Antibiotic Resistance, Alternatives, and the U.S. Poultry Industry

MISSISSIPPI STATE UNIVERSITY EXTENSION

Antimicrobial resistance (AMR) is a global public health issue with important implications in the U.S. For years, antibiotics and antimicrobial compounds have widely been used across the U.S. poultry industry to treat and prevent disease threats and to promote growth (Chapman and Johnson, 2002; Sneeringer et al., 2015).

The connection between antimicrobial use and selection for AMR has been extensively studied, as reported by Hedman et al. (2020). Within the U.S., **80 percent of antimicrobial agents produced are applied to animal production** (Food and Drug Administration, 2019). Intensive animal food production can lead to resistance resulting from extended use of antibiotics for promoting growth, preventing disease, and treating infection (Laxminarayan et al., 2013; Silbergeld et al., 2010; You & Silbergeld, 2014).

Antibiotic Usage Decreasing

Even though AMR genes occur naturally (Durso et al., 2012), agricultural practices can influence the prevalence and occurrence of AMR genes in soils. For example, soil applications of swine manure increased erythromycin resistance gene abundance that remained high for a decade post-application (Scott et al., 2018). Today, the poultry industry is keenly aware of the antimicrobial resistance issue, and there is widespread, ongoing research targeting safe and effective antibiotic alternatives.

Antibiotic use in the poultry industry is not a recent phenomenon. The discovery that antimicrobials fed in subtherapeutic concentrations to poultry expedited their growth was accidental. The first use of antibiotics in poultry was reported in nutritional studies by Moore et al. (1946). This was soon followed by the first report of antibiotic resistance in food animals (turkeys) by Starr and Reynolds (1951).

However, several FDA reports over the past 25 years have documented decreased antibiotic use by the U.S. poultry industry. For example, in a survey from 1995 to 2000, there was a substantial decrease in the use of antibiotics by the broiler industry (FDA, 2014). However, a 2011 report estimated that 20 to 52 percent of broiler operations used **antibiotics for production purposes not related to disease control** (USDA, 2011). But this report also found a **long-term decline in antibiotic use** in broiler production (Sneeringer et al., 2015).

More recently, FDA (2017) reported that domestic sales and distribution of all medically important antimicrobials intended for use in food-producing animals **decreased by 33 percent between 2016 and 2017**. The U.S. Poultry and Egg Association (2019) reported a **decrease in the percentage of broiler chicks that received hatchery antibiotics** from 93 percent in 2013 to 17 percent in 2017, a 95 percent drop in in-feed tetracycline use in broiler chickens, a 67 percent reduction in in-feed tetracycline use in turkeys, and a 42 percent drop in hatchery use of gentamicin in turkey poults. In addition, *Poultry Health Today* (2020) reported broilers raised in "no antibiotics ever" **(NAE) systems accounted for 58 percent of total U.S. production in 2019**, a seven-point increase over the previous 12 months.

While there has been discussion on the links between antibiotic use in animal production and human health (Vaughn and Copeland, 2004), perhaps the greatest contributing factor to the recent decline in antibiotic use in livestock is the **demand by consumers for NAE poultry products**. These demands have occurred even though NAE products often cost more to produce and consumers are often unwilling to pay the increased cost. However, there is growing consumer interest in sustainable food production and knowing how food is raised. As a result, current research is devoted to identifying antibiotic alternatives that can support sustainable bird growth and defend against disease threats (Sneeringer et al., 2015; Gadde et al., 2017). This has led to the broiler industry taking the lead in livestock production systems that have as their mission to meet consumer demands and be "no antibiotics ever."

Poultry Litter Management

A major issue today for growers, researchers, and the entire poultry industry is the area of poultry litter management. The **U.S. is the world's largest poultry producer**, with more than 9 billion broilers produced in

2019; roughly 58 percent of broilers are produced in five southeastern states (Georgia, Arkansas, Alabama, North Carolina, and Mississippi; National Chicken Council, 2020). Poultry litter is a combination of bedding material (shavings, sawdust, rice hulls, etc.), manure, wasted feed, and feathers.

The amount of litter produced by broiler chickens is significant. A 20,000-bird broiler house will produce **approximately 150 tons of litter per year** (Ritz and Merka, 2013). Therefore, in areas of concentrated poultry production, large volumes of poultry litter are produced in relatively small geographic areas. While this litter can serve as a valuable source of nutrients, it may also be a **possible source of AMR bacterial populations** in the environment (Thanner et al., 2016).

Some estimates indicate that nearly 14 million tons of poultry litter is produced on U.S. broiler farms annually (Moore et al., 1995; Gollehon et al., 2001). Poultry litter-amended soil may serve as a non-point source for antibiotics that enter surface and ground waters via runoff and leaching (Yang et al., 2019), because approximately 30 to 80 percent of veterinary antibiotics administered to animals are excreted in manure and urine (Sarmah et al., 2006).

Many antimicrobial compounds we use in animal healthcare today were originally isolated from the soil (Yang et al., 2019). This is not surprising considering that soils are a large reservoir of microbial diversity. In fact, 1 gram of soil may contain 10^6 to 10^9 bacterial cells from 10^3 to 10^6 different bacterial species (Girvan et al., 2003; Torsvik, 2002). Furthermore, antibiotic-resistant genes are not a new occurrence.

Antimicrobial-resistant genes have been recovered from 30,000-year-old permafrost samples, indicating **AMR is an ancient phenomenon** that existed long before antibiotic usage became common (D'Costa et al., 2011). Therefore, even though it has been suggested that there is a relationship between antibiotic use in agricultural animals and AMR emergence, it is not the only explanation for AMR prevalence (Yang et al., 2019). Administration of antibiotics to agricultural animals is only one possible explanation for AMR.

Approaches for Decreasing AMR

There is **concern that land application of poultry litter may transport AMR microorganisms** to the environment outside the poultry house. However, there are currently several approaches being undertaken by poultry operations to address AMR. These include multidisciplinary strategies aimed at developing new drugs, antibiotic alternatives, and management practices (FDA, 2013), along with reducing total antibiotic use, as discussed previously. Of these various approaches, developing new drugs is likely the least promising. Only a small handful of new antibiotics have been approved since the 1960s (Butler and Buss, 2006) because developing new antimicrobial drugs is extremely labor intensive, time consuming, and costly.

Research surrounding **antibiotic alternatives is proving more promising**. Society is pressing for reduced antibiotic use and greater efforts to find effective alternatives to control infectious diseases on farms (Gadde et al., 2017). In response to this pressure, several classes of antibiotic alternatives have been proposed and tested in poultry production, including probiotics, prebiotics, symbiotics, organic acids, enzymes, plant extracts, metals, antibacterial vaccines, immunomodulatory agents, antimicrobial peptides, bacteriophages, and different broiler chicken growth systems (Montoro-Dasi et al., 2020).

The most popular of these alternatives currently appear to be **probiotics, prebiotics, and a variety of plant extracts**, which are in various research trials aimed at finding antibiotic alternatives that provide both growth promotion and microorganism defense benefits. Prebiotics, such as fructans and galactans, and more recently, dietary fibers (Ricke, 2015, 2018) are selectively used by host microorganisms to confer a health benefit (Gibson et al., 2017). Probiotics such as *Bifidobacterium, Bacillus, Lactobacillus,* and *Lactococcus* are live microorganisms that confer a health benefit on the host (World Health Organization, 2011).

Plant extracts are plant-derived compounds that represent a relatively safe, effective, and environmentally friendly source of antimicrobials despite their sometimes-inconsistent nature. In other words, research sometimes finds an encouraging response, and other times, it doesn't. However, plant extracts have been used for many years in numerous different cultures as food preservatives and dietary supplements to reduce spoilage and promote growth. Products currently being researched include coconut oil, cinnamon, thyme, oregano, clove oil, pine oil, and others.

Despite the research, much remains unknown about how management practices may affect AMR—not only poultry litter management, but also pasture management and grazing practices after poultry litter is land applied. The ability of pasture management practices (i.e., filter strips and continuous versus rotational grazing) to reduce AMR gene sequence, prevalence, and movement to soils is largely unknown (Yang et al., 2020). Yang et al. (2020) reported that poultry litter had lower abundance of AMR genes relative to cattle manure, although long-term applications of poultry litter on pastures increased the abundance of AMR genes in soil. However, indications were that conservation **pasture management practices and select poultry litter inputs may minimize the presence and abundance of AMR genes in grassland soils**.

In addition, the poultry industry is researching a variety of management practices that address AMR but also have an added welfare component. Practices such as reduced stocking densities, additional downtime between flocks, and investigating slow-growing broilers are aimed at lessening the need for antimicrobial interventions while providing an improved animal-welfare environment.

Summary

Much remains unknown concerning antibiotic resistance and its connection with the U.S. poultry industry. However, something we do know is that antibiotic resistance has been ongoing for thousands of years. As a result, AMR genes are ubiquitous and represent a huge reservoir of genetic material that we can potentially affect with production practices and management efforts related to poultry litter and grass and croplands. A better understanding of soil and poultry litter and the role each plays in the creation of antibiotic-resistant genes will allow the poultry industry to better address antimicrobial resistance. Additional research on antibiotic alternatives such as prebiotics, enzymes, probiotics, organic acids, and plant extracts could provide new tools for the poultry industry to meet consumer demand for NAE products. As the poultry industry strives for increasingly sustainable production practices, careful evaluation of antibiotic use should lessen or prevent further dissemination of antimicrobial resistance.

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