

3 Mastitis vaccines: Past, present, and future. G. M. Tomita^{*1}, B. G. Talbot², P. Lacasse³, A. A. Potter⁴, X. Zhao⁵, J. Lee⁵, and D. T. Scholl¹, ¹University of Montreal, Saint Hyacinthe, Quebec, Canada, ²University of Sherbrooke, Sherbrooke, Quebec, Canada, ³AAFC-Dairy and Swine R&D, Lennoxville, Quebec, Canada, ⁴University of Saskatchewan, Saskatoon, Saskatchewan, Canada, ⁵McGill University, Montreal, Quebec, Canada.

Recommended mastitis control practices are at times inadequate in coping with the complex epidemiology of this disease. Therefore, the concept of immunization to enhance resistance to mastitis is a logical approach to augment existing mastitis control procedures. Mastitis vaccine research in the past has led to the commercialization of several products. Cows vaccinated with coliform mastitis vaccines are reported to have a lower incidence and duration of clinical mastitis. However, vaccinated cows are still infected at the same rate as nonvaccinated cows. The administration of vaccines against *Staphylococcus aureus* mastitis has been shown to enhance spontaneous cure rates, but vaccination did not prevent new infections. Therefore, improvements are needed. Advancements in the field of microbial pathogenesis, genomics, and bovine immunology have made the identification of protective antigens a relatively straightforward task. The challenge has been to incorporate these antigens into an effective product. Researchers are currently formulating the next generation of mastitis vaccines which are based on cross-protective antigens from coliform bacteria, *S. aureus*, and *Streptococcus* species. Most vaccines in use today are still formulated and delivered in the same manner as those produced 30 years ago and this will likely be the rate limiting step in the improvement of mastitis vaccine efficacy. The incorporation of novel immunomodulators such as CpG oligodeoxynucleotides, and the employment of alternative vaccine delivery methods such as antigen microencapsulation have the potential to increase the magnitude and quality of the immune response. A successful mastitis vaccine will serve as an additional mastitis control tool in a comprehensive udder health management program. Immunization will complement, but not replace management practices that promote reduction of teat end exposure to pathogens.

Key Words: Mastitis, Vaccines, Immunization

4 Management strategies to maintain udder health. D. Kelton^{*}, University of Guelph, Guelph, ON, Canada.

Management strategies employed by Canadian dairy producers to maintain udder health are based on the National Mastitis Council's Ten-Point Plan, encompassing the three broad areas of monitoring, prevention and therapy. The adoption of this plan is supported by an informal network of dairy veterinarians, extension workers and regulatory personnel, who together with the research community are in the process of formalizing a national mastitis network.

Prevention of mastitis is encouraged through the enforcement of somatic cell count (SCC) regulatory limits and the staged implementation of the Canadian Quality Milk (CQM) program. A key component to the CQM is the establishment of standard operating procedures on every farm to ensure that milk is harvested in a manner that safeguards the health of the cow and the product. Current emphasis on providing each cow with a clean and comfortable environ-

ment, and on reducing peri-partum disease, are also key components of this effort. A recent study involving over 300 Ontario tie-stall dairy farms confirms the relationship between inadequate stall size and increased SCC at the herd level.

Treatment of sub-clinical mastitis is based on sound dry cow management, which includes the standard recommendation of treating every quarter of every cow. The strategic use of teat sealers/sealants plays a role in preventing new infections during the dry period in some herds. Clinical cases must be appropriately identified, etiologically classified and where appropriate treated based on clearly defined protocols which are consistent with the guidelines established in the CQM program.

Monitoring of udder health is critical to the process, and with approximately 75% of Canadian dairy producers enrolled in milk recording and subscribing to monthly SCC services, there is a strong foundation for this process. Current and future efforts to link diagnostic laboratory culture results to on-farm herd management systems containing clinical case records and SCC data will greatly enhance the monitoring capacity.

5 Mammary tissue damage during mastitis: causes and controls. X. Zhao^{*1} and P. Lacasse², ¹McGill University, Ste Anne de Bellevue, Quebec, Canada, ²Agriculture and Agri-Food Canada, Lennoxville, Quebec, Canada.

It is well known that mastitis reduces milk production. However, exact underlying mechanisms are not fully understood. Mammary tissue damage causes a reduction of the number and activity of epithelial cells and consequently contributes to decreased milk production. There are two distinct types of cell death, apoptosis and necrosis. Both have been reported to occur during mastitis. Various factors contribute to epithelial tissue damage. Certain bacteria produce toxins that destroy cell membranes and damage milk producing tissue, while other bacteria are able to invade and multiply within the bovine mammary epithelial cells before causing the damage. Breakdown of the extracellular matrix by the plasmin/plasminogen system can also lead to death of epithelial cells. Probably more important but less obvious players are somatic cells, in particular neutrophils. They are predominant cells in the mammary gland during infection. Their major function is to phagocytose and destroy infectious agents. In addition, they limit the growth of some microbes. At the same time, they can potentially harm the mammary tissue by releasing reactive oxygen intermediates and proteolytic enzymes. Different signaling and biochemical pathways leading to tissue damage are being delineated. An *in vitro* co-culture system with activated neutrophils and mammary epithelial cells has been adopted by us to study the potential value of various antioxidant, chelators and enzyme compounds for reducing the damage. The promising compounds were further evaluated using *in vivo* challenge studies. The future challenge is to find economical feed containing active compounds for field study and application. Understanding the biochemical and cellular changes in the mammary gland during mastitis will ultimately lead to means of manipulating mammary function to alleviate the loss of milk production during mastitis.

Key Words: Bovine, Mammary Gland, Mastitis

CSAS Vitamin: Vitamin Nutrition of Livestock Animals

6 Vitamin nutrition of livestock animals: Overview from vitamin discovery to today. L. McDowell^{*}, University of Florida, Gainesville.

There are 15 vitamins that are of significance to livestock. The term vitamin(e) was first used in 1911-1912. What were later to be known as vitamin deficiency diseases, such as scurvy, beriberi, night blindness and xerophthalmia had plagued the world from antiquity. Around the turn of the 20th century laboratory animals were found not to survive on purified diets containing only fat, protein, carbohydrate, salts and water. Natural foods (e.g. milk) was found to contain small quantities of "unknown substances essential to life?". Experiments with animals contributed greatly from 1900 through the 1930s to the discovery of vitamins. The development of the concept of vitamins can be roughly divided into four

(broadly overlapping) periods. 1) Empirical healing of some diseases by administration of certain foods. 2) Development of analytical capabilities to identify classes of nutrients in foods. 3) Experimental induction of dietary diseases in animals; and 4) Administration of synthetic diets to discover essential nutritional factors. In the 1950s to the present, vitamin deficiencies became more common place when livestock were denied pasture and moved into confinement. Today typical grain-oilseed meal (e.g. corn-soybean meal) monogastric diets are generally supplemented with most vitamins, thiamin and vitamin B₆ seem to be less likely deficient. A number of factors influence vitamin requirements and vitamin utilization and include: physiological make-up and production function; confinement rearing without pasture; stress, disease and adverse environmental conditions; vitamin antagonist, use of antimicrobial drugs, and

body vitamin reserves. Under commercial livestock and poultry production conditions, vitamin allowances higher than NRC requirements may be needed to allow optimum performance. Generally, the optimum vitamin supplementation level is the quantity that achieves the best growth rate, feed utilization, health (including immune competency), and provides adequate body reserves.

Key Words: Vitamins, History, Requirements

7 Enhancing the vitamin content of meat and eggs: Implications for the human diet. A. Sahlin and J. D. House*, *University of Manitoba, Winnipeg, MB, Canada.*

Enhancing the vitamin content of meat and eggs provides an opportunity to increase the level of key nutrients, especially those deemed to be at marginal or insufficient levels in the human diet for optimal health and well-being. In general, enhancement efforts have focused on the development of feeding strategies to achieve optimal vitamin levels in meat and eggs. The definition of an optimal strategy however is influenced by such factors as: 1) the efficiency of transfer of the vitamin into the final product, 2) the impact on animal performance or health, 3) the impact on the quality characteristics of the final product, and 4) economic considerations. Vitamins are an extremely diverse class of nutrient, in terms of chemical and physical properties. Each vitamin differs with respect to stability during processing, susceptibility to bioconversion within the intestinal tract, digestibility, transport and storage within tissues. Therefore, the development of vitamin-enriched meat and eggs will be highly dependent on the interaction of multiple factors. Ultimately, the success of such strategies must be judged against the contribution the enriched products make to the human diet, in terms of vitamin intake, and in the acceptance of the products by the consumer.

Key Words: Vitamin, Meat, Eggs

8 Impact of B-vitamin supply on major metabolic pathways of lactating dairy cows. C. L. Girard* and J. J. Matte, *Agriculture et Agroalimentaire Canada, Lennoxville, Québec, Canada.*

Knowledge on dairy cow requirements for major nutrients increased substantially during the last decade and they have been extensively applied in dairy cow nutrition. However, little is known on the importance and the roles of B-vitamins. Most of those vitamins act as essential cofactors in energy, protein and lipid metabolism, it is likely that as milk yield increases, the demand for these cofactors also increases. In dairy cows, the supply in those vitamins from synthesis by the ruminal microflora is generally sufficient to avoid deficiency symptoms but could be suboptimal when it comes to optimize metabolic efficiency, production, composition and nutritional quality of milk. Results from recent experiments highlight how the supply in B-vitamins, especially folic acid, biotin and vitamin B₁₂, impacts on the major metabolic pathways. For example, supplemental biotin given during the first 100 days of lactation increased milk and true protein yield without effect on feed intake, plasma concentrations of glucose, insulin or non-esterified fatty acids (NEFA) nor on molar percentages of acetate, propionate and butyrate in ruminal fluid. Supplemental vitamin B₁₂ and biotin given between 118 and 174 days of lactation increased the amount of glucose and decreased the amounts of volatile fatty acids and ammonia from the gastrointestinal tract and increased milk, milk protein and casein yields without changes in dry matter intake. Vitamin B₁₂ utilization was increased in cows fed simultaneously supplementary folic acid and possibly, more so in extra-hepatic tissues. Moreover, in those cows fed supplementary folic acid, plasma glucose was increased by vitamin B₁₂ supplementation while plasma biotin tended to be decreased. Vitamin B₁₂ also reduced accumulation of lipids in liver that was observed when folic acid was given alone. In conclusion, it appears from those results that there is a need to review the paradigm according to which synthesis of B-vitamins by ruminal microflora is sufficient to meet dairy cow requirements under all circumstances.

Key Words: Dairy Cow, B-Vitamins, Metabolism

9 Fat-soluble vitamins in reproducing animals: physiological and nutritional basis. F. J. Schweigert*, *University of Potsdam, Potsdam, Germany.*

The general importance of fat-soluble vitamins especially vitamin E, vitamin A and its nutritional precursor b-carotene in reproducing animals has been characterized based on response variables such as the prevalence of overt signs of deficiency, reproductive performance and milk production rate. The substantially increase in performance in farm animals such as milk production in cows has substantially changed the feeding and management e.g. for cows (less pasture, less forage, and more total confinement) and thus resulted in changed (increased) vitamin requirements. The review will focus on the importance of fat-soluble vitamins (especially vitamin E, vitamin A and its precursor b-carotene) in reproducing animals under these changed variables. Both, vitamin E and β-carotene might exert their function due to their antioxidant properties. Especially vitamin A through its active metabolite retinoic acid but possibly also b-carotene as molecule per se or by products of its metabolism as well as vitamin E can modulate gene expression through interaction with nuclear receptors. This aspect is of specific importance in ovulation, embryonic development and mammary gland development. Additionally an optimal supply of the mother is of importance for an early and efficient supplementation of the newborn through milk.

Key Words: Nutrition, Fat-Soluble vitamins, Reproduction

10 Choline metabolism for high-producing dairy cows: metabolic and nutritional basis. A. Baldi* and L. Pinotti, *University of Milan, Via Celoria, Milano, Italy.*

Choline, the beta-hydroxyethyltrimethylammonium ion, is a strong base containing a trimethylated quaternary nitrogen. Choline occurs widely in biological materials as the compound itself, as acetylcholine and as various phospholipids. In feed ingredients and crude unprocessed fat sources most choline is present as phosphatidylcholine (lecithin). Relatively rich sources of choline are soyabean, soyabean meal, rapeseed meal, fish meal and dried yeast. However in these feedstuffs, the dietary bioavailability of choline is considered "moderate". In dairy ruminants, choline is extensively degraded in the rumen; for this reason dietary choline contributes insignificantly to the choline body pool and methyl group metabolism is generally conservative with a relatively low rate of methyl catabolism and an elevated rate of de novo synthesis of methyl groups via the tetrahydrofolate system. The primary source of methylneogenesis, via the tetrahydrofolate system, is derived from gluconeogenic precursors, which depending of the energy balance and of physiological state, can be deficient in ruminants. Consequently, in time of glucose imbalance, for instance at the onset of lactation in dairy cows, the extra demand for methyl groups may have a negative impact on milk production, making reasonable to hypothesize that choline could be limiting nutrient for lactating dairy cows. Moreover, choline as a lipotropic substance may optimise the balance between the fat retained and metabolized by the liver, and hence improve lipid metabolism in general. Our findings herein presented are in line with these assumptions indicating that supplementation of choline, which can escape degradation in the rumen, may help to improve not only methyl groups metabolism but also other nutrient status (e.g. vitamin E).

Key Words: Dairy Cow, Choline, Metabolism

11 Folic acid and vitamin B₁₂ in reproducing sows: New concepts. J. J. Matte* and C. L. Girard, *Dairy and Swine R & D Centre, Agriculture and Agri-Food Canada, Lennoxville, QC, Canada.*

In pig nutrition, the lack of and/or the outdated information on B-complex vitamins is an important factor for empiricism and disparities in dietary recommendations. This is particularly the case for folic acid (B₉) and vitamin B₁₂. Recent studies suggest that the beneficial effects of B₉ on sow prolificacy would be due to enhanced embryo development and survival. Embryo synthesis of oestrogens and uterine secretions of prostanoids and cytokines during attachment appears to be key factors involved in this B₉ regulation of embryo devel-

opment. Nevertheless, those embryo and uterine responses to B₉ are often more pronounced in multiparous sows than in gilts. This parity effect on B₉ responses could be attributed to the metabolic interaction with another vitamin, B₁₂. Those two vitamins are essential to modulate the transfer of one-carbon groups for protein and DNA synthesis, methylation and gene expression. The metabolic pathway involved is the remethylation of methionine from an intermediary metabolite, homocysteine (Hcy). A deficiency in B₉ or B₁₂ may induce a local or systemic accumulation of Hcy, a powerful pro-oxidant known to impair embryo development. It appears that the B₁₂ status, which is about 2 times lower in gilts than in multiparous sows, could be a limiting factor to the B₉ action on uterus and embryo metabolisms during the first pregnancy. This B₁₂ status is

particularly critical since the sow uterus drained in early gestation massive amounts of B₁₂, representing 2 to 3 times the B₁₂ plasma pool. Dietary B₁₂, at levels 10 times higher than recommended, maximized B₁₂ status and minimized Hcy accumulation in first parity sows. It appears that an optimum ratio B₉:B₁₂, yet to be estimated, would allow the full beneficial response of B₉ on sow prolificacy. In the future, it is likely that the need for updated information on requirements for B-complex vitamins will be enhanced taking into account the "dietary fine tuning" required with the highly producing pigs selected during the last decades.

Key Words: Folic Acid, Vitamin B₁₂, Sow

Genomics: Functional Genomics for Livestock Improvement

12 What is functional genomics? J. Pérez Laspiur* and T. Ferris, *Michigan State University, East Lansing.*

In the past, we have attempted to understand the physiological responses of livestock to stressors, such as environmental conditions and husbandry practices, and their impact on performance traits. Further, we have selected livestock using quantitative approaches that involve estimating the effects of all genes affecting these traits without knowing the specific role of any of these genes. Evident phenotypic traits are a combination of internal (genetics) and external (environment) factors working jointly. Although we have advanced in our understanding of the role that external factors play on the occurrence of important phenotypic traits, we lag behind in our understanding of the genetic factors that affect these same traits. With the recent completion of the bovine genome sequence and availability of high-throughput technology, a functional genomics approach can now be used to simultaneously investigate disturbances in expression of thousands of genes in relation to environmental and physiological challenges. This approach allows us to determine what groups of genes and pathways are responsible for, or correlated with, - metabolic changes and how these may be manipulated to improve performance and well-being of cattle. Functional genomics therefore has the potential to highlight significant new candidate genes to improve genetic selection programs and to evaluate the effect of various practices on multiple systems within an animal. A vital contribution of these studies is the integration of physiological, nutritional, and genetic data to develop public resources for cattle. These resources will help answer questions concerning genes involved in milk production, milk quality and composition, and response to husbandry stressors. Eventually, this knowledge will further aid in selection and management of livestock.

Key Words: Functional Genomics, Genetic Improvement

13 Implications of functional genomics for animal breeding programs. J. C. M. Dekkers*, *Iowa State University, Ames.*

Current selection programs in livestock are primarily based on selection on EBV for traits of economic importance, that are estimated from phenotypic records. These EBV provide an estimate the collective effects of all genes that affect the trait, without knowing where the genes that control the trait are located in the genome or what their individual effects are. Thus, although this quantitative genetic approach to selection has been effective for many traits, it is essentially a black-box approach. In the past decade, much research has been conducted to locate so-called Quantitative Trait Loci (QTL), which are regions in the genome that contain genes that affect the trait and which can be identified using molecular markers that are linked to the QTL. In most cases, however, the actual location, identity, and functional role of the QTL remains unknown. Thus, QTL mapping has essentially subdivided the black box of quantitative genetics into multiple smaller black boxes. Examples where the causative gene for the QTL has been identified are limited. Although markers that are linked to QTL can be used to enhance genetic progress through marker-assisted selection, there are limitations to such selection. In addition, the ability to identify QTL is limited for traits that are difficult or expensive to record. The purpose of this presentation is to describe and discuss how functional genomics

can enhance the discovery of genes that control traits of importance and how the knowledge functional genomics promises to provide on gene function could be used in the future to enhance selection programs, management programs, and the integration of selection and management programs.

Key Words: Functional Genomics, Selection, Marker-Assisted Selection

14 Use of functional genomics in genetic selection programs for environmental stress tolerance in dairy cattle. R. Collier*, C. Stiening¹, B. Pollard¹, M. VanBaale¹, and P. Coussens², ¹*University of Arizona, Tucson,* ²*Michigan State University, East Lansing.*

Selection for tolerance to environmental stress has traditionally been counterproductive in domestic animal production. As animals acclimatize to environmental stressors they reduce or divert metabolizable energy from production to balance heat gain and loss. Thus, it has generally been faster and easier to obtain production increases by altering the environment around animals. However, environmental modification comes at a high cost and in some cases these costs cannot be economically justified. Ideally, one would like to simultaneously select for increased production and thermal resistance to increased thermal load. In order to do this the genes associated with acclimatization need to be identified. In acclimatization, the body's response to the environment is coordinated in two phases (acute and chronic) over a several week period at the structural, organ, cellular and molecular level to respond the stress or stressors with alterations in the organism's capacity to tolerate the stress. These changes include alteration in gene expression, enzyme activity, cell receptor populations, body organ size, fat deposition, energy consumption and a wide variety of other possible effector mechanisms depending on the stressors. Targets of potential genetic manipulation would include increased efficiency and capacity of thermal effectors and delayed onset of temperature threshold for thermal injury. We have identified a group of genes associated with the heat shock response in bovine mammary tissue. We have also identified factors associated with altered sweating rate in cattle. Presentation will focus on strategies to improve heat shock response and sweating rate to improve thermal tolerance in dairy cattle.

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Key Words: Acclimation, Heat Stress, Functional Genomics

15 Functional genomics of reproductive tissues: Creating new knowledge that can be used to solve infertility in farm animals. M. C. Lucy*, *University of Missouri, Columbia.*

Reproductive tissues express mRNA for a large number of genes. The full complement of expressed mRNA is unknown and sequencing projects typically find a large number of unique mRNA within the reproductive tract. The function of the proteins that arise from the expressed mRNA is either unknown or poorly understood. Furthermore, genes with recognized functions may have alterna-