

8 Government perspective on animal production food safety. Alice Thaler*, *USDA/FSIS, Washington, DC/USA.*

The Food Safety and Inspection Service (FSIS) is committed to ensuring food safety for meat, poultry and egg products using a farm-to-table approach. Issues affecting producers include regulatory requirements at slaughter, humane handling, and residues. FSIS has no direct regulatory authority on the farm; however, regulatory requirements at slaughter establishments will impact the relationship between producers and processors. The FSIS has 35 cooperative agreements with state regulatory officials and universities to educate producers about these impacts. These educational efforts in animal production are part of a larger change whereby FSIS will redefine the role of its veterinarians who will become public health professionals overseeing the effectiveness of farm-to-table food safety systems.

Humane issues potentially impact producers. FSIS considers humane methods of handling animals and humane slaughter operations a priority, and is committed to ensuring that there is compliance with the Humane Methods of Slaughter Act in federally inspected establishments that slaughter livestock. FSIS participates in the USDA Animal Well Being Task Group, which is comprised of agencies with regulatory authority over humane treatment of animals under prescribed circumstances, such as animals under exhibition. FSIS plans to develop objective criteria for determining whether observed handling and stunning practices for livestock are humane. Also, beginning with School Year 2000-2001 purchase, USDA will no longer accept ground beef that includes product from non-ambulatory cattle.

Residues continue to be an important issue in the minds of consumers. FSIS is developing an approach to regulatory enforcement that will be compatible with a HACCP environment. This may include condemnation of carcasses whenever a target tissue is found to exceed the regulatory tolerance for a pesticide or drug.

All in all, responsibility to prevent, reduce or eliminate hazards will be shared throughout the farm-to-table continuum. Industry quality assurance programs are expected to address more food safety issues in the future. This will be a major change for producers who do not currently have programs in place to address microbiological, chemical, and physical hazards.

Key Words: residues, HACCP, food safety

9 Overview of environmental protection concerns and potential solutions. H. F. Tyrrell*, *U. S. Department of Agriculture, CSREES, PAS.*

The impact of livestock production on the environment has evolved into a major issue confronting livestock producers in the United States. The U.S. Environmental Protection Agency has proposed new regulations for Animal Feeding Operations which will have major impact if enacted as proposed. The Supreme Court has upheld new Air Quality Standards which, for the first time, will include ammonia as a criteria pollutant under the National Ambient Air Quality Standards. The bottom line is that it will not be business as usual for livestock producers. The livestock industry is going to have to factor in the cost of dealing with nutrients entering and leaving the animal feeding operation by whatever route. The starting point for the development of nutrient management

systems has to be the application of mass balance principles to the total livestock production system. We have to be able to accurately identify source and fate of each nutrient as it moves through the production system. Route of loss will be different for each nutrient. Loss of nitrogen to the atmosphere, for example, can be the primary route from the production system to the environment whereas phosphorus loss via this route would be negligible. Only when one considers total mass flow of all nutrients through a livestock production system can realistic comparisons of alternative nutrient management strategies be made.

Key Words: Nutrient, Regulation, Environment

10 EPA's Vision—the Next Steps. Roberta Parry*, *U.S. Environmental Protection Agency, Washington, D.C..*

The U.S. Environmental Protection Agency (EPA) proposed new Confined Animal Feeding Operation (CAFO) regulations in January 2001. The regulations focus on preventing animal manure from reaching surface waters. Nutrients are the major pollutants of concern, since they are the number one cause of water quality impairments in lakes and the number three cause in rivers. Pathogens and sediment are also important pollutants from CAFO operations. In order to update the 25-year old CAFO regulations, EPA has proposed several changes to better protect water quality. These changes focus on three major areas: 1) who needs a permit (all CAFOs including dry poultry, immature swine and heifer operations, and integrators with substantial operational control over growers); 2) feedlot requirements (existing beef and dairy CAFOs and all new CAFOs—zero discharge to groundwater that is hydrologically connected to surface water), (veal, swine, and poultry—zero discharge with no overflow allowance); and 3) land application of manure (Permit Nutrient Plans including rate, timing, and method of application; 100' setback from water; maintaining records on manure transferred off-site). EPA has taken public comment on the proposal and will be revising the regulation for final action by December 2002. In addition to the CAFO proposal, the Total Maximum Daily Load regulation may require animal operations to adopt additional practices if the operations are in watersheds where agriculture impairs water quality. Livestock producers will need assistance from many different sources to understand their responsibilities under these regulations and implement changes on their operations.

Key Words: Confined Animal Feeding Operation, Water Quality, EPA Regulations

11 Industry View of Environmental Issues. C. Itle*¹, ¹*National Milk Producers Federation.*

As a result of various federal, state, and local environmental initiatives, livestock producers are having to become increasingly aware of minimizing any potential environmental impacts on their farms. This presentation will review various initiatives to manage livestock waste from both regulatory and educational/technical assistance standpoints. In addition, we will discuss producer-led efforts to address their environmental concerns.

Key Words: Environmental, Livestock

Current Concepts of Animal Growth X: Metabolic and Cellular Regulation of Protein Deposition

12 Amino Acids: Regulators of Global and Specific mRNA Translation. S.R. Kimball*¹, ¹*Pennsylvania State University.*

A continuous supply of a complete complement of essential amino acids is a prerequisite for maintenance of optimal rates of protein synthesis in both liver and skeletal muscle. Deprivation of even a single essential amino acid causes a decrease in the synthesis of essentially all cellular proteins through an inhibition of the initiation phase of mRNA translation. However, the synthesis of all proteins is not repressed equally. Specific subsets of proteins, in particular those encoded by mRNAs containing a 5-terminal oligopyrimidine (TOP) motif, are affected to a much greater extent compared to most proteins. The specific decrease in TOP mRNA translation is a result of an inhibition of the ribosomal protein S6 kinase, S6K1, and a concomitant decline in S6 phosphory-

lation. Interestingly, many TOP mRNAs encode proteins involved in mRNA translation, such as elongation factors eEF1A and eEF2, as well as the ribosomal proteins. Thus, deprivation of essential amino acids not only directly and rapidly represses global mRNA translation, but also potentially results in a reduction in the capacity to synthesize protein.

13 Cellular Control of Protein Degradation. Didier Attaix*¹, Lydie Combaret¹, M-Noelle Pouch¹, and Daniel Taillandier¹, ¹*Human Nutrition Research Center of Clermont-Ferrand and INRA.*

A few years ago protein degradation was considered to be a global, non-selective and poorly regulated metabolic process that was mainly involved in housekeeping functions. This area of research has developed exponentially in the last decade, and it is now clear that many major biological functions are controlled by the breakdown of specific proteins. In

this respect, the ubiquitin-proteasome-dependent pathway is the most elaborate protein-degradation machinery known. The formation of a polyubiquitin degradation signal is required for proteasome-dependent proteolysis. Several families of enzymes, which may comprise hundreds of members to achieve high selectivity, control this process. The substrates tagged by polyubiquitin chains are then recognized by the 26S proteasome and degraded into peptides. However, the 26S proteasome also recognizes and degrades some non-ubiquitinated proteins. Indeed, several ubiquitin- and/or proteasome-dependent systems degrade specific classes of substrates and single proteins by alternative mechanisms and are presumably interconnected. They may also interfere or cooperate with other proteolytic pathways.

Key Words: Protein breakdown, Proteasome, Ubiquitin

14 Stress and Muscle Cachexia. P.O. Hasselgren^{*1}, ¹*University of Cincinnati.*

One of the metabolic hallmarks of sepsis and severe injury is a catabolic response in skeletal muscle. Muscle cachexia in these conditions is mainly caused by increased protein breakdown, although inhibited protein synthesis contributes to the negative nitrogen balance in skeletal muscle. Muscle protein breakdown during sepsis and following severe injury mainly reflects degradation of the myofibrillar proteins actin and myosin. There is evidence that a calcium-calpain-dependent release of the myofilaments from the sarcomere provides substrates for the ubiquitin-proteasome proteolytic pathway. Proteins degraded by this pathway are ubiquitinated and subsequently degraded by the 26S proteasome. Research in our laboratory has provided evidence that the gene expression of calpains as well as various components of the ubiquitin proteasome pathway is upregulated in skeletal muscle during sepsis and following severe injury. In addition, proteasome inhibitors block the increase in muscle protein breakdown seen in these conditions. Muscle cachexia in patients with stress has important clinical implications because it can prevent or delay ambulation, increasing the risk for thromboembolic complications and prolonging rehabilitation. In addition, when respiratory muscles are affected, there is an increased risk for pulmonary complications and a need for prolonged ventilatory support.

Key Words: Muscle, Proteolysis, Sepsis

15 Developmental Regulation of Protein Metabolism. T.A. Davis^{*1}, M.L. Fiorotto¹, and A. Suryawan¹, ¹*USDA/ARS Children's Nutrition Research Center.*

Growth and development are characterized by high rates of protein turnover that support rapid rates of protein accretion. The rate of protein deposition varies among tissues, with the growth rate of the skeletal musculature being amongst the highest. The efficiency with which dietary amino acids are utilized for protein deposition is high in neonates and decreases as the animal matures. This high efficiency is likely due to the enhanced stimulation of protein synthesis after feeding. The rise in protein synthesis in response to feeding and its developmental decline are more pronounced in skeletal muscle than for other tissues. In the neonatal pig, the postprandial rises in insulin and amino acids independently stimulate protein synthesis in skeletal muscle, whereas amino acids are the principal anabolic stimulus for liver. These developmental changes in protein synthesis are regulated by alterations in the expression and activity of components of the signaling pathway that controls the initiation of translation.

Key Words: Protein Synthesis, Insulin, Amino Acids

16 Muscle Wasting and Protein Metabolism. C. Castaneda-Sceppa¹, ¹*Jean Mayer USDA Human Nutrition Research Center on Aging.*

Accelerated muscle proteolysis is the primary cause of muscle wasting in many catabolic diseases such as diabetes mellitus, renal and liver failure, HIV infection and AIDS, and cancer. In individuals with catabolic diseases, as it is the case of fasting states (anorexia and starvation), protein breakdown increases while protein synthesis declines resulting in negative muscle protein balance. The pathway responsible for accelerated proteolysis in catabolic conditions is the ubiquitin-proteasome dependent system. Muscle proteolysis increases under conditions of acidosis,

up-regulation of branched-chain ketoacid dehydrogenase, the presence of catabolic hormones (glucocorticoids, thyrotoxic states), insulin resistance, and multiple cytokines (interleukin-1 and 6 and tumor necrosis factor). In contrast, factors that suppress muscle proteolysis and wasting leading to a state of adaptation include dietary protein deficiency with adequate energy intake, use of anabolic agents, and resistance exercise training. The understanding of the biochemical adaptation that reduce protein degradation and improve nitrogen balance are important for the development of effective therapies to combat muscle wasting and improve protein homeostasis with catabolic illnesses.

Key Words: Skeletal muscle loss, Protein turnover, Catabolism

17 Hormonal Regulation of Regional and Tissue Protein Turnover. S. Nair^{*1}, ¹*Endocrinology Unit, Mayo Clinic.*

Hormones are major regulators of protein turnover in humans. Whole body protein balance and tissue concentrations of specific proteins are determined by the balance between synthesis and degradation of proteins. Most of the hormonal actions are tissue and protein specific and the same hormone may inhibit synthesis of one protein but directly or indirectly stimulate synthesis of another protein. Hormonal effects are targeted at different levels of regulation of protein synthesis and degradation. Examples of hormonal imbalance resulting in profound changes in protein turnover is evident in type I diabetes. Insulin deficiency results in elevated glucagon and growth hormone levels in human. Insulin deficiency has been shown to result in profound muscle wasting by a net increase in muscle protein breakdown. High glucagon causes increased metabolic rate and accelerated leucine oxidation thus contributing to the catabolic state in diabetes. Other catabolic hormones such as cortisol also may contribute to catabolism. Insulin also is a key hormone involved in regulating the trafficking of amino acids across organs especially making amino acids available for synthesizing essential proteins in between meals. Recent interest has focused on insulin specific effects on certain proteins with specific functions such as mitochondrial proteins. Hormones also act in conjunction with substrates which modulates hormonal effect on protein turnover.

18 Exercise and Protein Metabolism. R.R. Wolfe¹, ¹*University of Texas Medical Branch and Shriners Burns Hospital.*

Resistance exercise training produces an anabolic effect on muscle, yet during exercise muscle protein synthesis is not stimulated, and muscle protein breakdown may be accelerated. The anabolic response begins after the exercise is completed. Muscle protein synthesis is elevated by about one hour after exercise, and remains elevated for as long as 48 hours. A simultaneous increase in muscle protein breakdown blunts the effect of the stimulation of synthesis on the net protein balance. Net muscle protein balance is improved after exercise, but remains negative unless nutrients are ingested. Thus, the "anabolic" response to resistance exercise occurs in the fed state, where ingested amino acids are incorporated into muscle protein to a greater extent than when ingested at rest.

19 Nutritional Regulation of Protein Metabolism. P.J. Garlick^{*1}, ¹*State University of New York at Stony Brook.*

Protein homeostasis depends on the balance between protein synthesis and protein degradation. In muscle of growing animals, feeding is accompanied by an increase in protein synthesis, resulting in net protein deposition. This has been shown to depend on amino acid supply and insulin secretion. In contrast, in the liver, protein deposition after feeding results mainly from an inhibition of protein degradation. At the whole body level, increasing nutrient intake in human preterm neonates has been shown to be associated with increased protein deposition, resulting from enhanced protein synthesis. In healthy adults there is no growth, but there is a need to retain protein after meals to counter the protein loss that occurs postabsorptively. The adult rat shows little stimulation of muscle protein synthesis by food intake or insulin infusion, whereas in human muscle the responses to nutrients or insulin remain controversial. Pathological conditions such as trauma and infection are characterized by muscle protein loss and a decrease in muscle protein synthesis, and much effort has been spent on strategies for reversing muscle wasting by nutritional and pharmacological means. However, nutritional support, even when supplemented with branched chain amino acids or glutamine, have not yet been shown to be effective.