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# A one health perspective on dairy production and dairy food safety

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ABSTRACT

As the global population approaches 9.7 billion inhabitants by the year 2050, humanity faces enormous challenges to feed, house, and provide basic living requirements for the growing population while preserving the health of wildlife and the ecosystem. Dairy source foods play an important part in providing nutrient and energy dense sources of calories and establishing *Bifidobacterium* as a keystone species in the gut for positive health outcomes in infants and children. In developed countries, dairy products have a high food safety record when pasteurized and properly processed. However, when milk is consumed unpasteurized, as often occurs in developing countries where regulation and oversight of the dairy industry is lacking, dairy can serve as a vector for zoonotic transmission of disease and can contain adulterants such as antibiotic residues. Here we provide an overview for the importance of dairy source foods for nutrition and with a One Health perspective and discuss the historical events that have resulted in a high standard of dairy food safety in the United States. This review article covers the Origins of One Health, the role of milk in transmission of disease, management practices and regulations to ensure safe dairy products reach consumers, current challenges facing the dairy industry and impacts on public health, and how these standards can be employed in low and middle income countries to improve public health, nutrition and economic benefits to farmers.

## 1. Introduction

By the year 2050 the global human population is expected to reach 9.7 billion inhabitants, creating a critical need to address global food security while also sustaining global health [1]. Dairy derived foods are a nutritious source of proteins, fats, micronutrients, prebiotics and probiotics, which can contribute significantly to food security and human health [2]. Consumption of dairy products has been shown to have a positive impact on bone mass, cardiovascular health and the gastrointestinal microbiome [3–6]. Milk as a source of nutrition is especially important for infants and children, who need nutrient and energy rich foods for growth and cognitive development. Numerous studies have shown consumption of milk correlates to reduced stunting and the World Health Organization (WHO) recommends 25–33% of dietary protein content should come from dairy for children suffering from malnourishment [7,8]. Furthermore, advances in genomics have opened the door to microbiome research, which has associated a symbiotic relationship between human and bovine milk bioactive compounds and the keystone bacteria *Bifidobacterium* [9]. Infants and children colonized with *Bifidobacterium* develop a protective intestinal microbiota, which blocks pathogens from binding to the intestinal epithelium by competitive inhibition and establishment of these bacteria in the gut are associated with reduced stunting, improved cognitive development and positive health outcomes [10,11]. Additionally, *Bifidobacterium* are highly susceptible to antibiotics and children prescribed antibiotics or who are exposed to antibiotic residues are at risk of upsetting the establishment of this keystone bacteria in the gastrointestinal tract [12]. Milk and dairy products provide an excellent source of nutrition and promote beneficial health outcomes. People in both developed and developing countries benefit from dairy producers and manufacturers that maintain a high standard of food safety, ensuring a safe and wholesome product for consumers.

The advent of antibiotic therapy has led to a boost in the health status of humans and animals around the world. However, the extensive use of antibiotics in humans, animals and industrial applications has resulted in antibiotic-resistant bacteria globally. As the world becomes more interconnected and global networks become smaller, the transmission of antibiotic-resistant bacteria has become an urgent global health crisis. In an unprecedented act, WHO has released a "Global Priority list of Antibiotic Resistant Bacteria [13]." This document outlines microorganisms that pose the greatest public health risk in an effort to prioritize and recognize the importance of research in creating

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new antimicrobials. As a global community, we now face the challenge of combating antibiotic-resistant bacteria, establishing prudent use of antibiotics, while improving livelihoods and meeting global food security needs.

This review is designed to deliver a One Health philosophy for dairy production medicine, highlighting the intersection of humans, animals and the ecosystem. Discussed are the origins of One Health, Critical Control Points in Dairy production, prevalence of antibiotic-resistant mastitis pathogens, prudent use of antibiotics, antibiotic residues and current research on alternatives to antibiotics. This review also summarizes effective techniques that should allow dairy producers and food safety experts to manage their way through animal health, human health, ecosystem health and on-farm challenges. These management techniques reaffirm that producers of dairy products in the United States supply milk that is safe, nutritious, and provides beneficial health outcomes and that these practices can benefit dairy production globally.

## 2. Origins of one health

In 1964, Dr. Calvin Schwabe, a UC Davis School of Veterinary Medicine Professor, coined the term “One Medicine,” the precursor to “One Health,” in his book Veterinary Medicine and Human Health. Dr. Schwabe was considered the “father of modern epidemiology” and the visionary behind the One Health concept. In his book, he outlines the roots of One Medicine noting that traditional healers did not differentiate between practices used to heal animals or humans, the course of disease and treatment are essentially the same and fundamentally “there is only one medicine.” In modern times, medical practitioners and scientists in human, animal and ecosystem health are trained in the same foundational clinical, laboratory, and epidemiological sciences. (Fig. 1) Medical practitioners and scientists are vitally dependent upon each other to advance both public health and social justice for the benefit of all and that health status cannot improve without access to clean water, sanitary food and hygienic living conditions [14].

WHO estimates 760,000 childhood deaths are attributed to diarrheal disease each year, making it the second cause of death among children under age five globally [15]. Prevention of diarrheal disease in developing countries is often focused on the role of water and sewage, while foodborne disease is often considered last [16]. Furthermore, uncontrolled and unregulated use of chemicals and pharmaceuticals in the food supply creates another hazard to public health. Foodborne illness places an undue burden on health status of people in these regions and can contribute to foodborne disease in developed countries if contaminated food products are exported [17,18]. Finally, to date there have been few food safety studies in developing countries that incorporate the cultural context of local food preferences, preparation, and eating habits, all of which contribute to food hygiene. These developing regions are in need of capacity building and knowledge base to implement public health programs capable of dealing with food safety from farm to table.

A One Health approach to dairy production medicine and food safety has the potential to improve global health and create best practices for producers to improve milk quality and production. (Fig. 2) This approach to dairy production takes into account the impact products entering and leaving the dairy farm have on the health status of the larger network and that food safety starts on the farm. As such, it is vital for producers to ensure they are using high quality water, feed, supplies and protocols to prevent spread of disease and chemical adulterants among the herd and animal handlers and to safeguard that dairy products and animal products are free of disease and safe for human consumption. Additionally, producers should take the necessary steps to ensure that waste generated on the farm is properly disposed of and does not contaminate the environment or downstream users.

Food safety requires the prevention of foodborne disease through safety assessment of food products, components and manufacturing

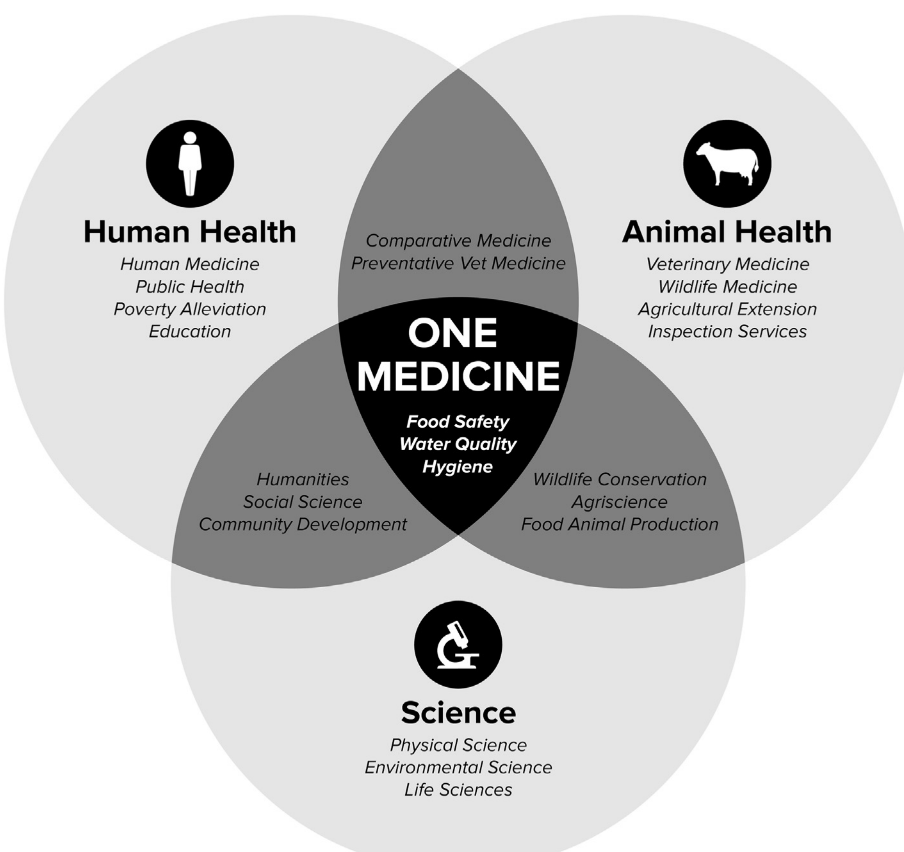


**Fig. 1.** One Medicine. Dr. Charles Schwabe described his vision of “One Medicine” in his textbook Veterinary Medicine and Human Health. This text details the role of human medical practitioners, animal medical practitioners and scientists in interdisciplinary scientific research to advance the health of humans, animals and the ecosystem for the benefit of all. This framework establishes that public health cannot improve without clean water, sanitary food and hygienic living conditions.


**Fig. 2.** A One Health Approach to Dairy Production Medicine. This approach to dairy production considers the impact of products entering and leaving the dairy farm on health status of the larger network and downstream users. Producers maintain high quality production by ensuring feed, water, supplies and protocols used on farm should meet specific standards and understand that food safety begins on the farm.

practices for both microbiological and chemical contaminants [19]. A One Medicine/One Health approach to dairy production medicine, herd health and food safety can lead to significant advances in food security, nutrition, food hygiene as well as advance global health. This integrative approach to solving complex problems impacting health and conservation where animals, humans and the ecosystem intersect reduces foodborne zoonotic disease, and is imperative in developing countries [14]. Zoonotic diseases are passed from animals to humans and vice-versa, and pathogens causing zoonotic disease are capable of entering the environment, contaminating water and soil, thus having a detrimental effect on the health of humans, animals and the ecosystem [20].

## 3. Critical control points in dairy production

Historically, zoonotic diseases associated with the consumption of milk have been due to bovine tuberculosis and brucellosis. Both of these diseases cause severe illness in humans and were difficult to diagnose and control in animals. At the turn of the 20th century, tuberculosis and brucellosis eradication programs were implemented in the United States and began to make an impact on human health. In 1947, there were 6321 reported cases of human brucellosis and by 1966 it was reduced to 252, more than a 95% reduction. In the case of tuberculosis, it is estimated that one out of nine deaths was caused by tuberculosis in 1900 and a modest estimate is 10% of humans infected with tuberculosis harbored the bovine strain. Eradication of bovine tuberculosis is estimated to have saved 25,600 lives in 1940 [14,21].

Henry Koplik, an American Pediatrician at the Good Samaritan Dispensary in New York City, first promoted heat treatment of milk for infants in 1889, providing it as “medicine” to sick infants and children. Soon, Koplik had a following of physicians, mothers and children and in 1890 he revealed his methods and sterilization equipment to the New York County Medical Society [22]. In June of 1893 Nathan Straus, a New York philanthropist and follower of Koplik, opened his first milk depot in New York City selling low cost pasteurized milk. With the advances in microbiology and sanitation, Straus was outraged by the high rate of child mortality due to tainted milk, which he viewed as preventable. Milk was a staple for children of poor families, and Straus and other “sanitary reformers” saw the need for a “clean” milk supply as part of the fight against tuberculosis and childhood mortality. Straus' milk depots quickly grew in popularity and by 1910 they were throughout the city and provided milk that was monitored and controlled from the farm with the guidance of a veterinarian. He contracted milk only from the most hygienic dairies and the milk was then transported in refrigerated trucks to his pasteurization laboratory. The sterilized bottled milk was then transported again on a refrigerated truck to the milk depots throughout town, where it was sold at a minimal cost to the city's poor. Straus provided free education on infant care and feeding by doctors as well as medical care for sick children [23]. Straus was a pioneer in advancing public health through applying scientific knowledge and establishing control points in dairy production. He recognized the importance of sourcing milk only from healthy cows living in hygienic conditions. His work was the foundation for city, state and eventually federal requirements of milk pasteurization.

Although tuberculosis and brucellosis eradication programs and pasteurization of milk made great strides in reducing these diseases, foodborne illness due to consumption of unpasteurized milk contributed to outbreaks of *Salmonella*, *E. coli*, *Campylobacter* and *Listeria* continued through the 1970's [24,25]. Contamination of milk and dairy products with pathogenic organisms is often derived directly from the animals or the farm environment and these sources are known reservoirs of foodborne disease [26]. *Salmonella*, *E. coli*, *Listeria* and *Campylobacter* are microorganisms that contribute to the majority of foodborne disease in the US and all of these pathogens are shed in the milk and feces of cattle [27]. These microorganisms can enter the food chain through fecal contamination of foods, equipment or carcass processing.

Before the FDA established federal guidelines in 1987 “requiring the pasteurization of all milk and milk products in final package form intended for direct human consumption,” local and state participation in pasteurization programs was voluntary [28]. The most current version of the “Grade A” Pasteurized Milk Ordinance (PMO) recognizes milk as the most important source of nutrients for proper health, especially among children and the elderly as well as a source of foodborne disease. In order to ensure the safety of milk and dairy products, the PMO outlines provisions “governing the processing, packaging, and sale of Grade “A” milk and milk products.” As a result of the various programs administered by the United States Public Health Service and the Food and Drug Administration, foodborne disease originating from milk has fallen dramatically. In 1938, an estimated 25% of all foodborne disease and contaminated water outbreaks originated from milk. Currently, less than 1% of such outbreaks are associated with milk [21]. The combined efforts by the USPHS, FDA and USDA has resulted in the safe supply of milk to the US population and set the gold standard for inspection and control of milk and milk products globally.

## 4. Foodborne pathogens: from farm to table

Mastitis, an infection of the mammary gland and source of foodborne pathogens, occurs when pathogenic bacteria enter the mammary gland through the teat end and colonize the mammary tissue. Mastitis pathogens are generally categorized into 3 categories: coliform, streptococci, and staphylococci. These organisms can be spread from infected quarters to uninfected quarters of the same cow or other cows and to equipment, the environment, animal handlers and humans who handle or consume unpasteurized milk products. These pathogens can enter the food chain directly or through the contamination of equipment [29]. Milk is an ideal nutrient broth for the proliferation of bacteria and once microorganisms from the farm environment enter the milk supply they can quickly multiply and establish biofilms in milk processing plants. Contamination of equipment at facilities that produce dairy products are a significant source of foodborne disease, organisms such as *Listeria* have the ability to proliferate at low temperatures [30]. While most milk in developed countries is pasteurized before it reaches consumers, some consumers prefer unpasteurized products, thus putting themselves at risk for developing foodborne diseases [31,32]. Furthermore, milk in developing countries is often consumed by smallholders unpasteurized and contributes to high rates of diarrheal disease [33,34]. A critical control point for organisms causing foodborne disease in dairy products is the teat end. By emphasizing management of mastitis through establishment of hygiene and animal health Standard Operating Procedures, foodborne disease and environmental contamination can be prevented while simultaneously improving milk quantity, quality and animal health and welfare. A One Health approach to management of livestock is vital for sustainable and successful production of animal based foods and the ability to address food security globally.

Best management practices have been commonplace in developed countries and have contributed significantly to increased milk production and economic livelihoods of producers. It is estimated that mastitis costs US dairy producers up to $2 billion per year and is the number one cause of economic loss to farmers [35]. The National Mastitis Council outlines a 10-point checklist for mastitis control for best practices. Table 1 highlights the main points for producers to follow based on the NMC 10-point mastitis control checklist. This plan outlines key practices to control mastitis on the farm and incorporates management practices vital to an economically successful dairy business. These include management of clinical mastitis, udder health, proper procedures, maintenance of equipment, biosecurity, dry cow therapy, hygiene and good record keeping [36]. By addressing each of these issues, dairy producers can reduce mastitis, which is their most significant cost of economic loss, and improve milk quantity and quality. Through a combination of education, economic incentives and consumer preferences, producers have begun to adopt these practices [37–40]. However, more work needs to be done to implement these practices in developing countries.

## 5. One health and antibiotics

Antibiotics are chemical compounds with bactericidal and bacteriostatic properties and have revolutionized the treatment of disease. Many of these compounds originate from natural sources such as bacteria and fungi. Since the introduction of antibiotics in the early 20th century, they have had a profound influence on reducing morbidity and mortality in both humans and animals, and are considered one of the most important achievements of modern medicine [41]. However, overuse of antibiotics in human, animal and industrial sectors has created a global public health threat of antibiotic-resistant organisms. A problem recognized by Alexander Fleming, who discovered Penicillin in 1928, "The thoughtless person playing with penicillin treatment is morally responsible for the death of the man who succumbs to infection with the penicillin-resistant organism [42]." While de novo mutations resulting in antibiotic-resistant bacteria are possible, it often requires multiple mutations to occur [43]. The most significant mode of acquiring resistance is through Horizontal Gene Transfer (HGT) [44]. Antibiotic resistance is not a new phenomenon created by human use of antibiotic therapeutics, but an evolutionary mechanism for fitness of bacteria [45,46]. Barlow et al., estimated OXA B-lactamase genes originated ~2 billion years ago, and most of the diversity seen in this family of genes was the result of ancient mutational events. Modern use of antibiotics has selected for bacterial communities that are capable of passing these genes through HGT. The appearance of resistance in bacterial communities cannot be entirely blamed on medical use. However, selection for and mobilization of these resistance genes has been aided by human misuse, creating the need for prudent use of antibiotics in human, animal and industrial sectors [47]. In this section, we outline prudent use of antibiotics in dairy production, prevalence of antibiotic-resistant mastitis pathogens, and cutting edge research into alternatives to antibiotics.

## 6. Prudent use of antibiotics

In the 1990's, driven by political and public opinion, the European Union passed a ban on the use of antibiotics as growth promoters in livestock in an effort to control non-therapeutic use of antimicrobials in agriculture. The consequence of this ban on human health was a decrease in vancomycin resistance of *enterococci* (VRE) in human fecal carriers, however this did not translate into a reduction of VRE infections in humans [48]. Bacteremia caused by VRE strains among humans increased from 2000 to 2014, a similar trend was seen in the United States, and corresponds to an increased prevalence of *Enterococci* in these populations, peaking in 2008–2009 and decreasing since [49]. Other nosocomial infections such as Methicillin Resistant *Staphylococcus aureus* (MRSA) followed similar patterns of increasing infection followed by a subsequent decrease [50]. While difficult to directly pinpoint the reason for decreases in VRE and MRSA, during the years 2006–2007 these bacterial infections became such a concern, legislators and professional medical associations began implementing infection control measures to prevent the spread of these organisms within hospitals, between healthcare providers and patients [51]. Implementation of restricted use of antibiotics in the European Union (EU) for animal agriculture use had a negative outcome for animal welfare. Morbidity and mortality of livestock and poultry increased the use of therapeutic antibiotics, which constituted a shift from antibiotics that did not have overlap with human medicine to those that are used in human medicine. Use of therapeutic antibiotics increased despite improved animal husbandry practices [48].

Currently legislative guidelines for the prudent use of antibiotics in agriculture are lacking and California has become the first state in the United States to require a veterinarian to prescribe antibiotics in livestock and poultry, with the passage of bill SB 27. The American Veterinary Medical Association outlines Judicious Use of Antimicrobials in Cattle. These guidelines are meant to aid veterinarians in judicious use through management, prevention of disease and animal welfare, while protecting farmers' economic livelihood and providing safe and nutritional foods to consumers [52]. Regulatory authorities should outline and monitor prudent use practices for operators and veterinarians that will benefit animal health, food safety and human health.

**Table 1**

Ten-point Mastitis Control Plan based on National Mastitis Council Recommendations. [36].

1. Establish Udder Health Goals
   - Set Somatic Cell Targets.
   - Establish Goals with Veterinarian, Site Manager and Workers.
2. Maintain a Clean, Dry, Comfortable Environment
   - Provide hygienic stalls, yards and bedding.
   - Ensure cow comfort through stress reduction.
3. Follow Proper Milking Procedures
   - Clean and dry teats before milking.
     Milkers adhere to wearing clean gloves during milking.
   - Forestrip and examine milk for clinical mastitis.
   - Apply Pre-dip teat disinfectant with 30 s of contact time.
   - Ensure proper attachment of cluster to teats make adjustments as necessary.
   - Apply Post-dip teat disinfectant.
     Ensure cows remain standing for 30 min following milking.
7. Effective Dry Cow Management
   - Reduce feed rations before dry off to facilitate decreased milk production.
   - Administer Dry off treatment to each quarter immediately following last milking using hygienic procedures.
   - Use J-5 core antigen vaccine to prevent coliform mastitis.
   - Remove excess body hair on flank and udder.
8. Establish Biosecurity Protocols for Contagious Pathogens and Chronically Infected Cows
   - Collect Somatic Cell Count on bulk tank and individual cows.
   - Monitor microbiological causes of mastitis on-farm
   - Isolate and screen new cows entering facility for disease for mastitis.
   - Isolate and monitor chronically infected cows.
4. Maintain and Use Milking Equipment according to Manufacturer
   - Ensure proper installation, validation and maintenance of equipment.
   - Replace liners and seals regularly.
   - Establish protocol for cleaning and sanitation following each milking.
5. Follow Good Record Keeping Practices
   - Establish a database for animal health, which includes: Cow Identification, days in milk, cases of mastitis, treatments received, outcomes of treatments, milk culture results.
6. Appropriate Management of Clinical Mastitis During Lactation
   - Establish a Mastitis Treatment Protocol.
   - Collect pretreatment milk sample for microbiological analysis.
   - Administer therapeutic treatments according to manufacturer directions.
   - Cull animals that do not respond to treatment.
   - Observe drug withdrawal times.
   - Ensure proper storage and disposal of pharmaceuticals.
   - Maintain animal health records.
9. Monitor Udder Health Regularly
   - Monitor somatic cell count of Individual cows.
   - Monitor distribution of high somatic cell count cows.
   - Conduct milk microbiological culture on high somatic cell count cows.
   - Calculate mastitis rates and distributions regularly.
   - Use somatic cell count data to establish and update udder health protocols regularly.
10. Review Mastitis Control Program Regularly
    - Consult with Veterinarian, Extension Specialist or Product Technician regularly.
    - Establish protocols to review and evaluate on farm procedures.

## 7. Prevalence of antibiotic-resistant mastitis pathogens

The USDA National Animal Health Monitoring System Dairy 2014 (NAHMSD 2014) reports clinical mastitis in 25% of all cows during 2013 and that 87.3% of those cows were treated with an antibiotic therapeutic in their treatment procedure, with 73% using cephalosporins [53]. Furthermore, intramammary (IMM) treatments are routinely used during dry off as "Dry-Cow Therapy" to treat and prevent infections in the initial stage of the dry period. The NAHMSD 2014 estimates 93% of cows were treated with dry-cow antimicrobials, which is the use of an antibiotic treatment at the end of lactation. The purpose of dry cow therapy is to treat current intramammary infections as well as prevent new infections during the dry period [54]. These uses of antibiotics are concerning for the selection of antibiotic-resistant mastitis pathogens as well as entry of antibiotic residues into bulk tank milk.

Rajala-Schultz et al. [55] conducted a study on antibiotic resistance of Coagulase Negative Staphylococcus (CNS) at calving in first lactation cows and cows which were past their first lactation in the Krauss Dairy Research Herd at the Ohio Agricultural Research and Development Center. Two hundred two isolates were obtained from 147 cows over the course of the 16-month study. They found a majority of first lactation cows (84%) had an infection in at least one quarter, while 58.6% multiple-lactation cows had an infection in at least one quarter. The majority of isolates recovered were CNS (158 out of 202) and 139 CNS out of 180 isolates were tested for susceptibility. Most resistance among CNS isolates was to penicillin, 44 out of 139 (31.7%), 28 out of 139 isolates were resistant to two or more antibiotics (20.1%), and 11 (7.9%) were multi-drug resistant, meaning the isolates were resistant to three or more antibiotics. The major findings show a lower rate of penicillin resistance among isolates from first lactation cows when compared to isolates from multiple lactation cows, 26.5% versus 39.3% respectively. The $MIC_{90}$ was also higher in isolates from cows that were passed their first lactation. Comparison of all other antibiotics (Ampicillin, Oxacillin, Cephalothin, Ceftiofur, Erythromycin, Pirlimycin, Tetracycline, and Sulfadimethoxine) showed less than a 5% difference in resistance between the groups. These results seem to indicate antibiotic use does select for resistant pathogens although none of the differences were statistically significant [55].

To compare the change of resistance patterns over time Park et al., [56] monitored resistance of mastitis pathogens on dairies converting from conventional operations to organic operations. They followed two herds in their last year of conventional production, through transition to the end of their first year in organic production. They found an increase in IMM infections during the transition and through organic production. Infection rates were: 1st year (conventional production) 47%, 2nd year (transition) 61.8%, 3rd year (organic) 69.8%. There were not any significant differences of infection at dry-off. Furthermore, they found a decrease in β-lactam resistance in CNS followed the conversion to organic farming and indicates a discontinuing use of antibiotics decreases the rates of antibiotic-resistant mastitis pathogens [56].

These studies reveal resistance among mastitis pathogens is not growing or widespread and even among individual cows, resistance could only be found immediately following IMM treatment and return to baseline resistance following termination of treatment. Furthermore, discontinued use, as on organic dairy farms, can be associated with an increase in IMM infection and increased therapeutic use of antimicrobials increasing the burden of foodborne pathogens entering the milk supply. These studies and others indicate the use of mastitis treatments can select for antibiotic-resistant mastitis pathogens and also shows with prudent use resistance profiles are reduced in dairy herds [57–61]. Available literature indicates prudent use of antibiotics in the dairy industry is the appropriate method to minimize selection for resistant organisms, while maintaining animal health and welfare for the prevention of foodborne pathogens and antibiotic residues from entering the food chain.

## 8. Antibiotic residues in milk

Ensuring milk is antibiotic residue free has a major impact on public health and economic livelihood of producers. Milk containing residues originates from unhealthy animals, has the potential to contain foodborne pathogens and is a potential allergen to consumers. These concerns are even greater in developing countries where there is virtually no oversight in the use of antibiotics in animals, milk and meat withdrawal times or antibiotic residue testing. The presence of antibiotic adulterants in milk can have a profound impact on the health of infants and children in regions already facing high rates of diarrheal disease and malnutrition. Numerous studies have shown a link between the gut microbiome, health status and disease [62–64]. Antibiotic residues can negatively impact the microbiome of those consuming adulterated milk, resulting in dysbiosis, a change in microbiota associated with disease states [12,65]. *Bifidobacterium* spp. are a keystone species that play an important role in intestinal homeostasis and infant health. This bacterium is highly susceptible to antibiotics and exposure to antibiotic residues from food can greatly impact the microbial diversity of the gut microbiome resulting in reduced levels of *Bifidobacterium* and increases in *Proteobacteria* [66,67]. Dysbiosis can last for years resulting in long-term health risks, especially in infants and children, such as stunted growth, compromised immune response, and recurring diarrheal disease [12].

A guideline for prudent use of antimicrobials in agriculture animals helps to improve safety of foods from animal origins. Antibiotic residues in milk have been a cause for concern and the majority of antibiotic residues in milk are derived from mastitis therapeutics in dairy cattle, failure to withhold milk for the appropriate withdrawal time, and feed contaminated with antibiotic residues are also a mode of entry into the milk supply [21,68,69]. Currently, an overlooked sector of antibiotic residues remains commercial ethanol production. Corn-based ethanol is produced in a fermentation process using yeast cultures. These cultures are often contaminated with Lactic Acid Bacteria (LAB), which compete for nutrients and result in lost yield of ethanol. In order to prevent proliferation of bacterial contaminants and limit yield losses, many ethanol producers use large amounts of antibiotics in the fermentation process. This is cause for concern as residual corn mash and slurry is sold as an animal feed, mainly to beef and dairy producers. Antibiotic residues in animal feed has recently become a concern and the dearth of scientific information on how these residues alter the microbiome of economically important agricultural animals is unknown. There may be a similar outcome as found in humans in that antibiotics alter the microbiome such that beneficial bacteria are depleted from the gut providing an opportunity for resistant bacteria to proliferate resulting in an increase in diarrhea and fecal shedding of pathogens [70–72]. This seemingly unrelated industry presents an avenue for antibiotic residues to enter the dairy farm impacting food safety, human and animal health, and highlights the importance of a “One Health” approach to animal production.

To address concerns of antibiotic residues in milk, the Milk and Dairy Beef Quality Assurance (MDBQA) program was established in 1991 as a Hazards Analysis Critical Control Point (HACCP) program for antibiotic residue avoidance in dairy products and is an effort by the American Veterinary Medical Association and the National Milk Producers Federation to be an industry sponsored program for best practices and eliminating antibiotic residues from dairy products [73]. By 1992, the PMO required all tanker trucks of milk be tested for β-lactam residues before they entered milk-processing plants [73]. The 2015 PMO states all raw milk is to be sampled before it enters the milk processing plant and requires all other drug residues to be tested based on a random sampling program. Due to these regulations, β-lactam residues are rarely found in tanker trucks of milk. In 2015, β-lactam residues were found 0.012% of tanker trucks, resulting in discarding of the entire truck of milk and possible penalties for the producer [53]. For producers to ensure a milk supply free of antibiotic residues, they should follow milk and meat withdrawl times as specified by the label use of the manufacturer's product and periodically testing individual cows and bulk tank milk. Observing the withdrawl period for antibiotic treatments is of importance as this is the period of time to discard milk or hold animals from slaughter to ensure drug residues are below the determined maximum residue limit allowed by the FDA after an animal has received an antibiotic treatment [74]. The majority of operators surveyed in the NAHMSD 2014 reported some form of on-farm residue screening, 89.7% tested individual cows after receiving IMM treatments [53]. Overall, the system of milk production in the United States ensures our dairy products are high quality, safe and free of antibiotic residues before entering the food chain.

## 9. Dairy dynamic management

Dairy Dynamic Management (DDM) is a One Health management approach to dairy production medicine with the premise that food safety and milk quality begin on the farm [75]. This approach incorporates the One Medicine/One Health philosophy and can be implemented to address the previously discussed challenges in food safety. DDM uses a protocol based management system to establish clear goals and objectives tailored to the farmers needs through the establishment of standard operating procedures and good record keeping, ensuring the team is properly trained and adhering to established practices. A DDM Specialist, in conjunction with a scientific consultant and the dairy manager, facilitates communication, team building and problem solving through clearly identifying each team member's roles on the farm and establishing a clear expectations of the team. These are the foundation of a successful dairy operation. The process of creating a DDM network (Fig. 3) and team, establishes critical control points tailored to the dairy producers' specific needs. By clearly defining practices and roles on the farm, farmers can track how their practices impact the broader network. DDM builds a team of specialists that understands food safety begins on the farm and diseases can be passed between humans, animals, wildlife and the environment [75]. The core concepts of Dairy Dynamic Management can be extended to any agricultural system or production network and will be crucial for increasing global food production to alleviate food insecurity and malnutrition through sustainable measures.

## 10. Alternatives to antibiotics

Initiatives such as the National Action Plan for Combating Antibiotic-Resistant Bacteria and the USDA “Alternatives to Antibiotics” have spurred new action and research into combating antibiotic resistant bacteria [76,77]. These initiatives outline guidelines and policies to address the emergence of antibiotic-resistant bacteria in human and animal health. The USDA “Alternatives to Antibiotics” sets out to emphasize research for preventing and treating disease in food animal production in the following areas: 1) Vaccines, 2) Microbial-derived products, 3) phytochemicals, 4) Immune products, and 5) Chemicals and Enzymes. By focusing scientific research to these areas emphasis can be placed on prevention and control of animal disease as well as treatments that do not select for antimicrobial resistance, thus preserving key therapeutics for human use. Here our discussion will focus on bacteriophages, enzymes and organic chemicals.

Microbial derived products such as bacteriophages, or phages, are a re-emerging area of research. Phages are viruses that infect and replicate in a narrow range of host bacteria, which are lysed when the phages are release into the environment. During the 1930's and 40's, phage therapies were commonly used in Georgia, Russia, Poland and the US. However, interest declined in this research after the discovery of antibiotics in the 1940's and research in this field was abandoned [78]. With the rise of antibiotic-resistant bacteria in the 1990s, phage research is again gaining interest. Phages are ubiquitous in nature and can be easily isolated from water, soil and sewage. Phages have a very narrow host species range making them ideal for targeted killing of bacteria but also requiring therapeutic products to consist of cocktails of phages. There are few studies evaluating the efficacy of phage therapy for mastitis but current work indicates phage therapy as an IMM treatment may have many hurdles and also has the potential to mediate horizontal gene transfer of pathogenic genes among bacteria [79–82]. Studies indicate the use of antimicrobial enzymes, such as endolysins, may have more success [83–86]. Endolysins are phage

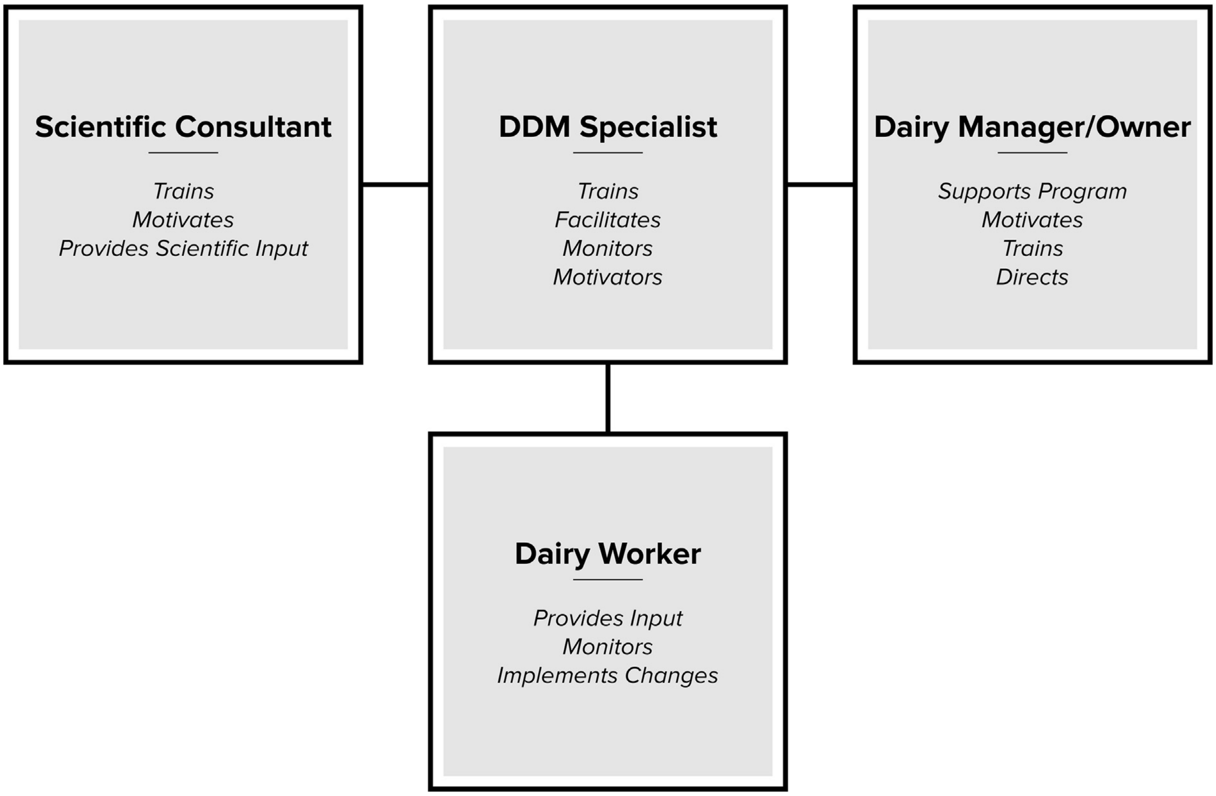


**Fig. 3.** Dairy Dynamic Management Hierarchy. The DDM Specialist facilitates communication and establishment of DDM practices in conjunction with a scientific consultant and the dairy manager or owner to build a team capable of managing on farm challenges.

encoded murein hydrolases, which cleave peptidoglycan structures in the cell wall of bacteria upon release of bacteriophage into the environment and present a novel source of enzymes capable of killing bacteria without selecting for antibiotic-resistance. Furthermore, these enzymes have the potential to be used in human medicine to combat antibiotic-resistant bacteria [87]. Finally, teat dips are the first line of defense in udder hygiene and the most effective method of preventing mastitis [88]. Organic farming and prudent use of antibiotics has prompted exploration into organic and environmentally friendly compounds for udder hygiene and biocontrol in the dairy industry. While scientific research on formulations of organic teat-dips is limited, many dairy industry leaders such as DeLaval offer a variety of products approved for use on organic farms in both the United States and European Union [89–91]. Further investigation of organic chemicals and acid washes currently used as additives and preservatives in food to extend shelf life and reduce microbial contamination may prove valuable to advance this area of research. Additional research on the harmful effects these formulations may have on animal health, environmental impact or residues in foods is warranted and current information is limited. For example, use of organic acids may alter the pH of the skin and result in teat end damage [92]. Creating and validating the use of these substances in organic farming as teat dips and biocontrol agents fits into the One Health paradigm of dairy production medicine by preventing disease with organic and environmentally friendly products that do not pose a health risk to humans, animals or the ecosystem.

## 11. Conclusion

The global challenges faced by our generation and the next are difficult and numerous. As the global population continues to grow we must find solutions to meet food insecurity, improve global health and face emerging health crisis such as antibiotic-resistant bacteria. There is not one solution to these problems, but in order to successfully navigate these issues a holistic approach is needed. Calvin Schwabe had the insight to pioneer the One Health/One Medicine philosophy to create solutions to improve animal, human and ecosystem health with a holistic mindset. Key components of which are access to clean water, safe food and hygiene. A One Health philosophy for dairy production medicine and management addresses these issues through effective farm management systems such as Dairy Dynamic Management, prudent use of antimicrobial agents and consideration of the entire system of dairy production. These management techniques reaffirm that producers of dairy products in the US supply milk that is safe, nutritious, and provides beneficial health outcomes and that these practices are needed in developing countries to improve nutrition, health and wellbeing.

## Conflicts of interest

The authors declare no conflict of interest.

## Contribution of authors

SG drafted the manuscript and created the figures. All co-authors provided input for the literature review, manuscript preparation, proofreading, and critical analysis of the submitted review.

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