multiparous from d 2 to 5, d 2 to 14, d 2 to Peak, d 5 to 10, d 5 to 14, d 5 to Peak and d 10 to 14 (0.2, 1.0, 1.0, 1.2, 1.6, 1.4 and 2.2 vs. −0.1, 0.8, 0.9, 0.9, 1.4, 1.3 and 2.0, respectively). Cows that conceived, regardless of whether or not they suffered pregnancy loss, had greater P4 concentrations (except on d 2) and a greater rate of P4 increase than open cows. Also, primiparous cows consistently had greater P4 concentrations and rate of increase than multiparous cows.

Key Words: in-line milk progesterone, estrous cycle, fertility

CSAS SYMPOSIUM: REDUCING THE USE OF ANTIBIOTICS IN LIVESTOCK PRODUCTION

0492   Alternatives to antibiotics in swine and poultry.
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To reduce the risk for the spread of antibiotic resistant bacteria from livestock to humans, the European Union banned the use of antibiotics as growth promoters in animal feeds for pigs and poultry since January 2006. As a result, the use of veterinary prescribed antibiotics increased in a sort of compensation phenomenon. In intensive husbandry systems, veterinary prescribed antibiotics are mainly used around birth and in newborn animals.

To study the effects of antibiotic usage during early life stages, we performed several experiments in piglets and poultry. We analyzed both the short-time and long-term effects at the level of intestinal microbiota and intestinal mucosal functions. To this end, we applied metagenomics, transcriptomic and immunologic analytical approaches on intestinal tissues and luminal contents, taken at different intestinal locations and at different time-points after treatment. These studies clearly demonstrated both short-term and long-term effect on the expression of immune related genes. We hypothesized that that these long-lasting effects are due to differences in the programming of the gut immune system as induced by the temporary early life perturbation of the gut microbiota.

To search for alternatives for antibiotic growth promoters, a large variety of farming approaches are proposed, including organic acids, probiotics and prebiotics, enzyme, clays and minerals, trace elements, and botanicals. In this presentation, we will show the effect of the administration of fructooligosaccharides (FOS) to suckling piglets on intestinal microbiota and gene expression. Twelve days of intervention with FOS resulted in a bifidogenic effect in the colon of treated piglets. Furthermore, after 23 d of intervention with FOS, decreased

expression in immune related gene sets was observed in treated piglets.

In this context, it is also important to identify major intrinsic and extrinsic factors that (co)determine the early life gut microbial colonization of livestock species. From literature it is already known that several extrinsic factors are important, including the sow/mother-hen and the environment. Here we show data that indicate that also the genetic make-up of host is an important factor in the early life microbial colonization of the gut and consequently for immune system development.

In conclusion, during early life, the interplay between the host (genetics), environment (nutrition and/or management), in association with the microbiota modulate bacterial colonization, drives gut development and immune maturation. The use of antibiotics during early life stages perturbs this interplay significantly with serious consequences for the functionality of the host immune system.

0493   Management of dairy cows to improve resistance to infectious diseases.
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The incidence of infectious diseases varies greatly during the lactation cycle. Most new cases of clinical mastitis appear at the beginning of lactation (transition period), and the incidence increases with the level of milk production. In addition to mastitis, the majority of other infectious diseases becomes clinically apparent during the first 2 wk of lactation. During this time, cows are in negative energy balance and they must mobilize body reserves to balance the deficit between food energy intake and energy required for milk production. Cows undergoing energy deficit have a weakened immune system, which increases their susceptibility to infections. Therefore, we evaluated the effects on blood metabolite concentrations and immune functions of limiting milk production in early lactation to reduce the negative energy balance. In a first experiment, multiparous Holstein cows were milked either once a day or twice a day for the first postpartum week. In a second experiment, the amount of milk harvested was limited by milking cows incompletely (about one-third of expected milk production was collected) twice a day until d 5 after calving. In a third experiment, first-wk milk production was limited by administering a prolactin secretion inhibitor, quinagolide, during the first days of lactation. Globally, the results of these studies indicate that reducing the amount of milk harvested postpartum while maintaining milking stimuli reduces metabolic stress and immunosuppression without compromising productivity of high-yielding dairy cows. The second period that has the highest incidence of new intramammary infections

(IMI) is the period immediately following drying-off, during early mammary gland involution. The importance of the dry period is often underestimated as many of these new infections are only detected after the next calving. A cow's risk of acquiring a new IMI during the dry period increases with milk production at drying-off but decreases as mammary gland involution progresses. In this context, we tested whether prolactin inhibition could be used to reduce milk production at drying-off and to accelerate the rate of mammary involution after cessation of milking. In late-lactation cows, quinagolide decreased milk production within the first day of treatment and induced more rapid changes in concentrations of several markers of mammary gland involution after drying-off. In addition, quinagolide improved the resistance to IMI suggesting that prolactin inhibition could be a new strategy for facilitating drying-off. Innovative management can be used to reduce dairy cow's susceptibility to infection and antibiotic utilization.

Key Words: mastitis, transition period, blood metabolites

0494   Selection for disease resistance in swine.
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Infectious disease is a major problem for swine production around the world despite successes in terms of biosecurity and vaccination. Perhaps the best known examples of disease resistance pertain to infection with *E. coli* F4 (K88) or F18, which cause scours in young pigs and can result in significant morbidity and mortality. In other cases, there is variation in susceptibility but all pigs become sick. Porcine respiratory and reproduction syndrome (PRRS) is an example of a disease where all pigs are infected by PRRSV but the impact on the host varies. For example, the amount of virus produced and the growth of the infected pigs varies significantly between individuals. Genome wide association studies identified a relatively large effect on chromosome 4 (SSC4) and Boddicker et al. (2012 *J. Anim Sci* 90:1733) reported that this region explained 15.7% of the genetic variance for viral load and 11.2% for gain. Subsequently a putative functional variant in *GBP5* was identified as the likely causative mutation (Koltes et al., 2015 *BMC Genomics* 16:412). Two regions of the genome were identified as explaining a similar amount of variation in PCV2 susceptibility (Engle et al., 2014 *Proc. 10th WCGALP).* Although these findings offer potential tools to reduce the impact of these two major viruses through genomic assisted selection, it would be very difficult to combine such tools for all of the important diseases. One option may be to select for animals that respond better to infection, maintaining growth and/or rapidly recovering. This is described as resilience or robustness. A new study is underway to investigate resilience using a "natural challenge" model consisting of a number of different agents including PRRSV as well as Swine Influenza

Virus, *Haemophilus parasuis* and *Streptococcus suis*. A number of approaches are being used to try to identify biomarkers that will predict resilience in high health status pigs to reduce the impact of infection and contribute to reducing the use of antimicrobials in production. For example, Kommadath et al. (2015 *BMC Genomics* 15: 452) used RNaseq to identify gene expression patterns before infection with *Salmonella* that predict different outcomes in terms of carriage of the pathogen. A second option in the future may be to use gene editing to manipulate the early stages of infection and develop novel resistance as was recently demonstrated so remarkably for PRRSV by Prather and colleagues (Whitworth et al., 2016 *Nature Biotechnology* 34:20).

Key Words: health, pigs, resilience

0495   Genomic approaches to characterizing and reducing antimicrobial resistance in beef cattle production systems.
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The current rate of resistance development against antimicrobials (AMR) available for use in human medicine is a global health threat. The discovery and design of new antibiotics is nearly at a standstill and as a result, the approximately 700,000 global deaths attributed to AMR infections yearly is expected to rise. Intensive livestock operations, including beef production systems require the use of antimicrobials to ensure animal health and to optimize growth efficiency. As a result the microbes present in the feedlot environment can be exposed to multiple classes of antimicrobials and have the potential to harbor, acquire or develop resistance. To understand the magnitude and risk of AMR in this setting, it is important to assess the prevalence and diversity of AMR determinants in the microbial population. AMR bacteria are traditionally identified by isolation and growth in the presence of selective antibiotics. However, more recent advances in genomics have enhanced the precision of AMR characterization. Whole-genome, metagenomic, and RNA sequencing provide new avenues for the rapid detection of AMR determinants in microbial communities, including unculturable organisms. Metagenomic approaches can be used to identify both previously characterized and novel AMR mechanisms in recalcitrant bacteria which may serve as an environmental reservoir of resistance genes. Metagenomic approaches can also be used to place AMR genes within the context of mobile genetic elements, providing information with regard to the likelihood of their dissemination among microbial communities. Genomics may also play a key role in mitigating and developing alternatives to antimicrobials such as probiotics. RNA-seq-based

transcriptomics and Tn-seq may also provide new ways to examine the cellular mechanisms that may promote AMR or prevent it. Finally, CRISPR-Cas gene-editing shows promise as a tool to directly reduce AMR by killing AMR-resistant organisms without harming beneficial microbes. All these technological developments provide new opportunities to better identify, quantify, and mitigate resistance to antimicrobials as well as develop alternatives.

Key Words: antimicrobial resistance, bacteria, beef, cattle, CRISPR-Cas, genomics, metagenomics

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0496 Nurturing healthy gut microbiome: route to increased disease resistance in ruminants.
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Perturbations in gut microbiota colonization during early life have been shown to present long lasting influences to the host immune responses, health and metabolism as well as subsequent microbial succession. These perturbations can be caused by nutritional imbalances, differing feeding methods, nutritional regimes and antibiotic treatments during the early life. Management of ruminants can vary significantly due to different feeding practices and it relies heavily on antibiotics prevention/treatments for diarrhea and pneumonia in pre-ruminants. However, our understanding on the influence of such management practices on gut microbiome as well as ruminant health and metabolism is very limited. Our recent study has revealed that feeding of heat-treated colostrum soon after birth enhances the colonization of beneficial bacterium, bifidobacteria, which is well-studied using mouse models and has been shown to have greater impact on mucosal immune system development as well as weight gain in children. Besides, the colonization of bifidobacteria in calf gut has been suggested as a preventive mechanism of pathogenic *E. coli* that causes neonatal calf diarrhea. The use of next generation sequencing approaches to study calf gut microbiome and linking the early microbial composition with that of calf phenotypes have reported that higher abundance of *Fecalibacterium* is associated with decreased diarrhea incidences and increased body weight, suggesting linkages between gut microbiome, calf health and growth. Moreover, diet-driven changes in rumen microbiome are related to the development of subacute ruminal acidosis, a prevalent metabolic disorder in adult cattle. Thus, understanding on gut microbiome and their link to gut/rumen development and metabolism will provide means to improve health in ruminants via microbial manipulation. Such manipulation methods toward nurturing a healthy gut microbiome not only improve the disease resistance in ruminants, but may also decrease the heavy antibiotic usage that is in practice in the industry.

Key Words: disease resistance, gut microbiome

0497 Pre- and probiotics for increased disease resistance in the nonruminant animal.
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In addition to formulating diets for poultry and swine to optimize performance outcomes, an equally important goal is to apply nutritional interventions to support a healthy and functional gastrointestinal tract. The latter has gained considerable interest as the utilization of in-feed antibiotics and some ingredients (such as those derived from animals) has come under increased scrutiny and may no longer be an option. To this end, feed additives such as pre- and probiotics have been suggested as feed additives with potential to mitigate enteric diseases in poultry and swine raised under antibiotic-free feeding programs. Prebiotics are ingredients that are selectively fermented and lead to specific changes in the composition and (or) activity of gut microbiota (e.g., bifidobacteria and lactobacilli) that confer beneficial effects to the host. Various carbohydrate components, including fructooligosaccharides and transoligosaccharides and other fiber types (e.g., inulin, sugar beet pulp, and coarsely ground wheat bran) have been reported to cause prebiotic effects in poultry and swine. Moreover, it has been reported that dietary supplementation with carbohydrases may generate carbohydrate components in the gut that could enhance gut health and function partly by acting as prebiotics. Probiotics are live microorganisms which when administered in adequate amounts confer a health benefit on the host. The beneficial effects of these additives are mediated through one or more of the following mechanisms in the gut: stimulation of a healthy microbiota, prevention of enteric colonization by pathogens, improving digestive capacity and lowering the pH, improving mucosal immunity, or enhancing gut tissue maturation and integrity. Bacillus, yeast and lactic acid-producing bacteria such as *Lactobacillus*, *Bifidobacterium*, and *Enterococcus* are the most common groups of organisms used as probiotics. This presentation will highlight recent studies on the utilization of pre- and probiotic utilization in the nutritional management of gut health and function in the nonruminant animal. Also, the mechanisms underlying the effects of these additives will be discussed along with the possible reasons for the inconsistencies often seen among studies with regards to the efficacy of these additives.

Key Words: prebiotics, probiotics, poultry, swine