens for 62 cents per pound to local families (Sawyer, 1971). Shortly thereafter, other surrounding families, hearing of her good fortune, sought to also profit from raising broiler chickens; and by 1925, Delaware was producing approximately 50 000 broiler chickens per year (Sawyer, 1971). At about the same time, a disease that was referred to as 'range paralysis' hit the southern portion of Delaware and affected Leghorns of 12 weeks of age or older that were being used for egg production. This helped make younger birds of heavier breeds as the best alternative for poultry meat production, which increased the growth of the broiler industry (Sawyer, 1971). Although Cecile Steele has been noted by some as the woman who started the poultry meat industry, the first commercial broiler operation was actually established in 1880 in Hammonton, New Jersey

(Strausberg, 1995). Soon thereafter, the raising of chickens for meat production became common place in the northern and middle eastern parts of the United States and southern farmers soon began following the lead of their northern neighbors in producing chickens for meat consumption.

During the beginning of the twentieth century, cotton was the main cash crop for the southeastern United States. However, as times changed and government agencies became involved, cash incentives were provided for farmers who would stop producing cotton through the Agricultural Adjustment Administration (1933) and later through the 1936 Soil Conservation and Domestic Allotment Act (Gisolfi, 2006). This drastically changed the agricultural landscape of the south and spurred major changes in agricultural production. Georgia was especially affected by the diminishing harvest of cotton, and many of the cotton growers who remained no longer had a market in which to sell their products. This led individuals such as Jesse Jewell to enter the poultry raising industry (Sawyer, 1971; Gisolfi, 2006). Jesse Jewell and many others began selling chicks and feed on credit to farmers who eventually became known as poultry growers. When the birds reached their market weights, generally at about 12 to 16 weeks of age, they were hauled to a processing plant, sold, and the creditors and the growers were paid off (Gisolfi, 2006). Later, this method would eventually be coined vertical integration (Gisolfi, 2006). The decrease in cotton production, and the shift toward broiler production in Georgia would increase that state's poultry production to about 500 000 broilers by 1935 (Gisolfi, 2006). Although Georgia played an important role in the beginnings of the US broiler industry, a number of other southern states also made major contributions to the onset of the broiler industry.

Arkansas has not been widely accepted as the first state to raise poultry for meat, but it is well documented that the Arkansas broiler industry also had its beginning very early in the twentieth century. In fact, Arkansas' beginning was very similar to that of the Delmarva area. Arkansas found its start in 1916 when J. J. Glover and his daughter Edith raised 20 White Wyandottes purchased by mail, sold them for $1 a bird, and coined them as 'Arkansas Broilers' (Strausburg, 1995). However, poultry was not widely produced during this time as apples were the main commodity produced in northwest Arkansas in the 1920s, with there being over four and a half million apple trees in the state at that time (Strausberg, 1995). Around the same time, the northwestern Arkansas apple industry experienced drought and blight brought on by coddling moths, forcing the area to pursue other alternative commodities (Strausberg, 1995). One of those commodities was poultry. In 1921, the first Arkansas poultry hatchery was built by Jeff D. Brown, and in 1922, J. J. Glover raised 324 broilers with the promise of 55 cents of profit per bird (Strausberg, 1995). Although northwest Arkansas did have existing poultry farms, it was not until 1927, when a severe freeze ravished the apple industry, that poultry production became a highly sought-after activity (Strausberg, 1995). In the same year, Lloyd Peterson of Decatur, Arkansas, raised 500 Rhode Island Red chickens and made a $107 profit (Strausberg, 1995). As a result, Jeff Brown's hatchery group began lending credit to farmers in the form of chicks, feed, or both to entice others to invest in commercial broiler production (Strausberg, 1995). With assistance from county Extension agents, and scientists at the University of Arkansas and the Arkansas Experiment Station, Arkansas would eventually become one of the major leaders in the poultry industry, producing 6.9 billion pounds of broiler meat in 2017 (The Poultry Federation, 2017). Furthermore, a number of poultry companies such as George's Inc., Simmons Foods Inc., Cobb-Vantress Inc., Tyson Foods Inc., OK Foods Inc., and Twin River Foods, Inc. all originated in the state of Arkansas (The Poultry Federation, 2017).

As the broiler industry expanded after its humble beginnings, it did so with the support of the assistance provided by the US government and universities. Basic support for the modern poultry industry was really initiated during the late 1800s and early 1900s with the passage by the US government of the federal Hatch Act. That Act established the Land Grant University system for each state, and the Smith Lever Act which followed provided recurring funding for Agricultural Experiment Stations and extension programs in each state. A large number of the Land Grant universities developed poultry programs during the above time frame and hired professionals for doing teaching, research, and extension programming for poultry producers. At one time, 44 university-based Poultry Science programs were in existence in North America, but during the 1970s through to the 1990s, as poultry operations became larger and the industry became more and more concentrated in certain geographical areas of the country, many of those departments were either closed or merged with Animal Science Departments. So, by the early part of the twentieth century, only six Poultry Science Departments continued to exist, and all of those units are currently located in the Southeastern United States. A few other universities, however, have continued some poultry research, extension, and teaching as part of their integrated Animal Science Departments, and, most Veterinary Colleges also included poultry-related teaching, research, and extension activities. Contributions of these university-based programs were extensive, and probably the best example of how extensive those university-based poultry programs were can be seen via the history that Havenstein (2012) developed related to the poultry programs that were carried on at North Carolina State University from the year 1881 through 2010. All of the current and former university-based programs around the nation made similar contributions to the growth of the industry.

Of course, the US Department of Agriculture for many years has also led extensive research and development programs related to poultry. Numerous state- and/or regional university-sponsored extension conferences on nutrition, poultry management, poultry waste, and by-product management, and so forth, have also contributed greatly to the industry's growth and development; as have many annual state and national industry conventions and technical programs such as Fact Finding, the Southeastern Egg and Poultry Association, the Pacific Egg and Poultry Association, the National Poultry Breeder's Roundtables, and through meetings sponsored by a number of state-based industry associations. All of these university-, federal-, and industry-based programs have provided and are continuing to provide valuable inputs to the development of today's industry.

Even though the US broiler industry was started in the early 1900s, broiler production did not become a fully developed agricultural industry with major economic impact until the onset of the Second World War (Williams, 1998). Since then, the poultry industry has steadily grown and made drastic changes in its breeding, its production management (i.e. in hatchery operations; grow-out housing; ventilation and light control systems; feed milling systems; transportation systems; and litter source and management systems, etc.), its nutrition, and its animal health veterinary care practices (Hunton, 1990). Even with all of the developments that the industry has significantly benefitted from, it still faces many challenges for the future.

3 Vertical integration

Poultry production began as family backyard operations, and subsequently grew into a multibillion-dollar industry with approximately 35 major poultry businesses that control its operations from start to finish (NCC, 2018b). The rapid and successful development of the industry can largely be attributed to its willingness to incorporate scientific advancements, and to vertically integrate the various aspects of its overall production and marketing processes. The term 'vertical integration' was coined by Jesse Jewell of Gainesville, Georgia who in the mid-1930s was a visionary who had the foresight to begin furnishing farmers with chicks and feed on credit until the birds were heavy enough to sell back and settle the debt (Gisolfi, 2006). To begin this concept, Jewell contacted feed companies such as Ralston-Purina and Quaker Oats and local banks to receive credit for the feed and chicks (Gisolfi, 2006). He received credit easily and in turn, extended credit to farmers who were given baby chicks and feed in advance of their growouts. Balances were settled 12 to 16 weeks later when their broilers reached market weight, or when another processing merchant or distributor purchased them (Gisolfi, 2006). In the mid-1930s, farmers were not required to sell the broilers back to the dealer who had provided them as baby chicks, because farmers were not contractually bound to a specific processor.

By 1940, poultry businesses purchased and owned hatcheries, distribution facilities, and processing plants (Gisolfi, 2006). These early integrators limited their reliance on outside sources to maximize profits. They subsequently began to create contracts in the mid-1950s with individual farmers or growers and eventually implemented a contract payment system that was based on body weight and a 'feed-conversion plan' (Gisolfi, 2006). The contracts defined expectations for the farmers who supplied their own growing facilities, equipment, labor, heat, and litter; and, it indicated that they were to sell the grown broilers solely to the supplier they were in contract with. The 'feed-conversion plan' represented a method to determine the income the farmers would receive based on the pounds of chicken the merchants received from the pounds of feed the farmers used to raise the birds (Gisolfi, 2006). The contracts and the 'feed-conversion plan' may have taken away the independence of the farmer involved; however, it did establish uniform practices for contractual farming as a part of this vertically integrated business.

The business style of merchants such as Jesse Jewell and many others revolutionized the industry of today where vertical integration is still heavily relied upon. It is also apparent that the advancements made, especially in genetics (Havenstein et al., 2007), nutrition, housing, veterinary care, transportation, processing, product development, and marketing, have jointly allowed the broiler industry to become a much more efficient business, and one that has expanded to become the leading supplier of meat for human consumption worldwide. As such, the industry is an integral part of the US economy and the United States possesses the largest broiler chicken and turkey industries in the world. The US public consumes more chicken per capita now than any other country in the world, having consumed more than 93.5 pounds per capita in 2018 (NCC, 2019b). The wholesale value of industry shipments and consumer retail expenditures for chicken was 65 and 95 billion dollars, respectively, in 2018 (NCC, 2019b). Since the broiler industry is such an important aspect of the US economy, and of our citizens' diets and lifestyles, it is evident that the industry must continue to be vigilant in order to meet consumer demands in the future.

4 Nutrition

As the poultry industry on the eastern shore began to flourish in the Delmarva area in 1925, and then in the southern United States about 10 years later, so did the development of poultry feed systems and diets. Although Delmarva alone had ten major feed manufacturers present during the onset of the broiler industry, poultry feeds were primarily supplied by local feed mills, who held monopoly over the market (Sawyer, 1971). Large feed milling companies were more competitive, however, because of their greater resources which allowed them to develop substantial research on improving broiler diets. In 1925, the first complete broiler feed was developed by The Beacon Milling Company

(Sawyer, 1971). And as early as 1929, that company developed and introduced a coccidiosis control mash that drastically changed the developing field of poultry nutrition (Sawyer, 1971).

At the conclusion of the Second World War, the first high-energy broiler diet was introduced into the broiler industry (Sawyer, 1971). However, that diet was inadequate in its energy-protein ratio, and because of that the concept of 'calorie-protein ratio' was first introduced in 1955 (Sawyer, 1971). In an attempt to describe the energy-protein content in feed, in 1940, scientists at the Texas Agricultural Experiment Station investigated the metabolizable energy (ME) content in poultry feedstuffs (Fraps et al., 1940). Although the same group proposed a system for determining productive energy (PE), PE was shortly replaced with ME determination (Elwinger et al., 2016). In the second half of the twentieth century, research determining ME was conducted to evaluate apparent ME when corrected for zero nitrogen retention (AMEn) (Elwinger et al., 2016). Not long after, Ian Sibbald published an alternative method for determining ME that became known as the true metabolizable energy (TME) (Sibbald, 1976). Scientific advancements in the understanding of energy composition from poultry diets helped create our modern poultry feeding programs. However, that was only one of the components that contributed over the years to the development of improved nutritional practices for the poultry industry.

The primary components of poultry diets include water, carbohydrates, fats, proteins, minerals, and vitamins. The coining of the term 'protein' was first described in 1834, so throughout the second half of the nineteenth century biochemists and nutritionists began determining and elucidating the basic substructures of various proteins, the amino acids. At the onset of the first World Poultry Congress held in 1921 in The Hague, the Netherlands, there were no technical papers related to the evaluation of protein content in poultry diets. However, during the second Congress (Barcelona, Spain, 1924), there was one paper that described the protein structure of 30 different feedstuffs, as well as the digestibility coefficients of those feedstuffs. During the third Congress (Ottawa, Canada, 1927), a joint discussion of the importance of the theoretical and experimental foundation of protein requirements was held (Elwinger et al., 2016). Although the National Research Council's (NRC) *Nutrient Requirements of Poultry* was first published in 1944 (NRC, 1944), it was not until 1954 that the NRC elaborated on the actual requirements for crude protein, essential amino acids, and glycine for chicks, poults, and laying hens (NRC, 1954). Within the same 1954 publication, the NRC also described the arginine, lysine, methionine, cysteine, tryptophan, and glycine contents of various poultry feedstuffs (NRC, 1954).

After the 1950s, there were numerous elaborate attempts to better describe the requirements for protein and essential amino acid requirements of different poultry species, breeds, ages, and sex (Elwinger et al., 2016). The rapid expansion of knowledge through research led the NRC to compile the results from around 440 experiments and to publish those compilations in the NRC guidelines in 1994 (NRC, 1994). More recently, a meta-analysis was published by Sauvant et al. (2008) describing the various requirements affected by the previously mentioned fixed factors. However, there continues to be a need for updated requirements, so in 2016, the NRC announced that there would be a renewed effort to update the NRC *Nutrient Requirements of Poultry* (Elwinger et al., 2016) in the near future.

One of the greatest advances in poultry nutrition was initiated through the discovery of the animal protein factor (APF), B_{12} from the liver in 1948 (Rickes et al., 1948; Smith et al., 1952). Long before that, vitamins were known to be necessary components of poultry diets. As early as 1913, vitamin A (retinol) was detected by McCollum (Semba, 2012) and by the 1940s, all of today's vitamins had been elucidated with the last being vitamin B_{12} (Elwinger et al., 2016). Before the identification of vitamins was made, the poultry industry fed various microbial, plant, and animal origin ingredients in attempts to benefit production. After the identification of all of the various vitamins, it was realized that the supplementation of poultry diets with grain germs and maize germ oil, dried beet pulp, yeast, fish oil, and dried fish soluble were due to the presence of ß-carotene, vitamin E, vitamins of B-complex except B_{12}; vitamin D_2 after UV exposure; vitamins A, D_3, B_{12}; and vitamins of the B-complex, respectively (Elwinger et al., 2016).

In addition to the discovery of vitamins, improved knowledge of minerals and other feed additives and their requirements has also increased the success of the poultry industry. Minerals are required by all animal species for the formation and replacement of skeletal structure. Minerals also contribute to poultry health by being activators of enzymes and hormones, and through the maintenance of osmotic and acid-base homeostasis (Elwinger et al., 2016). For laying hens specifically, calcium (Ca) and phosphorus (P) and carbonate ions are required for metabolism to promote eggshell formation (Elwinger et al., 2016). Previously, it was believed that 1% Ca and 0.5% of available P would meet the requirements of growing chicks; however, this was costly and led to increased excreted P from poultry (Elwinger et al., 2016). The elucidation of the available phytase activity in cereal grains was determined in the early 1940s and promoted the decreased use of inorganic phosphates in poultry diets. The available phosphorus from wheat, triticale, and barley was high (50–70%), while the available P from corn, leguminous grains, soya meal, and rapeseed meal was less than 25% (Hoshi and Yoshida, 1977; Sauveur, 1983). Another advancement in meeting the optimal P level in poultry diets was the development of exogenous microbial phytases in the 1970s by Nelson et al. (1971). After the first phytase feed enzyme became commercially available in the Netherlands (Simons et al., 1990), the use of phytase became widespread and led to the innovative discovery that bone mineralization should be utilized to adequately determine and reduce the supplementation of C and P in poultry diets (Letourneau-Montminy et al., 2010). With phytase becoming a valuable resource to properly meet P requirements in poultry diets, other feed additives have been developed to meet requirement demands.

Although exogenous enzymes have been utilized in poultry diets as early as 1925 (Clickner and Follwell, 1925), their widespread distribution was not available until the 1980s (Elwinger et al., 2016). Many of the enzymes developed in the 1980s were created to degrade the non-soluble polysaccharides (NSP) that are present in various feedstuffs, thereby allowing for better nutrient absorption. Exogenous enzymes such as β-glucanase, xylanase, and protease have been effective in improving the nutritive value of barley (Hesselman and Aman, 1986), wheat and rye (Petterson and Aman, 1988), and protein sources, respectively. Currently, additional exogenous enzymes are being developed to further enhance nutrient absorption and reduce the overuse of feedstuffs in poultry diets, thus enabling poultry nutritionists to make considerable advancements in feed formulation.

Improvements in feed formulation were substantial from 1929 to 1969 and contributed to increased average bird weight from 2.82 pounds (1.28 kg) to 3.81 pounds (1.73 kg) (Sawyer, 1971). To evaluate the relative contribution of genetics and nutrition over time on the performance of commercial broilers, a study conducted by Havenstein et al. (2003) looked at changes in growth, livability, and feed conversion of 1957 and 2001 broilers when they were fed diets that were typical of diets used in those 2 years. The data showed that the average body weight of a Ross 308 fed a diet from 1957 reached a body weight of 2.126 g compared to 2.672 g when the same strain was fed the typical 2001 diet (Havenstein et al., 2003). Feed formulation and the ingredients utilized have continued to advance and improve the production and profitability of broilers, but the primary change in the growth performance of broilers has been brought about by the application of quantitative genetics by commercial poultry breeding companies. Genetic improvement has also been shown to be a major player in changes in the performance of turkeys (Havenstein et al., 2007) and commercial egg production stocks (Anderson et al., 2013).

5 Genetic selection

Although nutrition is an important factor that has led to the increase of broiler growth and size, genetic improvements have also played a major role in the change in development and growth of broilers. Improved nutrition was shown to have accounted for 10–15% of the change seen in broiler performance over the 46-year time span from 1957 to 2003, and genetics has contributed the rest

(Havenstein et al., 2003). During the twentieth and now well into the twenty-first century, the broiler and turkey industries have constantly demanded faster and faster growth and more and more efficient broilers and turkeys. Poultry breeders have responded by selecting each generation for improved growth rate and better feed efficiency. As a result, the days to market have continued to decrease, and the amount of feed required per unit of weight has also decreased dramatically. This decrease in efficiency has partially been brought about by shorter and shorter growing times being required to reach heavier and heavier market weights. The industry has also recognized that overhead costs per unit of meat processed also decline dramatically as heavier birds are processed. Therefore, the marketing of broilers has also changed from the sale of whole birds to the sale of further processed and cut-up products. Of course, in turn, the development of further processing has also spurred tremendous growth development in fast food restaurant chains, a number of which specialize in chicken products.

Previous to the concept of raising chickens solely for meat production, chickens were predominantly kept for egg production. Over the last 70–80 years, the breeders of egg production stocks have developed both white and brown strains that are smaller and more feed efficient. Those strains produce far more eggs, with better shell quality, with a specific average egg weight, and with better general livability over a given period of time, than did their ancestors. Egg production stocks have shown dramatic changes in performance (Anderson et al., 2013). Breeding for egg production has gone almost in the opposite direction (i.e. down in body weight and up in egg number and egg quality) from broiler and turkey breeding, but all three industries have been dramatically improved by the breeding process, thereby contributing greatly to the overall poultry industry's success.

Egg laying and broiler production are diametrically opposed, thus a breed designed solely for meat production would need to become a reality (Roberson et al., 1993). By the onset of the Second War World, there were numerous breeds of poultry that were used primarily for meat production; however, there was not a breed with the desired characteristics of a broad breast, such as the broad breasted turkey possessed (Gordy, 1974). The Chicken-of-Tomorrow Contest was first held in 1946 to address the need for a larger bird for poultry meat production, and in 1948 the first national contest was held at the University of Delaware (Gordy, 1974). In 1974, the winning bird, a White Cross, reached a weight of 5.7 pounds (2.59 kg) at approximately 7 weeks and 5 days, whereas the winning bird back in 1949, a New Hampshire-Rock Red Cross, required 13 weeks and 2 days to achieve the same weight (Gordy, 1974). One major advancement in genetics following the Chicken-of-Tomorrow Contest was the innovative development of a cross of a White Plymouth Rock male with a Cornish Gamebird female, that cross produced a broader breasted bird with more potential for breast meat development (Skinner, 1974). The Cornish Game breed originated in England, where it had been developed from Asiatic fighting stock that had traditionally been used for cockfighting, whereas the White Plymouth Rock had its origin in the New England area of North America (Crawford, 1990b). This innovative cross eventually became the primary foundation stock for most, if not all, of the male lines eventually used in modern broiler production. The Vantress organization was one of the major developers of such a male line, and eventually Vantress joined forces with the Cobb Breeding Company to form the current Cobb-Vantress Breeding organization. Several other breeding companies were also deeply involved in utilizing the descendants of the game bird cross as foundation stocks for their broiler male lines, including Ross, Hubbard, Cobb, Arbor Acres, Pilch, Ledbreast, and several others.

In the early 1950s, the description and application of quantitative genetics (initially led by Dr. Jay Lush and his students at Iowa State University, and subsequently followed by many others at a number of US Land Grant Universities) spurred the development of numerous commercial poultry breeding operations. Those commercial breeders hired quantitative geneticists to select and improve their stocks on an annual basis. The Chicken-of-Tomorrow Contest had demonstrated that some strains grew faster than others, but the application of the science of genetics and the development of specialized breeding companies for improving performance was the real driving force that led the broiler industry to point where flocks grown in 2016 reached market weights of 6.16 pounds (2.79 kg) at 47 days of age with a 1.86 feed-conversion ratio (NCC, 2017). It is apparent that breeding has contributed greatly to the overwhelming changes in broiler performance over the past 70–80 years. Of course, nutrition, housing, veterinary care, and many other factors have also played important roles in the broiler industry's success.

Over 25 years ago, Havenstein et al. (1992) predicted that the implementation of developing biotechnology methods and tools would benefit the industry. Specifically, they predicted that those tools would not only benefit the manufacturing of feed amendments such as modified feed grade enzymes and improved vaccines, but also for the direct genetic improvement of poultry breeding stock. Since then, the emergence of next-generation sequencing (NGS) technology in the Human Genome project has accelerated the development of sequencing instrumentation such that whole genome sequencing (WGS) has now become relatively commonplace (Heather and Chain, 2016; Hamdoun and Ehsan, 2017). These advancements led to a virtual explosion of applications ranging from WGS of specific foodborne pathogens for identifying and tracking specific causative organisms in a foodborne illness to characterizing gastrointestinal microbial communities in host animals such as chickens using 16S rRNA gene sequencing to generate taxonomic profiles (Ricke et al., 2017; Sekse et al., 2017; Pightling et al., 2018).

In poultry, the application of WGS has also advanced the understanding of the evolution of avian genome and the emergence of modern birds and progenitors of domestic chickens (Jarvis et al., 2014; Lawal et al., 2018). Application of RNA sequencing and differential transcriptomic analyses has led to the identification of genetic markers for chick resistance to *Salmonella* Enteritidis colonization (Li et al., 2018) while genotyping based on single nucleotide polymorphism (SNP) and microsatellite markers for quantitative trait loci mapping in commercial laying hens have been used to identify resistance to fowl typhoid caused by S. Gallinarum (Psifidi et al., 2018). It is likely that further elucidation of host resistance mechanisms should be useful for pathogen vaccine construction to enhance host immune response. It may also be possible to delineate host factors that while antagonistic to pathogen colonization in the gut are supportive of colonization by beneficial bacteria such as probiotic cultures.

Progress in the understanding of production traits is also becoming a reality. Liu et al. (2018) used a high-density SNP array to screen a population of laying hens from day of initial egg lay to 80 days of egg production to align specific SNPs with egg weight phenotypes and identify specific genes that could account for variation in age-dependent egg weights. Yuan et al. (2018) conducted a genome-wide association study of indigenous Chinese chicken breeds at the single marker and haplotype level loci mapping to establish that body weight should be considered polygenic with sufficient variability to suggest different genetic mechanisms accounting for the observed phenotypic variability in poultry breeds. As more fundamental genetic understanding is gained on commercial production, it is anticipated that detailed genetic information will be further linked to phenotypic traits and a more focused selection process can be implemented to optimize disease resistance, host gut health, and bird performance.

6 Housing

Improvements in broiler performance can be directly connected to improvements in the welfare of the birds involved, whether this includes housing, water, or veterinary care to treat and prevent diseases and mortalities. Before the onset of the modern poultry industry, many farms that had chickens were not concerned with their housing and let them roam free to roost in trees and be susceptible to predators and other external dangers (Skinner, 1974).

As the development of the broiler industry began, birds were raised in small sheds that had access to the outdoors. The sheds may have contained small heaters for the winter, but little else as the sheds were not controlled environments (Sawyer, 1971). One of first automated houses was developed in the late 1940s by the DeWitt brothers of Zeeland, Michigan. The brothers started with the production of an automated chain feeder (Sawyer, 1971). The automated feeder later became known as the ‘Big Dutchman’ and led to the DeWitt brothers to invent automated waterers, ventilation equipment, egg coolers, chick sorters, feed cleaners, and brooders (Sawyer, 1971). The Big Dutchman organization became one of the founding industries in automated housing.

The housing of the twenty-first century is vastly different than what was seen in the early 1900s. Broiler housing in the industry currently employs complete climate control facilities with the ability to manipulate temperature, relative humidity, air composition, air speed, air movement, and lighting. Because of the advancements in housing technology and machinery, poultry producers are able to maintain optimum control of the climate and environmental conditions in which their poultry are housed, which is also directly linked to the flock’s growth rate, feed efficiency, and livability (Liang et al., 2013).

In more recent times, there has been some public movement for preference of organic, free-range, or pasture flock production of market birds. There are a multitude of reasons for this increase in popularity such as perceived benefits in animal welfare, bird health, and food safety (Berg, 2001; Van Loo et al., 2012). Under these circumstances, particularly for free-range birds, housing is minimal and environmental exposure is much greater than what birds would encounter in conventional commercial industry housing (Fanatico et al., 2007; Jacob et al., 2008). Consequently, challenges such as predation on birds and feed costs are primary concerns of pasture flock farmers (Hilimire, 2012). In addition, slow growing breeds may be used in these small operations resulting in a longer grow-out period (Fanatico et al., 2007). Given these differences in breed of birds, dietary modifications, and environmental challenges, it remains to be determined how these inputs would influence GIT health and function but one would anticipate there could be some detectable differences between birds raised in this type of operation compared to conventionally raised birds.

7 Veterinary care

Improvements in growth rate, feed efficiency, and livability of poultry have also been a direct effect of developments in veterinary care. From the beginning of the industry, medications and drugs were a considerable area of concern for the industry as growers sought to improve efficiency in the production of their market birds. Drug companies were thus very interested in developing markets for their products for the industry. Companies such as Hess and Clark, American Cyanamid, National Remedy Products Company, Whitmoyer, Western Condensing, Sterwin, Monsanto, Elanco, Vinland, Pfizer, Wyeth, Consolidated

Products, Merck, Commercial Solvents, Abbott, and numerous others were involved (Sawyer, 1971).

Veterinary care, however, was not a common practice for the early poultry industry, because servicing poultry was not seen as needed or beneficial. However, 'Doc' Salsbury introduced the industry to the idea of providing poultry with veterinary care and providing growers with a means for identifying and treating diseases and afflictions found in poultry to improve their performance (Sawyer, 1971). 'Doc' Salsbury introduced the industry to numerous innovative products and ideas such as his annual poultry school that was started in 1931, an experimental farm for conducting research on proposed products (1935), a product called Ren-O-Sal that was a leader in the growth promotion movement, feed medications (1950), and vaccines that could be administered through the drinking water (Sawyer, 1971).

Currently, it is common practice in the broiler industry to not only employ preventative measures such as 'Doc' Salsbury had recommended, but to utilize service technicians who monitor broiler farms and advise the growers who manage the facilities. Through innovative measures taken by the broiler industry, the industry has seen a dramatic decrease in mortality among its flocks from 1925 to 2016 as mortality decreased from 18 to 4.4 percent (NCC, 2017). Of course, general overall management and housing, nutrition, and genetics have also contributed greatly to the considerable improvement in livability of the industry's broilers.

8 Poultry industry challenges in gut health

Even with the drastic improvements that have been made over the past 70 to 80 years in the poultry industry, some challenges still exist. Challenges such as the increase in the incidence of foodborne illnesses, and in the increase in poultry diseases originating from pathogenic bacteria and viruses. The gastrointestinal tract (GIT) of the modern broiler contains a complex mixture of hundreds of different microbiota that consists of both commensal and pathogenic bacteria. In addition, commensal bacteria in poultry such as *Campylobacter jejuni* are also pathogenic in humans (Ayllón et al., 2017). Due to the complexity of the GIT in both humans and broilers, health of both the poultry produced and of the humans that consume poultry products can be significantly affected. It is therefore important to understand each specific challenge of this type in order to elucidate effective solutions and the preventative measures associated with them.

8.1 Foodborne illness

Foodborne illnesses originating from poultry products are primarily related to the presence of *Salmonella*, *Escherichia coli*, and *Campylobacter*. In 2015,

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