

## Major Advances in Disease Prevention in Dairy Cattle

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### ABSTRACT

This paper describes some of the major points of progress and challenges in health management of dairy cattle in the last 25 yr. A selection of the leading contributors in the field is acknowledged. Specific advances in the areas of transition cow management, epidemiology, udder health, applied immunology, housing design, calf health, and health-monitoring tools are described. The greatest advances in dairy health in the last 25 yr have been the shifts to disease prevention, rather than treatment, as well as from focus on individual animals to groups and herds. A fundamental advancement has been recognition of the multifactorial nature of almost all diseases of importance in dairy cattle. Epidemiology has been a critical new tool used to describe and quantify the interconnected risk factors that produce disease. Another major advance has been redefining disease more broadly, to include subclinical conditions (e.g., subclinical mastitis, ketosis, rumen acidosis, and endometritis). This expansion resulted both from improved technology to measure function at the organ level and, just as importantly, from the evolution of the health management paradigm in which any factor that limits animal or herd performance might be considered a component of disease. Links between cattle and people through consideration of environmental or ecosystem health are likely to further expand the concept of disease prevention in the future.

Notable successes are decreases in the incidence of milk fever, clinical respiratory disease in adults, contagious mastitis, and clinical parasitism. There has also been improved protection through vaccination against coliform mastitis and bovine virus diarrhea. Since 1980, average herd size and milk production per cow have increased dramatically. Despite these increased demands on cows' metabolism and humans' management skills, the incidence of most common and important diseases has remained stable. Great progress has been made in understanding the biology of energy metabolism and immune function in transition dairy cows, the

time at which the majority of disease occurs. Coupled with an emerging understanding of how best to provide for dairy cows' behavioral needs, transition cow management promises to be the foundation for progress in maintenance and enhancement of the health of dairy cows in the next 25 yr.

**Key words:** dairy cow, health, preventive medicine, veterinary

### INTRODUCTION

Perhaps the single biggest advance in dairy health in the last 25 yr has been the paradigm shift from treatment of clinical illness to disease prevention. Shifts in philosophy, key assumptions, and priorities underlie the specific advances in science and technology. A fundamental advancement has been recognition of the multifactorial nature of almost all diseases of importance in dairy cattle. Epidemiology has been a critical new influence and tool to describe and quantify the interconnected risk factors that produce disease. In turn, health management or production medicine is characterized by an integrated, holistic, proactive, data-based, and economically framed approach to prevention of disease and enhancement of performance. Health management has been defined as the promotion of health, improvement of productivity, and prevention of disease in animals within the economic framework of the owner and industry, while recognizing animal welfare, food safety, public health, and environmental sustainability. Accordingly, disease prevention, considered broadly, is no longer the sole domain of veterinarians. Conversely, to deliver health management and effective disease prevention veterinarians must integrate consideration of nutrition, housing, and whole farm management systems into recommendations of best practices. Veterinarians are therefore evolving from task-oriented providers of therapy to advice-oriented consultants (Figure 1).

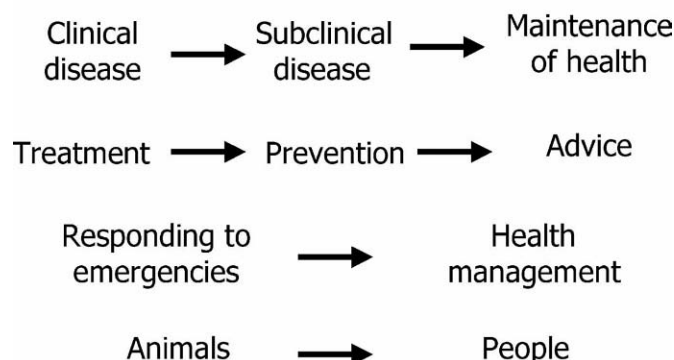
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## The Evolution of Dairy Veterinary Medicine



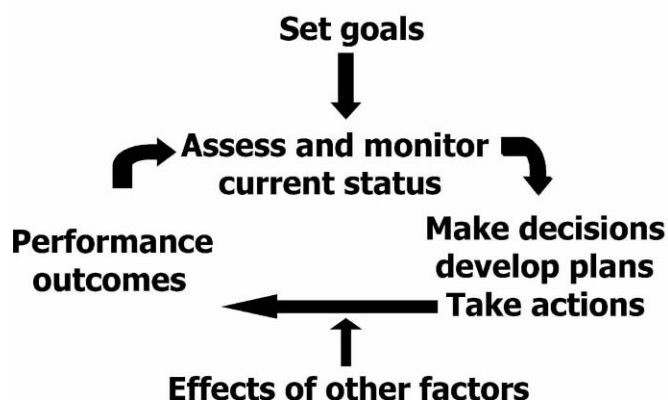
**Figure 1.** A schematic representation of the evolution of paradigms and practices in dairy cattle veterinary medicine over the last 25 yr.

mal or herd performance might be considered a component of disease.

### HISTORICAL PERSPECTIVE

Radostitis has described 4 phases in the development of preventive veterinary medicine. In the late 19th and early 20th centuries, as the profession of veterinary medicine was formalized, a major focus of activity was the eradication of clinical infectious diseases. Examples were the elimination of tuberculosis and brucellosis that were devastating to livestock, threatened the food supply, and had enormous public health significance. In the next phase, starting around 1940, the declining role of the horse for transport and labor shifted attention to food animals. Antibiotics became available, which revolutionized the treatment of common diseases and veterinary practitioners routinely performed successful surgeries, such as caesarean sections. Veterinary service was focused on treating the sick individual animal. This era was a time of unprecedented economic growth in the developed world, creating a constantly expanding demand for food and increased economic value of farm animals, making individual animal treatment profitable, and fuelling huge demand for veterinary services. Disease prevention efforts continued to be directed at eradicating potentially devastating conditions, but vaccination began to be used in parallel; for example, in control of brucellosis. A third phase began in the mid-1960s when efforts began to shift to proactive, rather than reactive, interventions. The major evolution in this era was the recognition of subclinical dis-

## The Health Management Cycle



**Figure 2.** The health management cycle. This conceptual framework can be applied to monitoring and continuous improvement of specific management areas on a dairy farm. Current measures of performance are quantified and compared with internal or external targets or benchmarks. A specific, measurable, and time-defined goal is set, and policies and practices are implemented to achieve the goal. Over time, performance will be affected by other influences or new variables. Actual performance is measured in a planned and systematic way, and a new iteration of the cycle begins. A key point is that the cycle is repeated routinely.

ease as a limiting factor on productivity. For example, internal parasite burdens could be measured and treated with effective new pharmaceuticals, with noticeable improvements in animal productivity. This period marked the beginning of producers paying for scheduled visits to the farm in the absence of an emergency or a clinically ill animal to be treated. Disease prevention efforts in dairy cattle focused on identification and treatment of infertility and mastitis. Among others, Douglas Blood was a notable leader in advancing dairy veterinary medicine in this period. The fourth phase outlined by Radostitis began in the late 1980s. Herd health programs were well established, and veterinarians increasingly collected quantitative data and analyzed records in an effort to identify production-limiting problems at an early stage. Reproductive management continued to be a fundamental task, but evolved from focus on problems of individual cows to systematic programs to prevent uterine disease and efficiently inseminate nonpregnant cows. Veterinarians sought new analytical skills, including the application of economics to dairy management decision making. The interconnected nature of the components of disease or reduced animal performance was increasingly recognized. Furthermore, there has been integration of other disciplines, notably nutrition, into the health management approach to preventive medicine (Figure 2). To this end, leading veterinarians have pur-

sued substantial continuing education to broaden their knowledge and skills to include computer literacy, epidemiology, nutrition, and design and ventilation of housing. Seminars at the annual conference of the American Association of Bovine Practitioners continue to be a key venue for exchange of new ideas and information across the dairy industry. Novel programs were created to respond to and advance this evolution, notably the Dairy Health Management Certificate Program, founded by Ken Leslie at the University of Guelph, which was adapted and replicated at veterinary schools in Pennsylvania, Wisconsin, Michigan, California, and Ohio. More recently, business training (MBA) programs have increasingly attracted veterinarians working in the dairy industry, starting with John Fetrow and David Galligan in a program at the University of Pennsylvania and including, among others, a web-based MBA in Agriculture offered at the University of Guelph.

Presently in the United States, disease prevention at the population level, and in particular dairy production medicine, is moving into a new era, in response to massive structural changes in the dairy industry. These changes are likely to accelerate further. In Canada, these trends and forces are somewhat muted and slightly lag behind the changes in the United States, but the fundamental directions are similar. The situation in Europe is somewhat different, in that social, land space, and legislative pressures constrain the growth of dairy herds in many parts of Western Europe, although recent additions of eastern European nations to the European Union will undoubtedly place new stress on those production systems. Several western European countries have well-established comprehensive national animal identification programs, livestock tracing schemes, and advanced disease recording systems. The fundamental evolution of disease prevention in dairy cattle is global. However, there are important differences in approaches. For example, several Scandinavian countries are well advanced in national programs to eradicate bovine virus diarrhea (BVD). Although the disease is recognized to cause significant economic losses in North American herds, there is presently little movement in the industry, and little likelihood of government resources or directives, to undertake the massive effort and the short- and medium-term costs that would be associated with such a scheme on this continent. This is an example of the differences in approaches to disease prevention even among countries with highly developed dairy industries.

#### **CHANGING STRUCTURE OF THE DAIRY INDUSTRY IN THE UNITED STATES**

The dairy industry in the United States is undergoing a profound and accelerating structural change. Based

on USDA statistics, researchers from Cornell report that approximately 3% of the 70,000 dairy herds in the United States have over 500 cows, with an average herd size of >1,100 cows, and these herds account for 36% of the milk supply. It is projected that in 2020, large herds (>500 cows) with an average herd size of almost 1,900 cows will account for 23% of the 15,000 herds that remain, and will produce 85% of the milk supply. Among his many contributions to the advancement of dairy production medicine, John Fetrow (with others) has recently highlighted these changes and articulated some of the implications for the veterinary profession and for disease prevention at the population level. Large dairy herds are characterized by business-driven decision making, seeking of operational efficiencies, specialization of labor, and use of standard operating procedures. Large dairies have offered, and will increasingly offer, unique challenges and opportunities for advances in disease prevention. The high density of cattle within farms, increasing concentration of dairy farms in regional clusters, and movement of animals between facilities for specialized management at different stages of life and within the production cycle may increase the possibility of propagation of infectious disease within and between farms. It is possible, but not necessarily true, that larger herd size might reduce the opportunity for early detection of diseased individuals. On the other hand, by their nature, large dairies may be more likely to successfully and consistently implement best management practices such as maintenance of clean, dry bedding, strategic vaccination protocols, hourly monitoring of maternity pens, prompt feeding of colostrum to newborn calves, and separation of sick from healthy animals. Additionally, large dairies have the critical mass of animals and the management systems in place to provide the opportunity for large-scale field studies that are the lifeblood of advances in disease prevention.

#### **THE UNIT OF INTEREST IN DISEASE PREVENTION**

In the last 25 yr, a major advance in applying new knowledge and effecting disease prevention has been a shift in focus from individual animals to groups and herds. Although dramatic increases in herd sizes have of themselves required this shift, the power of this approach is applicable to small or large herds. Ken Nordlund (1998) articulated this important philosophical premise, as follows, "Traditional veterinary medicine is focused upon diagnostics and therapeutics of the individual animal, with the assumption that if all the sick animals are handled properly, a healthy herd will result. Production medicine focuses upon the underlying herd management system with the assumption that if



the production system that produced the problem is fixed, a healthy herd will result.”

In fact, dairy cattle disease prevention has benefited from expansion of investigation from the individual animal level both up to the group and herd level, and down to the genomic level. Both of these avenues of research advance knowledge, and both are important and necessary. Recently (with increased concern over bioterrorism, zoonotic disease, and food safety), a significant component of disease prevention efforts have shifted to an even broader ecosystem and national scope. For example, there is renewed activity in public health not seen since the major campaigns for the eradication of brucellosis and tuberculosis. As the dairy industry, especially in the United States, but also in Canada, has moved to be heavily market-driven, the resources and infrastructure to study and respond to foreign animal disease were eroded. Recent cases of bovine spongiform encephalopathy in both countries have resulted in some constructive changes (e.g., improved national cattle identification systems) that will contribute to disease prevention in the future. However, this situation has also highlighted the chronic economic devastation that can be wrought by even isolated cases of disease in cattle. The risk of agri-terrorism has added another chilling dimension to the need for coordinated national and international systems to respond to animal disease at a population level. These situations provide a stark warning to policy-makers that animal disease prevention has major significance to society and to the economy. Although activity has been greatly increased, it is not clear whether North America is positioned to respond successfully to a substantial outbreak of animal disease.

### LINKS WITH HUMAN HEALTH

The relationship between dairy cattle health and human health warrants mention. The dairy industry strives to produce milk and dairy foods that are safe and nutritious, and that are seen to be healthful and wholesome. There are a number of diseases of dairy cattle and pathogens transmissible from dairy cattle that are zoonotic. Eradication campaigns and adoption of pasteurization through the 20th century provided for nearly complete control of the potential for brucellosis, tuberculosis, and Q-fever from cow's milk. More recently, it is worth noting that there have been very few major outbreaks of foodborne disease associated with dairy products, and that many of the episodes that have occurred were associated with illicit consumption of raw milk. However, milk is a potential source of zoonotic disease due to *Salmonella*, *Listeria*, and *Campylobacter*. Several public health issues presently confront

the dairy industry. For example, the possible associations of Johne's disease in cattle with Crohn's disease in people and bovine spongiform encephalopathy with variant Creutzfeldt-Jacob disease, as well as the possible contribution of antibiotic use in cattle to the development of antimicrobial resistance in human pathogens are important concerns. Additionally, more indirect links between cattle and people through consideration of environmental or ecosystem health (e.g., fecal shedding of *Escherichia coli* O157:H7, which does not cause disease in cattle, but is potentially highly pathogenic to humans) are likely to expand the concept of disease prevention in the future. The pathology of Johne's and Crohn's diseases are similar; the causative organism of Johne's has been detected in lesions from some Crohn's patients, and the association between the 2 conditions is the subject of active investigation by veterinary and human medical researchers. At present, there is no definitive evidence that Johne's disease causes or even contributes to Crohn's disease. However, the implications could be profound for the dairy industry if such a link were to be established. Accordingly, research on Johne's disease has expanded considerably in the last 10 yr. Programs have been developed to educate producers and assist them in implementing control measures for this disease. Johne's disease illustrates the evolution of clinical thinking with formal evaluation of diagnostic test performance and recognition of the limitations of the tests. In addition, there has been development of both new tests and new epidemiologic tools with which to evaluate tests. Although clinical cases and subclinically infected animals are a source of economic loss to dairy farms, for many farms this is not an economically limiting problem. However, many producers are seeking to be proactive in this regard, and an important spin-off effect is that the basic and most important management practices to limit the spread of Johne's disease are also best management practices for calf health and the prevention of other common and important diseases in calves.

Antimicrobial drug use exerts selective pressure on bacteria and eventually results in the development of antimicrobial resistance by some strains of bacteria. Depending on the mechanism of resistance, it may be passed to or amplified by successive generations of bacteria, or possibly exchanged among different strains of bacteria. This may result in pathogens of animals becoming resistant to certain antimicrobial drugs or classes of drugs. Of concern to public health is the possibility that antimicrobial resistance could be transferred from animals to people in zoonotic bacteria. More likely, transfer could occur in nonpathogenic bacteria that might be consumed in improperly handled or prepared food, which in turn pass resistance components to hu-

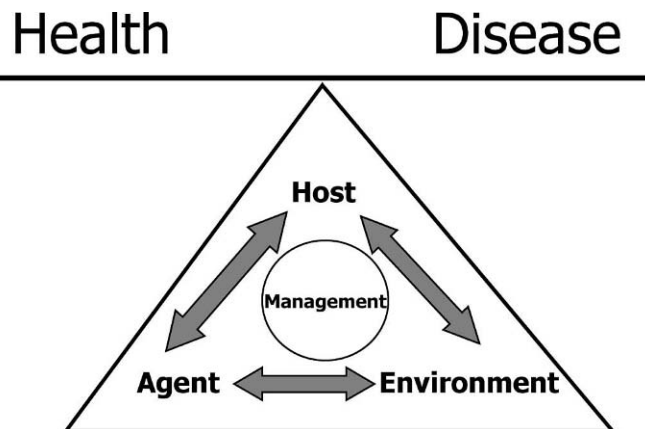
man pathogens. To the authors' knowledge, there are no examples of this occurring with milk as the medium of transmission. When disease prevention in dairy cattle is unsuccessful, antimicrobial drugs are used to treat certain conditions to maintain animal welfare and restore health and productivity. It is important to note that the vast majority of antimicrobial drug use in dairy cattle is therapeutic—that is, administered parenterally for a short time (3 to 7 d) at therapeutic doses for the treatment of a specific disease in selected individuals. This approach is in contrast to some applications in poultry, swine, and beef cattle, in which subtherapeutic levels of antimicrobial drugs may be administered in the feed for many weeks. Although there are numerous studies to support prophylactic use of antimicrobial drugs in feed, and at most conflicting evidence to argue against it, this is not a routine practice in the dairy industry.

### A QUESTION OF PERSPECTIVE

Have major advances in disease prevention been made in the last 25 yr? Is there evidence that the incidence of common diseases (calf scours and pneumonia, dystocia, stillbirth, retained placenta, metritis, endometritis, ketosis, displaced abomasum, mastitis, lameness, Johne's disease, leukosis, salmonellosis, abortion) has decreased? Tracking trends over time is confounded by the evolution of the necessary diagnostic tests, such as for subclinical ketosis, and for both clinical and subclinical mastitis. Given the lack of high-quality standardized data, it appears that the incidence of most conditions is stable, at best. Notable exceptions with decreased incidence are milk fever, clinical respiratory disease (in adults), clinical parasitism, and clinical infectious bovine rhinotracheitis and BVD (notwithstanding an epidemic in the early 1990s). Alternatively, is it a great success that milk production per lactation has doubled since 25 yr ago (and in some cases much more), and disease incidence has been held stable?

In contrast to the swine and poultry industries, it is worth noting that the North American dairy industry has largely not pursued disease exclusion (rigorous biosecurity) as a means of disease prevention.

Some failures in disease prevention must be acknowledged. For example, over the last 25 yr, digital dermatitis progressed from being largely unknown to an epidemic, and now to a firmly endemic status in most dairy herds in North America. Our current prevention and treatment strategies have produced a stalemate, at best, in the struggle with this important cause of lameness. Additional examples of diseases in which little progress has been made, or where prevention has even



**Figure 3.** A schematic representation of the determinants of disease. The balance of risk factors and protective factors that determine health status depend on the interaction of the components of the epidemiologic triad: host, agent, and environment, all of which are influenced by management practices.

regressed, include salmonellosis, leukosis, and calf diarrhea.

### SPECIFIC MAJOR ADVANCES IN DISEASE PREVENTION

The shift in philosophy and paradigms of disease control described above is arguably the biggest advance in itself, in that it is central to all of the specific developments.

#### Epidemiology

The concepts, analytic techniques, and critical appraisal from epidemiology constitute one of the greatest contributions to disease prevention in the last 25 yr. The tools of epidemiology were central to demonstrate and quantify the interrelated nature of most common diseases of dairy cattle (Figure 3). Calvin Schwabe at the University of California at Davis has been described as a godfather of veterinary epidemiology. Wayne Martin at the University of Guelph was an early leader in bringing epidemiology to the study of diseases of cattle. He coauthored one of the first major textbooks in the field (*Veterinary Epidemiology*, 1987), and recently coauthored an advanced textbook on study design and analysis (*Veterinary Epidemiologic Research*, 2003). The expansion in the body of knowledge in veterinary epidemiology over this time has been astonishing, fuelled by great strides in the sophistication and availability of statistical methods, software, and computing power to handle large datasets. Others, including Ian Dohoo at the University of Prince Edward Island and Yrjö Gröhn at Cornell University, have made sustained

contributions by quantifying the relationships among diseases, as well as among disease, production, reproduction, and culling in dairy cows. Although this information is taken for granted now, the application of epidemiologic approaches and methods to understanding disease in dairy cattle was in its infancy 25 yr ago. For example, there are now numerous departments within university faculties that include epidemiology, health management, or population medicine in their name or their mission statement, whereas essentially no departments with this focus existed in 1980. Some examples of the contributions of epidemiology include calculation of adequate sample size to address research questions; understanding the effects of correlation among animals in a study, how that may bias analysis, and use of methods to account for clustering; understanding the value of observational studies to investigate determinants of naturally occurring disease; understanding the sources of bias and confounding in the design and analysis of studies; and the use of multivariable models to measure and account for nontreatment effects in experiments. Additionally, epidemiology has brought thoughtful uncertainty to interpretation of tests and laboratory results, as well as methods to validate tests or quantify unavoidable uncertainty. As an example of one dairy health management research team, the authors and their graduate students and colleagues have sought to generate knowledge to inform decision-making by conducting large-scale observational studies and clinical trials (e.g., the prevalence and impact of subclinical ketosis and the use of moneisin to prevent it; diagnosis and treatment of endometritis; risk factors and prevention strategies for intramammary infections in the dry period).

#### ***Focus on the Transition Period and Exchange between Animal Science and Veterinary Medicine***

Perhaps the most important specific advance in the last 25 yr has been to focus research and management attention on the transition period, and in particular the close-up dry period. Approximately 75% of disease in dairy cows typically happens in the first month after calving. These problems are increasingly known to be rooted in immune function, and in turn, feed intake in the 2 to 3 wk before calving. It is difficult to overstate the central place of the transition period in dairy cow health and performance throughout lactation. The classic paper on homeorhesis by Bauman and Currie highlighted the challenges and complexity of the metabolic environment of high-producing dairy cows. Within a few years, several path models were published that described the interrelationships among diseases, and of feeding and management with disease in early lacta-

tion. These developments crystallized recognition of the importance of nutrition to many common disease and performance problems. As veterinarians increasingly sought upstream solutions; that is, prevention of disease, for many problems (milk fever, displaced abomasum, mastitis), an important realization was that nutrition played a key role. It is worth remembering that 25 yr ago, the notion that one could practically eliminate milk fever through diet was revolutionary. An early and notable success was the development and application of the concept of dietary cation-anion difference (DCAD) to prevent hypocalcemia. Elliot Block at McGill University advanced this approach, which was built on by David Beede, and Jesse Goff and Ronald Horst with the USDA. Refinements of manipulation of DCAD and new product development for its practical application continue through to the present.

Another example of successful research into links between nutrition and health is the very productive research effort from The Ohio State University in the 1990s on the associations of vitamin E and selenium with immune function and mastitis. Finally, research on feed intake, metabolic adaptation to negative energy balance, and the development and effects of fatty liver have been critical to improvement of understanding the pathophysiology of ketosis and displaced abomasum. Many investigators have contributed to this area, but David Morrow, Ric Grummer, Tom Herdt, James Drackley, and Tom Overton have particularly helped to advance knowledge toward disease prevention. This is an area of continuing research, with much still to be learned about both the fundamental biology of energy metabolism in transition dairy cows, and how to apply this knowledge to optimize health in commercial dairy herds.

In the last 20 yr, research on the physiology of bovine somatotropin and its implications for management has contributed massively to advancement of understanding of basic and applied aspects of metabolism and nutrition of high-producing dairy cows. Moreover, this technology has catalyzed debate over the relationship between production and health. It has helped to illustrate that high production is compatible with health, and requires attentive management to meet the needs of these "metabolic athletes."

These developments have helped to break down the compartmentalization of disease prevention between veterinarians, nutritionists, and animal scientists. Discussion and collaboration across disciplines has helped to broaden the approach to researchable questions from a reductionist perspective to a more holistic view. As such, the exchange of ideas and approaches between veterinarians and animal scientists, both in front-line



practice and in research, was a key development that continues to unfold.

### **Udder Health**

Mastitis control was already an important dairy health management initiative 25 yr ago. A 5-point mastitis control plan was developed in major extension efforts throughout the dairy industry. As a result, the practices of postmilking teat disinfection and blanket application of long-acting antibiotic therapy at drying-off were widely implemented. In addition, milking machine function, early detection and treatment of clinical cases, as well as identification and culling of chronically infected cows was emphasized. Starting about 25 yr ago, the use of somatic cell counts (SCC), as an indirect indicator of intramammary infection, became the standard method of monitoring bulk milk quality. Furthermore, DHI milk recording agencies began to offer the service of measuring SCC in individual cow composite milk samples on a monthly basis. Between these 2 sources of SCC data, dairy producers had the tools to accurately monitor their progress in the control of intramammary infections (IMI) and considerable progress was made. The European Economic Community, as well as other countries such as Canada, developed and implemented SCC penalty programs to force a considerable economic incentive for implementing the 5-point plan to bring herd level SCC under control. The industry dynamics, and the success associated with implementation of these programs are well documented. Several other countries, including the United States, have not emphasized aggressive SCC regulatory limits. In contrast, incentives for low SCC and other measures of milk quality have been offered at the local milk marketing level. A segment of producers are clearly motivated by such premium incentives. However, the overall success of these programs appears to be regional.

As the National Mastitis Council (NMC) mastitis control programs were widely adopted by the late 1980s, many of the major dairying regions of the world experienced changes in the expression of IMI in their herds. New IMI throughout the dry and periparturient periods, and clinical mastitis, became increasingly important. Understanding these changing dynamics of infection, as well as the prevention of both clinical and subclinical mastitis has been aided by the use of new nomenclature. Mastitis-causing bacteria have been classified into contagious and environmental pathogens, based upon important reservoirs and modes of transmission of each group. Changes in herd size, housing systems, and manure management have markedly increased the importance of environmental pathogens in the North American dairy industry. As emphasized

earlier, epidemiological studies have had a major impact on our understanding of the risk factors and biological interactions that result in an increase of environmental IMI. In addition, studies conducted in several countries have elucidated the incidence and risk factors involved with clinical mastitis on commercial dairy farms. Yet, significant challenges for the prevention of new IMI, primarily by environmental pathogens, remain an important focus of the dairy industry.

Meeting the challenges presented by environmental pathogens has required the emphasis of different aspects of mastitis control. For example, the management of milking, housing environment, and the dry period have become extremely important. Premilking udder preparation greatly influences the prevention of new IMI and maintenance of milk quality. In some regions, the practice of premilking teat disinfection has become widespread. Methods to improve and monitor stimulation of milk letdown, milk-out, and machine removal have also been widely implemented. The design and function of milking equipment, and milking techniques to optimize cleanliness, teat health, and milk flow have all been greatly advanced in last 2 decades. Appropriate installation, use, and evaluation of function of modern milking equipment continue to be extremely important. The design of free-stall housing systems has started to receive emphasis. The selection of stall surface and bedding material is known to have a major impact on the rate of new IMI by environmental pathogens. Although there is a large effect on manure management, considerable evidence points to sand as a preferred bedding material for both cow comfort and health.

There have been important revelations in our understanding of the role of the dry period on new IMI, and on subsequent clinical mastitis, in early lactation. Studies conducted in New Zealand, North America, and the United Kingdom have described the importance of management at drying-off, and the occurrence of teat-end closure in the dry period, as important factors for the prevention of infection. Long-acting dry cow antibiotic therapy has received renewed emphasis for the prevention of new IMI, in addition to its traditional role for the elimination of existing infections. However, methods to prevent new IMI in the dry period by protection of the teat-end with external or internal teat sealant products have been developed, evaluated, and implemented. The importance of the dry period for mastitis control, and for general health, remains as the focus of intense research and development.

Therapy of clinical mastitis remains a topic of considerable study and debate. No consistent approach to the early identification and treatment of clinical mastitis cases has been developed, even though a range of lactating intramammary and systemic antibiotic prepara-

tions is available, and their efficacies against the common mastitis pathogens are known. The risk and fear of antibiotic residues in milk, combined with a reasonably high rate of relapse and recurrent clinical signs, are valid reasons for concern. Thus, it remains that the management and advisory team for each farm needs to develop a farm-specific clinical mastitis treatment protocol that recognizes the predominant pathogens involved and monitors the success of the protocol. The usefulness of antibiotic treatment of subclinical IMI during lactation remains unknown, and merits further study. *Streptococcus agalactiae* has been greatly reduced. Conversely, *Staphylococcus aureus* remains a significant challenge, with very poor antibiotic treatment cure rates during lactation, and only moderate rates of cure with dry period therapy. However, the use of advanced epidemiological analytical tools has elucidated well-defined risk factors for failure of cure, allowing prospective decision-making on cows with particular chronic infections. In addition, the role of prepartum mastitis in heifers as an important aspect of mastitis control, especially for *Staph. aureus*, has improved. Rational use of antibiotics has become a major focus, and appropriate targeted treatment strategies remain extremely important in mastitis control programs.

Throughout the period in question, attempts to develop meaningful vaccination programs to prevent mastitis in dairy cattle have been described. In general, the progress in this area is disappointing. However, the development and widespread implementation of core-antigen coliform mastitis vaccines has reduced the incidence of severe clinical mastitis, and considerably reduced mortality due to coliform mastitis. This is also a major advance in that it was, and remains, one of the few disease prevention strategies with the economic benefits well described at the herd level and used in practice.

The development of record systems and monitoring tools has been particularly impressive and important for mastitis control. Clinical mastitis recording systems and automated incorporation and analysis of individual cow SCC data have allowed dairy producers and their advisors to make decisions and evaluate their success on an on-going basis. There is a need for greater incorporation of information on the microbiological identification of the bacterial agents involved. The prospects for substantial improvements in this area are encouraging. Recently, new diagnostic techniques such as DNA fingerprinting of mastitis pathogens have helped to better describe the epidemiology of mastitis, factors associated with virulence, and profiles determining the source and chronicity of infections. These tools have greatly increased our ability to follow infections, and in turn have challenged existing paradigms about the behavior of

environmental and contagious organisms. For example, situations where streptococci and *E. coli* have become persistent infections have been documented. Further studies are needed to continue to build our knowledge to combat the ever-diversifying nature of organisms that cause mastitis, as well as a more complex and conditional understanding of the interactions of animal, bacteria, and environment in mastitis.

Many scientists have contributed to advancement in the field of mastitis prevention. Ian Dohoo, Ynte Schukken, and Pamela Ruegg have significantly advanced our expertise with SCC and other diagnostic tests used in mastitis monitoring. Landmark work by Larry Smith and Joe Hogan has greatly improved knowledge in the area of environmental mastitis control.

Eric Hillerton, Murray Woolford, Elizabeth Berry, Andrew Bradley, and Randy Dingwell have clearly contributed to our understanding of the dry period, and the control of mastitis in dry cows. Ynte Schukken, Joe Hogan, Ron Erskine, and Herman Barkema have done seminal studies on clinical mastitis and its therapy. Stephen Oliver, Steve Nickerson, Woodrow Pankey, and Larry Fox should be recognized for advancing our knowledge of *Staph. aureus* and prepartum mastitis in heifers. Graeme Mein, Doug Reineman, and Jeffrey Reneau have been notable contributors to the advancement of knowledge and practice in the areas of machine function and milking management. It is important to state that throughout the last 25 yr scientific publications on mastitis control have been extremely abundant. Thus, many other authors have contributed to our knowledge in this area.

### Immunology

A key advance in the last 25 yr is recognition of the importance of immune function, and a better understanding of it, including normal function and insights into peripartum immunosuppression. Great advances have been made in describing elements of immune function in dairy cows in increasing detail. Studies in the 1980s and 1990s that documented impaired innate and specific immune function in the peripartum period were a significant advance in understanding the heightened risk and incidence of disease in the transition period. New molecular and genetic techniques promise to make this an area for huge advances in the next 25 yr. Recognition of the importance of immune function for mammary and uterine health continues to grow. Prevention of retained placenta, metritis, endometritis, and mastitis through enhanced immune function are still elusive, but increasingly refined recognition of where to focus investigative efforts is likely to yield more specific and effective preventive strategies in the foreseeable future.



Genetic markers for immune function, and genetic selection for disease resistance have just begun to be developed, but are likely to receive increasing attention. There remain substantial gaps between laboratory assays of immune function, the animal and herd level incidence of mastitis or uterine disease, and the ability to practically enhance immune function through nutrition, management, or genetic selection. For example, it was demonstrated over 20 yr ago that impaired chemotaxis of white blood cells was strongly associated with retained placenta, and that this was measurable at 1 wk prepartum. Recently, this work was confirmed and built upon to describe the specific cells involved (neutrophils), and particular aspects of their function (reduced chemotaxis and intracellular killing), as well as a specific cytokine (IL-8), that are predictive of the occurrence of retained placenta. Presently, genomic microarray technology is being used to investigate changes in particular genes that occur in the transition period and may be associated with the risk of immune function-related diseases. These developments are fascinating and should lead to better prevention and control of disease, in part due to improved genetic selection. Even though this knowledge reinforces the importance of immune function in the transition period, it has not yet translated into an ability to be used in management decisions to prevent disease. To apply new knowledge in immunology, field studies are required to complement laboratory-based investigations, to test the ability of differences observed at the gene, molecular, or cell function levels to be expressed and measured at the economically important cow and herd levels.

Advances have also been made in applied immunology. For example, veterinarians and producers are increasingly demanding well-designed disease challenge studies and clinical field trials to document vaccine efficacy. There has been a move to strategically timed use of vaccines, and new approaches and options for the use of modified live vaccines. In particular, modified live virus vaccines have become safer, allowing exploitation of their benefits for disease prevention. Notable progress has been made in understanding bovine virus diarrhea virus. In the last 25 yr, the unique ability of this virus to produce persistently infected calves by infection of the fetus in early pregnancy, and the role of these persistently infected animals as massive shedders of virus has come to be recognized. Additionally, numerous manifestations of BVD (mucosal disease, respiratory disease, abortion, congenital defects, infertility, hemorrhagic disorders, immunosuppression) have been described and are being targeted for protection through immune modulation. In the last 15 yr, 2 genotypes of BVD virus (types I and II, and subtypes) with different clinical behaviors were distinguished and vac-

cines have been changed to include both types. Recently, progress in the development and use of vaccines has improved the possibility of fetal protection against BVD virus, greatly reducing the risk of production of a calf persistently infected with BVD. Additionally, new diagnostic tools for BVD virus, immunohistochemistry in particular, have greatly advanced the ability to identify infected animals accurately and early.

### **Cow Comfort**

Although the concept of animal husbandry is as old as farming itself, renewed focus has been placed on understanding and meeting the behavioral and environmental needs of dairy cows in the last 10 yr. The development of open, curtain-sided free-stall barns has allowed the development of larger dairies in cold and wet climates while reducing the incidence of respiratory disease. Additionally, the health and performance effects of heat stress on dairy cows have been quantified, and new means to abate heat stress have been developed. Dennis Armstrong (University of Arizona) and John Smith (Kansas State University) have been leaders in this area. Broadening of the concept of disease as discussed at the outset makes the effects of failure to meet cows' behavioral needs a disease condition in itself. Additionally, as free-stall housing has come to predominate in the industry, there has been increased recognition of the prevalence and importance of lameness. The interactions of housing, nutrition, and physiologic changes that contribute to the occurrence of lameness have been investigated, but much remains to be learned. The science of lameness prevention is starting to accelerate and E. Toussaint-Raven, Sarel van Amstel, Jan Shearer, and Roger Blowey have been leaders in the advancement of the principles and practice of hoof trimming. Furthermore, the direct and indirect effects of heat stress (even in temperate regions), social stress, lack of lying time, and abnormal feed intake patterns on lameness, immune function, disease, and performance are being quantified. Although ongoing research is needed, a major advance recently has been application of both insightful empirical observations (Gordie Jones, Neil Anderson, Bill Bickert, and Doug Young) and formal studies in applied ethology (from the research group led by Daniel Weary at the University of British Columbia, and Nigel Cook and Ken Nordlund at the University of Wisconsin) to improve the design of stalls to optimize cow welfare. In part because of these advances in scientific information, the veterinary profession and the dairy industry must grapple with the difficult questions of how to strike a thoughtful balance between issues of animal preference, animal comfort, well-being, production, efficiency, environmen-

tal considerations, human working conditions, and economic sustainability in food production.

### **Calf Health**

Several large surveys of calf management, morbidity, and mortality in the United States and Canada have been conducted in the last 25 yr and have placed renewed focus on perinatal calf health. Research on passive transfer of immunity has resulted in new best management practices (e.g., tube-feeding 4 L of colostrum at birth) and strategies to monitor management (e.g., systematic measurement of serum total protein). The use of coccidiostats has greatly reduced disease in calves and heifers due to these parasites. Recently, techniques for and benefits of pasteurization of colostrum and milk for calves have been investigated, and this practice is increasingly being adopted in the field. There has been a major shift toward seeking improved calf health through timely and adequate colostrum feeding, and swift removal of calves from the environment of confinement housing for adult cows, particularly to calf hutches. During the last 25 yr, producers have been empirically investigating a variety of calf housing systems from hutches to individual pens in naturally ventilated barns to group housing and feeding in an attempt to balance calf health with systems conducive to attentive care by the people working with the calves. The investigation and education efforts of Sheila McGuirk and Sandra Godden related to calf health merit mention.

### **Tools for Monitoring**

As dairy herd advisors have become more numerate and analytical, the need for tools to collect and interpret data easily and validly developed rapidly. Veterinarians, notably Steve Eicker and Connor Jameson, have been major contributors to the development of on-farm dairy data management systems and herd analytic software. The objectives of this activity extend beyond disease prevention, but these tools nevertheless are an essential component of health management. There are a number of useful software tools available, and a particular advance has been the integration of DHI, herd, and veterinary software with largely successful sharing of data. The ability to integrate and analyze farm-specific data has led to earlier detection of health problems, and tailoring of disease prevention efforts to individual herd needs. Unfortunately, standardized, valid, and systematically recorded health data at the herd level, and especially at the regional or national levels are piecemeal at best, and nonexistent at worst. To quantify trends in disease prevention at the herd or population

levels will require more streamlined data capture and better incentives for producers to record data faithfully.

Rapid, relatively inexpensive metabolic tests (e.g., blood tests for calcium and nonesterified fatty acids, and urine and milk tests for  $\beta$ -hydroxybutyrate) which can be run on-farm, in local veterinary clinics, or cow-side have become available. These tools are useful for investigation of outbreaks of clinical disease and for routine monitoring of subclinical disease. The optimum strategies for collection, interpretation, and application of these data are still being developed, but promise to help to gain a window on the success of delivery of preventive health management in transition cows.

## **CONCLUSIONS**

Perhaps the single biggest advance in dairy health in the last 25 yr has been the paradigm shift to focus on disease prevention, rather than treatment. The key contributors to progress in health management in the last generation include using epidemiology to better study the determinants of disease, integration of the disciplines of veterinary medicine and animal science, and renewed focus on using science to advance health and husbandry of dairy cattle. Major advances have been made in the last 25 yr in the prevention of milk fever, contagious mastitis, and severe coliform mastitis. During this time, average herd size and milk production per cow have increased dramatically. Despite these increased demands on cows' metabolism and humans' management skills, the incidence of most common and important diseases has remained stable. Great progress has been made in understanding the biology of energy metabolism and immune function dairy cows in transition, the time at which the majority of disease occurs. This, coupled with emerging understanding of how best to provide for dairy cows' behavioral needs, promises to be the foundation for progress in maintenance and enhancement of the health of dairy cows in the next 25 yr.

There is an ongoing challenge for prevention of many diseases; although there is still much to learn, information already exists to substantially reduce or prevent the disease altogether—the challenge is in effectively and consistently implementing the required management practices. Ever-better understanding of epidemiology and pathophysiology will not in itself reduce the incidence of disease. The ability to translate emerging knowledge into on-farm application and actual prevention of problems requires understanding of the farm as an integrated system, a major component of which is educating and motivating humans to implement well-designed practices. Understanding and accomplishing

this final major step in the disease prevention process is both an advance and an ongoing challenge.

Over the past 6 decades, advances in disease control and dairy productivity have required that professionals repeatedly shift their focus to a broader perspective and expand the array of methodologies used. Thus, we have made the leap from the sick individual, to disease control and eradication in groups, to the health and productivity of cows on a dairy, to the health and productivity of a nation's herd. The focus today rests mainly on the production system until the milk truck leaves the farm. The next challenge will be to broaden the perspective once again, this time to encompass the entire food system, including issues of food safety, product development, environmental issues, consumer demands, food supply and security, and the role of the dairy industry in society as a whole.

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