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Review Article

Clinical Nutrition and Therapeutic Diets: New Opportunities in Farm Animal Practice

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Abstract

The science of animal nutrition gets increasingly involved with questions on how to supply nutrients that guarantee adequate physiological development, good health and reproduction. Clinical Nutrition provides clinically relevant nutritional advice for optimum health and welfare of farm animals without compromising the production output. Nutrition and medicine interface in a variety of ways and combine to serve as a dynamic force in health and disease and thus, a conceptual understanding of this interrelationship is critical to the continued and effective development of veterinary clinical nutrition. The therapeutic diets is an adjunct to balanced diets for supporting optimum production as well as for enhancing immunity and minimizing deterioration in health and production of animals during illness caused by inflammatory etiologies. This review will thus offer practical strategies for incorporating nutritional principles into daily clinical farm animal practice, provide a reliable resource on feeding practices in both healthy and diseased animals, and help veterinary practitioners to confidently and competently make nutritional recommendations. Moreover, there is an urgent need of explorative research for the prevention and control of occurrence of a disease or pathological condition; and for the management of clinical conditions through integration of clinical nutrition and other veterinary aid practices. Moreover, many metabolic and deficiency diseases are directly related to correction of imbalances and pre and post-natal nutritional and feeding management of farm animals. In this review, production stress and nutrition, stress of diseases and nutrition, metabolic effects of infection, nutrition-reproduction interaction, nutrition and immunity, transition nutrition, nutrition for gastrointestinal functionality, parasitism and host nutrition, nutrition-environment interaction, pharmaco-nutrition and ensuing nutritional support and dietary guidelines are briefed to introduce to a newer area of clinical nutrition that can have added strength to veterinary therapeutics.

Keywords: *Clinical Nutrition; Therapeutic Diet; Farm Animal*

Introduction

'Veterinary Clinical Nutrition' is recognized as one of the advancing new field of application in 'Animal Nutrition Research' that addresses the intrinsic issues of optimal health, production and welfare of livestock and pet animals. Keeping animals healthy and productive has, in many cases proven quite challenging, especially as management programs have become more intensive. A wholesome diet and balanced nutrition is essential not only for maintaining health but also for fighting diseases. Although 'Ayurveda' and later Hippocrates recognized the importance of a good diet for the prevention of diseases, clinical nutrition has emerged only recently as an important discipline in modern medicine and animal nutrition. Clinical nutrition of farm animals aims to understand and puts in practice the current knowledge of nutritional principles to the promotion of health of livestock through prevention of diet related diseases for the benefit of the healthy and unhealthy alike. The need of research and education on clinical nutrition is realized due to concurrent reports of several incidence of still birth, rickets, abortions, osteomalacia, fracture of long bones, drop in milk production and reproductive failure in the cows and buffaloes of military dairy farms and equines of breeding studs.

Clinical Nutrition can be defined as dietary management of clinically ill animals that is aimed at correction of nutritional deficiencies or excesses, replacement of nutrients to ameliorate a disease or disorder which does not have a nutritional cause and feeding of drugs or nutrients to aid in the inhibition of diseases [1]. The primary objective is to optimize nutrient intake, minimize catabolism and utilization of body nutrient stores, and maximize recovery process and immune competence in a sick animal. Environmental (climate, microbes, fauna, parasites, toxicants, electric current, and threat of injury) stimulus that initiates an adaptive change or stress response in the animal alters its normal physiological metabolism and hence the system is in need of therapeutic support, viz. therapeutic treatment and supportive diets. While assessing the nutritional requirement of such clinically ill animals, it involves assessment of the nutritional requirements for various life stages and productive functions, and formulations of balanced and complete diets and/or therapeutic diets for different patho- or pathophysiological conditions. It involves nutrition of clinically ill animals, supportive nutrition for the convalescent animals, and preventive nutrition to fight against the occurrence of clinical illness [2]. Disease and nutrition are closely interlinked and dietary modification forms an important part of the veterinary management of the case aided with right formulation of 'Therapeutic diets' that provides optimal health, production and welfare of animals.

Production stress and nutrition

Animal production refers to meat, milk, egg and wool production are phenotypic exhibition of an animal with respect to its genetic make-up sustained through improved scientific nutritional and managemental practices. A normal dairy cow experiences constantly changing nutrient demands and environmental stresses during the course of pregnancy and lactation. In the first part of the cycle the negative balance must be held to a minimum, later, the reserves must be replenished through fine-tuned nutritional support. Nature has accorded a high priority to the functions of pregnancy and milk secretion, allowing them to proceed at the expense of other metabolic processes even to the point that a disease state is averted and most of the production and metabolic diseases are associated with incomplete or imbalanced nutrition which fails to meet the high demands of production and an altered metabolic function. Identifying the physiological basis of differences among animals in milk and meat production is being recognized as high research priority for faster growth and nutrient partitioning in growing animal towards carcass composition with greater lean and reduced fat. The immunological manipulation of fat depots [3] suppression of somatostatin [4] and enhancement of GH activity by combination with monoclonal antibodies [5] are some of the potentially valuable possibilities but there is a need for better understanding of the nutrient and other requirement in response to these manipulations.

Alterations in tissue partition for growth, pregnancy, lactation, fiber growth as well as for meat production alter the nutritional strategy required to optimize both economics and resource utilization. Nutrients are partitioned to the areas of greatest need as determined by homeostatic and homeorrhetic controls. In high producing animals, homeorhetic demands on nutritional intake, digestion, and organ and nutrient reserves are high and at times it affects homeostasis and disease may occur. Of the homoerotic functions, the nutritional demands of lactation are greater than the demands of growth or pregnancy. During last two months of pregnancy the concepts unit plays a critical role in assuring adequate nutrient for its development as well as for the dam's mammary development and subsequent milk production. The resultant imbalances and nutritional insufficiency leading to metabolic and production diseases are ketosis, milk fever, grass tetany, acidosis, displaced abomasum, tympany, retained placenta.

Similarly, protein-energy malnutrition (PEM) is a frequent occurrence in field conditions due to a variety of factors, viz. i) declining grazing/pasture land, ii) seasonal scarcity of feed and fodder, iii) resources at farmers' hand, iv) production stress, v) disease stress, vi) wasting diseases, vii) anorexia, viii) micronutrient deficiency, and ix) other related factors. Prolonged PEM increases catabolic activity and drains the body reserve that lead to compromised antioxidant defense (reduced glutathione status) and immuno-depression [6]. Oxidative stress has been implicated in numerous disease processes including sepsis, mastitis, acidosis, ketosis, enteritis, pneumonia, respiratory and joint diseases [7].

Stress of diseases and nutrition

The metabolic effects of infection influence a wide variety and number of host biochemical pathways and molecular mechanisms function in support of many diverse defense systems used by the body to control, combat or to eliminate invading microorganisms. Infectious disease accompanied by fever are catabolic forms of illness causing washing effects marked by weight loss and a decrease in muscle mass and strength. Fever, the manifestation of a hypermetabolic state in illness utilizes body constituents such as glycogen stores, fat depot, and skeletal muscle protein to generate metabolic energy and substrate molecules for the activation of host defensive mechanism in order to control or terminate the infection. The mechanisms used for the defense of the body during the course and progression of an infection are production of fever, generation and release of phagocytic neutrophils, activation of macrophages and lymphocytes of the immune system, production of acute phase reactant proteins by the liver, synthesis of a variety of specialized proteins (interferon, component proteins of complement, lignin and coagulation systems), redistribution of certain nutrients and minerals, elimination of toxic products or metabolites and inflammatory and immune responses and tissue repair [8].

Nutritional deficiency apparently increases the severity of infection by viral, bacterial, fungal or parasitic pathogens. Studies indicate that most nutrition may affect pathogenesis either synergistically or antagonistically [9] and also has significant impact on cell mediated immunity [10]. Infection induced immune stimulation decreases appetite and muscle protein accretion, increases metabolic rate, body temperature and oxidative damage to cells. Increased incidence and severity of infections secondary to immunological impairment as a result of generalized malnourishment as well as selective nutrient deficiencies may result in vaccination failure, increased condemnation and mortality, poor feed conversion, and increased morbidity and medication costs. The potential for improved profitability and animal wellbeing had led scientists to investigate the mechanisms by which clinical and subclinical disease challenges influence growth and efficiency of gain. The challenge for food animal scientists is to develop technologies that encompass all aspects of the challenge from management strategies to nutritional and therapeutic intervention. Nutrients derived from dietary proteins, carbohydrates and fats as well as micronutrients, vitamins and minerals interact with immune cells systemically in the circulating blood, regional lymph nodes and specialized immune system of gastro-intestinal tract [11].

Metabolic effects of infection

Clinically the most visible metabolic effects of an infection appears catabolic; however, it must be kept in mind that equally important anabolic processes are taking place at the same time, that are of importance in host defense metabolism. Exposure of host to infectious agents, trauma or stressors stimulates the immune system. During this defence response, homeostatic balances modifies through a process called sometimes as homeorrhesis, which redistributes blood flow and mobilizes nutrients to facilitate both whole body and local tissue defence. A central component to this response to the invasion of the host by noxious stimuli is the activation of acute phase response (APR); the principal activators being the pro-inflammatory cytokines, interleukin (IL)-1α/β, IL-6, tumor necrosis factor (TNF) α and the type I interferons (IFN) α/β [12]. An important feature of APR is the overriding effects of pro-inflammatory cytokines on the anabolic effects of insulin, growth hormone and IGF-1. This induces sickness behaviour including decreased exploratory activity, fever, sleep and inappetance besides activation of the hypothalamus-pituitary-adrenal axis. There is reduced production of growth hormone releasing hormone and thyrotropin releasing hormone leading to reduced peripheral levels of IGF-1 [13]. In the context of livestock production, the activation of APR could lead to reduced utilization of nutrients by tissues producing fibre, meat, milk and skin. In addition to the changed profile of nutrient utilization by production tissues there can be direct metabolic cost of immune activation. Metabolic rate is elevated by 5 - 13% per degree of fever, while energy requirements of leukocytes increase 2 - 3 fold per cell following their activation [8]. Thus, a reduction in growth rate during immune activation will depend not only on homeorrhetic responses affecting accretion of nutrients in the production tissues but also on costs associated with pathology during infection. Overall, the competition between the tissues of the immune system and the production tissues for utilization of nutrients in the resource allocation theory, leads to a negative correlation between production and immune activation or disease resistance. The homeorrhetic response brought about by APR through the pro-inflammatory cytokines can induce metabolic changes in many target tissues including central nervous system, adipose tissues, liver, skeletal muscle, gut tissues and skeletal system.

General metabolic response

In general, the metabolic responses that take place in any infection, trauma and inflammatory stimuli can broadly be categorized as:

- Generalized acceleration of host metabolism,
- Generation of needed substrates from endogenous sources within the body: This includes synthesis of new or additional varieties of highly specialized proteins, and increased production of phagocytic cells, antigen specific lymphocytes and plasma cells. The production of the new cells and unique molecular products as needed for host defense.
- Generation of metabolizable energy from endogenous sources: The activated phagocytic cells need energy in order to initiate metabolic processes essential for cellular locomotion, particle uptake, lysozyme formation, killing functions and release of messenger molecules in the form of endogenous mediators. Here liver plays important role in the metabolic readjustments by reprioritizing the functions related to energy metabolism viz. initiation of glycolysis, prominence of gluconeogenesis, synthesis of fatty acids and triglycerides with concomitant reduction in ketogenesis.
- Redistribution of certain nutrients: Iron and zinc are taken up by liver and held in storage while the infection persists.
- Elimination of toxic products or metabolites: Excess of tryptophan produced is metabolized and excreted by in the urine as diazo reactants. Besides, the accelerated use of amino acids for gluconeogenesis leads to increased hepatic production of urea that also needs disposal.
- Direct participation in defense mechanisms such as inflammatory and immune responses and tissue repair.

Nutrition-reproduction interaction

Impact of nutrition on reproductive efficiency of livestock species is well documented, viz. it affects all aspects/events of reproduction including puberty (age at puberty), gametogenesis (folliculogenesis and spermatogenesis), oestrus cycle, fertilizing ability of gametes, maternal recognition of pregnancy, pregnancy, embryo development, implantation, foetal development and parturition and recurrence and maintenance of subsequent reproductive cycle. Regulation of normal reproductive development and physiology is a complex process involving the coordinated interaction of neurotransmitter systems, hypothalamic releasing factors, pituitary hormones, gonadal sex steroid hormones and various growth factors. This requires a clear understanding of both the nutrient requirement for reproduction and the mechanisms underlying partitioning of nutrients and prioritization for reproductive function via-a-vis various competing physiological systems. Currently, nutrigenomics provides new information and this technology is particularly well suited for studies of the complex metabolic interactions that dictate fertility and influence reproductive efficiency. At the molecular level, dietary energy intake affects the expression of mRNA encoding components of the ovarian insulin-like growth factor (IGF) system and these changes can directly influence the bioavailability of intrafollicular IGF [14]. This, in turn, can increase the sensitivity or response of follicles to FSH and is one mechanism through which nutrition can directly affect follicle recruitment. Further, the effect of short-term nutritional supplementation on follicle development is not mediated by an increase in FSH concentrations, but by increased concentrations of glucose, insulin and leptin acting directly at the ovarian level [15]. Thus, high concentrations of metabolic hormones in nutritionally-healthy ewes are associated with the development of more follicular waves and when a supplement is superimposed on this situation, changes in glucose and metabolic hormones allow more follicles to be selected to ovulate [16]. Dietary induced increases in intrafollicular IGF bioavailability also have a negative effect on oocyte quality. Thus, pre-mating nutrition is associated with alteration in the mRNA content in oocytes and surrounding follicle cells in ewes, which may account for the reduced reproductive performance typical of ewes that are on a restricted ration before mating [17] and it can also affect the expression of mRNA encoding components of the ovarian IGF system to regulate the sensitivity/response of follicles toward gonadotropins.

The interval from parturition to rebreeding, ovum quality, embryo development and embryo survival are the other major contributors to fertility and thus nutritional effects on fertility embrace the formation of the foetal gonads, their post-natal development, the timing of puberty and in multiple ovulating species, their ovulation rates. Recent research in ewes has also demonstrated that during its early development the foetal ovary is remarkably sensitive to maternal nutrition with subsequent lifetime effects on ovulation rate [18]. The timing of puberty in both sexes and adult ovulation rates in ewes are influenced by post-natal nutrition. Nutrition during the period when ovarian follicles emerge from the primordial pool (approximately 6 mo before they ovulate) can influence ovulation rate in ewes. Donor nutrition, in particular selenium status, can affect the resilience of spermatozoa to freezing and thawing. In contrast to spontaneously ovulating animals in which high-plane feed immediately before ovulation enhances oocyte and embryo quality, the opposite is the case in superovulated donor animals and those from which oocytes are harvested for *in vitro* embryo production. It is suggested that in farming practice, some of the most important effects of in-utero-nutritional programming may be those relating to behaviour and immune competence with the associated production and product quality benefits coming from improvements in health and welfare [19]. The goal of late gestation nutrition program is thus to insure adequate nutrient intake for strong vigorous lambs of moderate birth weight and also to sustain prolificacy (twining/triplets) ensuring against pregnancy-toxaemia. Additionally, ewes must enter lambing season in average to above average body condition to maximize production. Recent development with ultrasound scanning for foetal number allows for fine tuning the late gestation nutrition. The nutrients of greatest concern during late gestation feeding would be energy, crude protein (CP), Ca, Se and vitamin E. The energy requirement is affected by the number of foetuses and magnitude of environmental/climatic stress [20,21]. Supplementation of rumen protected fat (RPF) has dual effect of meeting higher energy and improved the number and size of ovarian pre-ovulatory follicles, and the ovulation rate [22]. Similar supplementation in ewes during out-of-the-breeding season was effective to maintain reproductive performance as reflected by increased levels of lipid profiles, glucose, and progesterone hormone, to improve the number and size of ovarian preovulatory follicles, and increased conception rate [23]. Thus, RPF may act as an important strategy to integrate nutrition, reproductive maintenance and per animal productivity. However, little is known regarding the potential interactions among differing maternal nutrition regimens in early and mid–late pregnancy [24] and also, level and period of supplemental nutrition to prolific (twins and triplets) ewe [25].

Energy balance and dry matter (DM) intake during first quarter post-parturition are critically important in determining oocyte and embryo survival/conception rate. Apart from the importance of the NEB and the associated endocrine and metabolic consequences, little attention has been given towards the effect of diets rich in energy and protein to sustain lactation and some studies indicate that excess energy intake reduces the response to superovulation [26] and also decrease the yield of embryos and alters expression of some gene constructs within the developing embryo [27]. Thus, key issue in improving reproductive efficiency and embryo production may be to supply the nutritional needs of the animal in a physiological way and avoid abnormal or unbalanced amounts of any one component in the diet.

Nutrition and immunity

Immunity is resistance to infectious agents, foreign particles, cells, toxins, etc. and the ability of animal to resist depends upon the competency of its immune system. Nutritional deficiencies contribute to a non-responsive immune system, which can be most easily regulated. In the face of an inflammatory reactions or immune challenge homeorhesis sets in which brings about interferences with normal physiological functions of an animal by redirecting the nutrient flow to meet the immediate challenge [28]. Because of the diversion of nutrients away from growth in support of immune related processes, immune challenge is considered a major obstacle to animals for achieving their genetic proficiency in respect of growth and production [29]. A reduced state of nutrition, malnutrition or depraved nutrition fails to meet both the homeostatic and homeorhetic requirements of an animal. Epidemiological observations have established the aggravation of infections in malnourished patients which is commonly associated with impaired immune responses, particularly cell-mediated immunity, phagocyte function, cytokine production, secretory antibody response, antibody affinity and the complement system [30]. A marked decline in cell-mediated and humoral immune response accompanied by alterations in related metabolic profile was observed in sheep exposed to periods of protein deprivation, which however showed a noticeable recovery after realimentation [31]. Infections activate the immune cells (T-cells, B-cells etc.), which then produce cytokines and malnutrition affects T-cells and modulates its production. Thus, the consequences related to immunity are diminished bactericidal activity, reduced reticulo-endothelial function, depressed production of interlenkin-1 by macrophages, decreased synthesis of complement proteins, depressed cellular immune response (delayed type hypersensitivity), decreased T-cell numbers, etc.

Deficiencies of vitamins (A, B, C, D_3, E) and minerals (Zn, Fe, Cu, Se, Cr) also have demonstrated impaired immune-competence [32,33]. Substantial evidence supports the supplementation of vitamin A, E, C, Zn, Fe and Se in excess of their requirement for enhanced disease resistance due to significant stimulation of humoral and cellular immunity and phagocytosis. Certain amino acids (methionine, lysine, arginine, choline, taurine), polyunsaturated fatty acids (PUFA) (ω3 and ω6 fatty acids) and carotenoids has significant immune-potentiation activity. However, factors affecting this immune-stimulatory role such as amounts needed, time of administration relative to periods of stress and infection, chemical form, route of administration, length of effectiveness and transfer to the fetus and neonate needs research applications and confirmation.

The acquired immunity has a significant role in newly-born animals as it depends on timely and adequate consumption of colostrum just after birth and then at least for a period of 72h. It is the most important factor associated with morbidity and mortality in neonates and therefore, in the face of inadequate passive transfer of immunity, animal welfare may be endangered. Acute respiratory distress syndrome is one of unknown etiology with high morbidity and mortality in weanling and suckling animals, but most often related to delay in the establishment of a competent immune system.

Transition nutrition

The transition period in dairy cows range from the last three weeks before parturition to three weeks after parturition, and they undergo large metabolic adaptations in glucose, fatty acid, and mineral metabolism to support lactation and avoid metabolic dysfunction [34]. Estimates of the demand by the gravid uterus at 250d of gestation and the lactating mammary gland at 4d postpartum indicate approximately a tripling of demand for glucose, a doubling of demand for amino acids, and approximately a fivefold increase in demand for fatty acids during this timeframe [35] and fourfold increase in calcium on the day of parturition [36]. On the contrary, the peculiar physiological change in this period is characterized by a decrease in intake around parturition. The NRC [20] recommended that a diet containing approximately 1.25 Mcal/kg of NEL be fed from dry off until approximately 21 d before calving, and that a diet containing 1.54 to 1.62 Mcal/kg of NEL be fed during the last 3 wk preceding parturition. The concept behind this recommendation trigger cows with moderately lower BCS to have increased DM intake to sustain potentially increased milk yield during early lactation and are more likely to have positive transition period outcomes than cows of greater BCS. In the week leading up to calving, DM intake has been shown to decline, with a drop of approximately 30% occurring in the 24 h before calving, 19% on the day after calving [37]. The NRC [20] delineated the following prediction equations for DM intake during the last 21 days of gestation:

Heifers: DM intake (% of BW) = 1.71 – 0.69 $e^{0.35t}$

Cows: DM intake (% of BW) = 1.97 – 0.75 $e^{0.16t}$

Where: "t" = days of pregnancy minus 280.

The last three to four weeks of gestation are characterized by a period of rapid fetal growth, colostrogenesis and mammary development, and metabolic readjustments favoring mobilization of fat and other nutrients. This phase should commensurate with slowly increasing DM intake in conjunction with rapidly increasing nutrient losses in support of milk production. Therefore, inability to meet the energy demand often leads to negative protein-energy balance (PEB) with the consequences of several metabolic disorders/diseases like milk fever, ketosis, retained placenta, metritis and displacement of the abomasum that primarily affect cows within the first two weeks of lactation. Physical and metabolic stresses of pregnancy, calving and lactation contribute to decrease in host resistance during the periparturient period, which may lead to increased susceptibility to mastitis and other infectious diseases [38]. We can enlist six important areas of concern during this transition phase 1) maximizing DM intake, 2) maintaining adequate mineral balance and homeostasis, 3) stimulating rumen papillae development, 4) minimizing negative PEB, 5) maintaining protein homeostasis, and 6) minimizing immune dysfunction. Monitoring the concentrations of four macrominerals viz. calcium (Ca), phosphorus (P), magnesium (Mg), or potassium (K) are of utmost importance, as inadequacy is often being involved in the metabolic syndrome (milk fever, downer cow, tetany) and less severe disturbances in blood concentrations can cause reduced feed intake, poor rumen and intestine motility, poor productivity, and increased susceptibility to other metabolic and infectious disease [39].

Nutritional management guidelines is provided [40] to optimize metabolic health of transition dairy cows, viz. i) strategies to meet glucose demands and decrease NEFA supply through balanced non-fiber carbohydrate (NFC) and starch supply ii) nutritional strategies to decrease conversion of NEFA to accumulated triglyceride in liver (addition or enrichment of diet with choline, methionine and lysine, linoleic and linolenic acid), iii) restricted feeding during the dry period, iv) direct supplementation with glucogenic precursors (propylene glycol, Ca propionate, monensin etc), v) enriching post-partum diet with added fat or fatty acids (trans-10, cis-12 CLA), vi) regulating calcium mobilization in support of lactation by lowering the dietary cation-anion difference (DCAD) of the diet fed during the prepartum period [41].

Nutrition for gastrointestinal functionality

It is inarguably stated that optimal GI functionality can promote livestock performances, health and welfare. The major determinants are diet, effective structure and function of the GI barrier, host interaction with the GI microbiota, effective digestion and absorption of feed and effective immune status [42]. The concept of "gut health" has emerged when we look at farm animal performance at par its genetic/physiological limits for high growth, reproductive traits and ultimate production output [43,44]. Since the ingested nutrients can play a significant role in the development and functionality of the GI tract, diet composition (ingredients, nutrients and additives) has an important role in the development and function of the digestive system, including the immune system and the microbiota. Dietary protein seems to be an important nutritional factor for maintaining immune homeostasis in the GI tract [45]. The potential of using feed supplements, functional foods and nutraceuticals in sustaining animal production performances while maintaining health and welfare cannot be ignored. Various nutraceutical strategies have been reported to support the immune system and to modulate the redox balance and the inflammatory response [42,46]. Antioxidants are supplemented in livestock's diet to counteract the negative impact of oxidative stress and to improve their health and productivity. There is significant interactions between redox homeostasis, metabolism, and the environment [46] and thus, supplemental antioxidants (e.g. Selenium, vitamin C, E, plant flavonoids, polyphenols etc.) or dietary substrates rich in these compounds can alleviate stress and sustain health and productivity of farm animals. Gut-friendly diets should have reduced levels of fermentable protein in the hindgut [47], minimal buffering capacity, negligible content of anti-nutritional factors (phytate, arabinoxylans, beta-glucans, lectins, protease inhibitors, saponins, tannins, etc.) and supply of beneficial compounds such as functional proteins and peptides (IgG, EGF, lactoferrin) and micro-nutrients such as vitamins and minerals [48]. The fiber component of diet plays a crucial role in the complex interaction between the diet, endogenous enzyme, microbiota, and hence digestion and absorption by the host and inducing a prebiotic effect [44], which are considered key components for optimal gastrointestinal functionality. The prebiotic effect of dietary fiber helps in competitive establishment of beneficial bacteria such as lactobacillus and sustain GI health.

A proper diet and normally functioning GI tract are thus integral for the delivery of nutrients, prevention of nutrient deficiencies and malnutrition, repair of damaged intestinal epithelium, restoration of normal luminal bacterial populations, promotion of normal GI motility, and maintenance of normal immune functions (e.g. both tolerance and protection from pathogens). An appropriate diet may have a profound effect on intestinal recovery and successful management of chronic or severe GI diseases [49]. Further, the amount of food, its form, the frequency of feeding, and the composition of diet each have important effects on GI function and may be used to help ameliorate GI disorders. Additionally, both nutrients and non-nutritional components of a diet are important to GI health, the later have multifarious role in ruminant nutrition based on its source, type and level in the diet. The pro-nutritional effect of plant secondary metabolites have been established in proper rationing of animals that confers better rumen environment, improvement in N utilization and energy usage, improvement in production and products quality and ultimately, a decrease in PEM [50].

Parasitism and host nutrition

Gastrointestinal parasitism (GIP) remains one of the main constraints to livestock production both in temperate and tropical countries. Confinement and pasture-based animals are most often exposed to worm infestation and the incidence is more prevalent in hot and humid regions. In general, it can be claimed that well-nourished animals cope better and overcome GI nematode (GIN) infection quicker than malnourished ones [51]. The groups that are most susceptible to parasitism are young pre-ruminants (calves, lambs and kids), when immunity has yet to be established and their mothers [52]. The peri-parturient relaxation of immunity and the demands of lactation, growth, and regaining body condition coincided with increased infection levels and the associated reduction of appetite [53]. Sub-clinical parasitism reduces the efficiency of food digestion and metabolic efficiency while increasing maintenance energy costs [54]. GIP, particularly those in the abomasum, cause pathological changes that disrupt digestion and reduce appetite [54,55]. The deficiency of specific amino acids could be due to reduction in net absorption of non-ammonia nitrogen [53], secretion of amino acid containing products in GI tract like higher secretion of threonine in intestinal mucus, leukotrienes rich in cysteine and incomplete reabsorption of these amino acids [55]. Following effects of GIP on nutrient utilization of host are described [51]:

- Reduce nutrient availability to the host through reduction in voluntary feed intake (VFI) and/or reduction in the efficiency of absorbed nutrients;
- Increased loss of endogenous protein into the GI tract, partly as a result of leakage of plasma protein, and partly due to increased mucoprotein production and sloughing of epithelial cells in to the alimentary tract;
- Effect on GI motility causing diarrhea enhances the loss of plasma protein, sodium and chloride with increase in potassium level thereby altering acid-base balance;
- An increase in metabolic protein/amino acids requirement as a consequence to endogenous protein loss;

- Diversion of nutrients and protein synthesis from production processes such as muscle, bone, wool, milk, egg, etc. towards repairment/replenishment of local tissue injury at GI level, mucus secretion and/ or loss of plasma or blood and other defensive and immuno-modulatory system during parasitism.

The interaction between the host and nutrition can be broadly discussed from two interrelated perspectives, i) the effects of nutrition on the metabolic disturbances and pathophysiology induced by parasitism; and ii) the influence of nutrient availability on the ability of the host to mount effective response against parasite establishment and/or development and to induce parasite rejection [56,57]. Most of the parasitic infection in domestic animals is caused by GIN, which may result in depression in appetite, impairment in GI functions, alteration in protein, energy and mineral metabolism and changes in water balance. In infested animals the protein deficiency occur via two processes, one due to leakage across damaged mucosa and second by diversion of protein from production to enhance immune response against worms and repair of damaged epithelial tissue of intestine. In high producing animals, periparturient relaxation in immunity is often associated with transitory increase in faecal egg counts during late pregnancy and lactation, and this effect was exacerbated during protein undernutrition. In multiparous ewes/does, it is suggested to integrate parasite management programs during periparturient period by making use of both protein supplementation and genetic selection to increase worm resistance and reduce dependency on anthelmintics for worm control [58].

Nutrition-environment interaction

Nutrition represents one of the greatest environmental determinants of farm animal's health. Therefore, livestock community would like to manipulate environmental factors, such as nutrients, to consequently yield the epigenetic mechanisms necessary to achieve phenotypes of interest. Improved or increased livestock productivity by using nutritional epigenetics has been observed through lower body fat (sheep) and higher protein mass (chicken) gains as well as altered expression of key gluconeogenic enzymes (pigs) [59].

Another aspect of nutrition-environment interaction is directly related to animal performance including intake and feed use efficiency within pastoral ecosystems and other adoptable rearing practice. Nutritional modulation and often catalytic supplements to augment metabolic activity and correct deficiency or meeting supra-nutritional requirements needs improved understanding of the interactions between livestock, plants and soils with a vision of improving productivity and efficiency needs. Further, semi-intensive and intensive system of rearing advocates housing that confers a micro-environment, which can be manipulated for better animal welfare and productivity. There is increasing interest in how to manage breeding females and their offspring to either minimise the consequences of adverse environmental effects or to enhance productivity and efficiency of offspring. Among the numerous variables affecting livestock production, thermal stress has been identified to be the cause of severe economic consequences and in view of climate change, the animals will every likely subject to multiple stress involving thermal, nutritional and walking stress in search of food and pasture that may severely hampers livestock production. Catalytic supplementation of mineral mixture and antioxidant has been seen to minimize the adverse effect of heat stress on the productive and reproductive efficiency of Malpura ewes [60,61]. In general, trace element deficiencies and toxicities are not commonly encountered in clinical practice, particularly in regions where there is access to adequate nutrition.

Pharmaconutrition

It focuses on the nutrients that are to be studied as therapeutic agents administered in physiologic and supraphysiologic (i.e. pharmacologic) doses, thus shifting the focus of specialized nutrition support to a study of active therapeutics [62]. The concept of pharmaconutrition advocates investigating the effects of pharmacologic doses of individual nutrients on immune function and ensuing clinical outcomes. Multiferous uses of pharmaconutrients are described [63] as i) to modulate the inflammatory and immune response associated with critical illness, ii) to modulate metabolic function in obese patients, iii) to improve gut microbiology and functional health of gastrointestinal tract and iv) to support or enhance drug delivery, disposition and pharmacokinetics and overall pharmacological action. The known physiological mechanisms of pharmaconutrients such as glutamine, arginine, ω-3 fatty acids, and selenium helps the clinician to recommend as an adjunct to drugs or as a special nutritional supplement to augment the therapeutic recovery process. Considering the overall treatment effect of immune-modulating nutrients, parenteral glutamine is recommended in patients receiving parenteral nutrition, while enteral glutamine is considered in burn and trauma patients [64]. Antioxidants, particularly selenium, should be considered for critically ill patients, and enteral formulas enriched with fish oils are recommended in patients with acute respiratory distress syndrome.

Nutrition-drug interaction

The nutrient-drug interactions may lead to clinical problems often resulting in adverse drug reactions/toxicity and even nutritional deficiencies. These interactions are significant when they diminish the intended purpose of the drug; when they impair the nutritional status of the individual; or when they cause acute or chronic drug toxicity. Various facets of drug-nutrient interaction are delineated [65], where drugs can affect the nutritional status in many ways:

- Influence appetite, taste acuity, and gastrointestinal function and thus increase or decrease nutrient intake,
- Affect carbohydrate metabolism,
- Alter lipid metabolism, causing increases or decreases in serum lipids,
- Have anabolic or catabolic effects on protein metabolism,
- Effect absorption, thus altering nutrient bioavailability.

The most commonly observed potential drug-nutrient interactions were gastrointestinal interactions affecting the drug bioavailability and the mineral status of the patients. Virtually every individual on multiple drug long term therapy incurs drug-nutrient interactions. Assuming that increased days of treatment or number of treatments is representative of disease severity, long-term calf performance is negatively affected by severe calf-hood disease [66]. Nutritional effects on drug metabolizing enzymes also have implications for endogenous substances and environmental toxins and carcinogens, which are metabolized by the same or related enzyme systems, and for related diseases [67]. Therefore, it would seem that designing clinical recommendations to maximize the effects of food and reduce the impact of toxins is essential. The complexity and the diversity in the type of interactions within the species, between the species and amongst the drugs warrant the Veterinarians to be more cautious while prescribing the drugs.

Surgical operations: In addition to post-operative care, the patients with various surgical conditions like gastrectomy and intestinal surgery, wounds or burns, surgery of joints or bones, etc. should have provision for complete and balanced diet with emphasis on pre and postoperative nutrition, viz. liquid preparations, high protein and calorie based diet, nutrient dense low volume diet, enzyme preparations, added vitamins (A, C and E), added minerals (Zn, Fe, Ca, P, etc.), supplemental amino acids (lysine, methionine, arginine).

Nutritional support and calculating requirements

Nutritional support replenishes tissue stores, improves immune function and wound healing and prevents death from cachexia. In persistent clinical illness nutritional status can be severely compromised by the combined effects of reduced feed intake and increased metabolic demands secondary to fever and tissue catabolism. Recommendations for dietary management of clinically ill animals are based primarily on data from healthy animals of a particular and/or related species because there are very few studies of nutritional needs of injured or ill farm animals. The clinically ill animals are usually less active and while calculating energy requirements, it is best to use the estimated requirement for animals confined to stalls and multiply these basal energy requirement by a "fudge factor" that reflects the severity of the disease and stress [68]. It is well established that both nutritional deficiencies and excesses alter susceptibility to infection both in humans and animals. Another aspect of concern is anorexia which may further limit the total nutrient uptake for meeting the requirements of animals. A variety of feeds should be offered in small amounts to determine preferences and some palatability enhancers may be added to modulate feed intake. Oral supplementation is preferred first, and extra-oral or parenteral nutrition are alternatives to feeding animals that do not respond to managerial or chemical stimulants of appetite. Following points should be taken into account while calculating the nutrient requirements of animals suffering from fever/pyrexia:

- Increase in the metabolic rate amounting to 13% for every degree celsius rise in body temperature, an increase also in restlessness and hence a greatly increased caloric need.
- Decreased glycogen stores and decreased stores of adipose tissue due to increased BMR and gluconeogenesis.
- Increased protein catabolism and additional renal output for excretion of nitrogen wastes.
- Accelerated loss of body water owing to increased perspiration and excretion of body wastes.
- Increased excretion of Na, K and altered serum concentration with decreased Fe and Zn and increased Cu.

Nutritional requirement for immune development may be different during the prenatal compared with the postnatal period and are strongly affected by the processes of growth and development, productivity operational use etc. Protein-caloric malnutrition is considered to be the commonest problem which predispose animals to infection like tuberculosis (TB), herpes, pneumonia, measles etc. caused by intracellular pathogens [69]. Besides specific treatment based on the aetiological factor and extent of liver involvement, the goal of nutritional therapy in animals with hepatopathy is to maintain metabolic balance and provide necessary nutrients for healing [70]. Amino acids mixture, especially those containing methionine, is used in hepatopathy with good results. Diets high in carbohydrate, calcium and protein of high biological value are known to have protective effects in hepatic disorders. In chronic hepatic diseases, diet needs to be supplemented with vitamins and minerals that are supposed to be depleted in hepatopathy. Antioxidant supplements such as vitamin E and beta-carotene help eliminate the free radical particles, which accumulate and can damage body tissues and contribute to the signs of aging. Antioxidants can also increase the effectiveness of the immune system. Clarity of understanding of the pathophysiology of oxidative stress in ruminants during peri-parturient period will allow the design of specific antioxidant therapies. Moreover, oxidative stress is also considered necessary to promote healing and repair of tissues. Routine care of production or disease stressed animals should involve adherence to a consistent daily routine, regular attention to normal health care procedures and periodic veterinary examinations for assessment of the presence or progression of chronic disease. Stressful situations and abrupt changes in daily routines should be avoided and if at all a drastic change must be made, attempts should be made to minimize stress and to accomplish the change in a gradual manner.

Nutritional advice for unhealthy or diseased animals

It is more logical to relate diet that can affect or modulate a disease condition and in general the adverse effects of inadequate caloric intake is associated with hyporexia or anorexia of illness. Proper nutrition can minimize the incidence or help control metabolic, infectious, and reproductive disorders in a dairy herd. Some of the indicators of possible nutritional problems in a herd can be evaluated from a set of observations as follows:

- Abnormally high incidence (> 10 - 15%) of metabolic disorders;
- Increased incidence of infectious disease and poor response of animals to vaccinations;
- Higher than normal occurrence of weak or silent heats and low conception rate;

- High incidence of off-flavors in milk, especially rancidity, oxidized or cardboardy milk, and malty or unclean tastes;
- Excessive decline in milk production, failure to achieve high milk yields during peak lactation, and generally lower production than what nutrition or genetics would warrant;
- If, there is more than 10% of the herd in the extreme categories of body condition
- Depressed DM intakes for the whole herd or within certain milking groups.

Supportive nutrition

- Administering feed additives: B-complex vitamins, dried brewer's yeast, probiotics (live yeast cell e.g. *Saccharomyces cerevisiae*, *Aspergillus oryzae*), or feeding sodium bicarbonate.
- Encourage intake by feeding unusual feedstuffs to those animals that are severely off-feed for several days. Items could include different forages like grass hay or straw, calf starter, or cereal grains. If at all possible, encourage forage intake over concentrates.
- Try sources of rumen bypassable or protected amino acids.
- Look for complicating infections or inflammations.
- Consider additional supportive treatments for ketosis (see next section).

Preventative nutrition

- Balance rations with an emphasis on crude protein, soluble intake protein, undegradable intake protein, forage and total neutral detergent fiber, calcium, magnesium, sodium, and chloride intakes for both dry and lactating cows. Maintain the proper mineral balance during the dry period.
- Avoid overfeeding concentrates to dry cows and recently fresh cows. Close-up dry cows should not receive over 30% of the total DM intake as concentrate. In conventionally fed herds, gradually increase grain from 1.0% of body weight after calving. In herds feeding a total mixed ration, recently fresh cows should not receive greater than 50 to 55% concentrate.
- Keep sodium bicarbonate in the lactating cow ration, especially for just recently fresh animals.
- Full feed good quality forage for the first one to two weeks after calving. Avoid or feed reduced amounts of abnormally fermented feeds for two weeks prior to and six to eight weeks after freshening. Upgrade forage quality two to four weeks prior to calving if a low digestible forage(s) is being fed during the early dry period. Check and monitor forage intake and particle size of the diet.
- Administer high-calcium boluses (75g calcium carbonate) as soon as possible after freshening and within eight hours of parturition.
- Sample and analyze total mixed rations for the dry cows and post fresh groups and compare with the programmed specifications. Check feeding rates on a routine basis.
- Test drinking water for heavy bacterial contamination, pH, and nitrates.

- Check that cows do not have access to excessive amounts of acorns, green-chopped corn silage, toxic weeds and heating forages.

Minerals and farm animal health

Interactions between minerals and other substances within the diet can occur within the digestive tract that impair mineral absorption. In the animal system, there is concentration dependent paracellular or transcellular absorption of minerals. In general, transcellular absorption is critical to allowing the animal to meet its mineral needs when diet mineral concentrations are marginal, and it depends on the ability of the diet to present enough minerals in an ionized form. Minerals can be categorized as positively charged cations and negatively charged anions and the relative amount of cations versus anions absorbed helps determine the acid–base status of the animal. Manipulation of dietary cation and anion content is commonly used as a tool in the dry period and during lactation to improve performance. Many microminerals play a role in the body as cofactors of enzymes involved in controlling free radicals within the body and are vital to antioxidant capabilities, but if consumed in excess, can become pro-oxidants in the body, generating destructive free radicals. This complex interactions between minerals can compromise the effectiveness of a diet in promoting health and productivity of farm animals.

Skeletal abnormalities: The major osteopathic conditions are rickets and osteomalacia, osteoporosis, arthritis and abnormal bone growth. The diet of diseased animals should be balanced for growing pups (extra protein for growth) and adult maintenance with meat and bone based supplement. It should have added Ca and P at proper ratio (1.3:1) and adequate vitamin A and D. In conditions like arthritis and joint pain, the protein content should be low to support minimum maintenance and should have prebiotics like inulin and oligofructans and nutraceuticals (glucosamine, chondroitin sulfate).

Conclusion

The interaction between illness, health, and nutritional status is multifactorial and complex. Nutrition of animal is ranked as one of the major area of importance amongst the acquired characteristics in relation to disease resistance. Stress on the other hand is an internal (Physiologic or psychogenic) or external (environmental, climate, microbes, trauma, parasites, toxicants etc) stimulus that initiates an adaptive change or stress response in the animal. Besides focusing on PEB and prepartum energy intake, the effects of dietary protein level, protein type, essential amino acids (e.g. methionine), or individual FA on the success of the cow's transition through calving need renewed attention. Understanding the molecular and metabolic changes associated with the level of feeding and feed ingredients on important biochemical processes will help validate the GI nutritional management and improve cow longevity, reproductive and productive efficiency, and animal welfare. Formulation of diets for stressed animals and fortification of micronutrients beyond the levels are needed to compensate for these effects. The possibility of dietary nutrient manipulation for optimization of immune response without compromising the genetic potential of animals for growth and production appears to be feasible and thus will economically benefit the livestock formers and the sector as a whole. There is also a need to consider the nutrition, disease control and flock/herd management together to ensure maximum profitability from livestock production. Therefore, the newer approaches should aim at:

- Metabolic effects of infection and dietary corrections.
- Homeostasis, homeorrhesis and nutrient flow.
- Stress and its relationship to mechanisms of disease and therapeutics.
- Metabolic limits to milk production: exogenic manipulation and interaction of cattle health/immunity and nutrition.
- Nutrition in immunostimulation and immunosuppression.

- Nutrition and antioxidants: role in immunity improvement following stress.
- Thermal stress, metabolic alterations, and nutritional strategies.
- Nutritional manipulation for the amelioration of the harmful effects of pollutants.
- Nutrition and drug interaction.
- Therapeutic nutrition and diet formulation.

This asks for a multidisciplinary approach to develop nutritional strategies that would allow farm animals to become more resilient to the environmental and physiological challenges that they will have to endure during their productive career. As we discover more about nutrigenetics and nutrigenomics, and as we expand our basic understanding of idiopathic diseases it is imperative to identify more nutritionally related causes, and be able to develop novel dietary strategies to manage disease processes, including the formulation of diets designed to alter gene expression to obtain beneficial clinical outcomes.

Conflict of Interest

The author has no financial or other conflict of interest in publishing this article.

Bibliography

1. Sahoo A. "Clinical nutrition- scope and significance". In: (Eds) VRB Sastry, A Sahoo, AK Pattanaik and DK Agarwal, Nutrition and Dietetics under Clinico-therapeutic Conditions of Pet and Farm Animals, CAS in Animal Nutrition, *Indian Veterinary Research Institute* Izatnagar, India (2001): 1-7.
2. Sahoo A. "Nutritional management of pet animals under different stress conditions". In: Proceeding, IV Biennial Conference & Exhibition, WBUAFS, Kolkata. India (2002): 69-83.
3. Spencer GSG. "Hormone manipulation of animal production by immuno neutralization". In (Eds) PJ Buttery, DB Lyndsey and NB Haynes, Control and Manipulation of Animal Growth. Battlerworth, London, (1986): 279-291.
4. Aston R., *et al*. "Enhancement of bovine growth hormone activity *in vivo* by monoclonal antibodies". *Molecular Immunology* 24 (1987): 143-150.
5. Wernerman J. "Glutathione status in clinically ill patients; possibility of modulation by antioxidants". *Proceeding of the Nutrition Society* 58 (1999): 677-680.
6. Celi P. "Oxidative stress in ruminants". In: (Eds) Mandelker L and Vajdovich P. Studies on Veterinary Medicine. Oxidative Stress in Applied Basic Research and Clinical Practice. Humana Press, Totowa, NJ. (2011): 191-231.
7. Beisel WR. "Metabolic effects of infection". *Progress in Food and Nutrition Science* 8 (1984): 43-75.
8. Scrimshow NS., *et al*. "Interactions of nutrition and infection". *Monograph Series of World Health Organization, Geneva* 57 (1968): 3-329.
9. Latshaw DL. "Nutrition mechanisms of immuno suppression". *Veterinary Immunology Immunopathology* 30 (1991): 111-120.

10. Saeed F., *et al*. "Studying the impact of nutritional immunology underlying the modulation of immune responses by nutritional compounds-A review". *Food and Agriculture Immunology* 27 (2016): 205-229.

11. Cray C., *et al*. "Acute phase response in animals: a review". *Comparative Medicine* 59 (2009): 517-526.

12. Petersen HH., *et al*. "Application of acute phase protein measurements in veterinary clinical chemistry". *Veterinary Research* 35 (2004): 163-187.

13. Armstrong DG., *et al*. "Interactions between nutrition and ovarian activity in cattle: physiological, cellular and molecular mechanisms". *Reproduction Supplement* 61 (2003): 403-414.

14. Vinoles C., *et al*. "Short-term nutritional supplementation of ewes in low body condition affects follicle development due to an increase in glucose and metabolic hormones". *Reproduction* 129 (2005): 299-309.

15. Vinoles C., *et al*. "The use of a 'first-wave' model to study the effect of nutrition on ovarian follicular dynamics and ovulation rate in the sheep". *Reproduction* 140 (2010): 865-874.

16. Pisani LF., *et al*. "Effects of pre-mating nutrition on mRNA levels of developmentally relevant genes in sheep oocytes and granulosa cells". *Reproduction* 136 (2008): 303-312.

17. Robinson JJ., *et al*. "Nutrition and fertility in ruminant livestock". *Animal Feed Science and Technology* 126 (2006): 259-276.

18. Ashworth CJ., *et al*. "The impact of in-utero-nutritional programming on small ruminant performances". In: (Eds) Papachristou TG, ZM Parissi, H Ben Salem, P. Morand-Fehr, Nutritional and foraging ecology of sheep and goats. Zaragoza: CIHEAM/FAO/ NAGREF, Options Méditerranéennes: Série A. Séminaires Méditerranéens; n. 85 (2009): 337-349.

19. NRC. "Nutrient Requirements of Dairy Cattle". 7th rev. ed. National Research Council, US National Academy of Science, Washington, DC (2001).

20. NRC. "Nutrient Requirements of Small Ruminants: Sheep, Goats, Cervids and New World Camelids". *National Research Council, National Academy of Sciences* (2007).

21. El-Shahat KH and AM Abo-El maaty. "The effect of dietary supplementation with calcium salts of long chain fatty acids and/or l-carnitine on ovarian activity of Rahmani ewes". *Animal Reproduction Science* 117 (2010): 78-82.

22. El-Nour HHM., *et al*. "Effect of calcium soap of fatty acids supplementation on serum biochemical parameters and ovarian activity during out-of-the-breeding season in crossbred ewes". *The Scientific World Journal* 1 (2012): 1-7.

23. Kenyon PR., *et al*. "Effects of twin-bearing ewe nutritional treatments on ewe and lamb performance to weaning". *Animal Production Science* 51.5 (2011): 406-415.

24. Sahoo A. "Nutrition and feeding of prolific sheep". In: PCR based FecB genotyping in sheep, Training Mannual, CSWRI Publication, Avikanagar, India. (2013): 88-95.

25. Lozano JM., *et al*. "Influence of nutrition on the effectiveness of superovulation programmes in ewes: effect on oocyte quality and post-fertilization development". *Reproduction* 125 (2003): 543-553.

26. Boland MP., *et al*. "Effect of nutrition on endocrine parameters, ovarian physiology, and oocyte and embryo development". *Theriogenology* 55 (2001): 1323-1340.

27. Bauman DE and WB Currie. "Partitioning of nutrients during pregnancy and lactation: A review of mechanisms involving homeostasis and chomeorhesis". *Journal of Dairy Science* 63 (1980): 1514-1529.

28. Spurlock ME. "Regulation of metabolism and growth during immune challenge: An overview of cytokine function". *Journal of Animal Science* 75 (1997): 1773-1783.

29. Flint DJ., *et al*. "Stimulatory and cytotoxic effects of an antiserum to adipocyte plasma membranes on adipase tissue metabolism *in vivo* and *in vitro*". *International Journal of Obesity* 10 (1986): 69-77.

30. Ozanne SE and CN Hales. "The long-term consequences of intra-uterine protein malnutrition for glucose metabolism". *Proceeding of The Nutrition Society* 58 (1999): 615-619.

31. Sahoo A. "Pharmaconutrition in canine practice: role of dietary fiber". In: Proceeding, National Congress on Canine Practice and 6th Convention of ISACP & National Symposium on "Modern Look on Canine Health Care Management in the Global Perspective". WBUAFS, Kolkata, India (2009)

32. Chandra RK. "Nutrition and immunology: from the clinic to cellular biology and back again". *Proceeding of The Nutrition Society* 58 (1999): 681-683.

33. Galyean ML. "Interaction of cattle health/immunity and nutrition". *Journal of Animal Science* 77 (1999): 1120-1134.

34. Roche JR., *et al*. "Nutritional management of the transition cow in the 21st century - a paradigm shift in thinking". *Animal Production Science* 53 (2013): 1000-1023.

35. Bell AW. "Regulation of organic nutrient metabolism during transition from late pregnancy to early lactation". *Journal of Animal Science* 73 (1995): 2804-2819.

36. Horst RL., *et al*. "Strategies for preventing milk fever in dairy cattle". *Journal of Dairy Science* 80 (1997): 1269-1280.

37. Huzzey JM., *et al*. "Prepartum behavior and dry matter intake identify dairy cows at risk for metritis". *Journal of Dairy Science* 90 (2007): 3220-3233.

38. Mallard BA *et al*. "Alteration in immune responsiveness during the peripartum period and its ramification on dairy cow and calf health". *Journal of Dairy Science* 81 (1998): 585-595.

39. Goff JP. "Macromineral physiology and application to the feeding of the dairy cow for prevention of milk fever and other periparturient mineral disorders". *Animal Feed Science and Technology* 126 (2006): 237-257.

40. Overton TR and MR Waldron. "Nutritional management of transition dairy cows: strategies to optimize metabolic health". *Journal of Dairy Science* 87 (2004): E105-E119.

41. Goff JP. "Invited review: Mineral absorption mechanisms, mineral interactions that affect acid-base and antioxidant status, and diet considerations to improve mineral status". *Journal of Dairy Science* 101 (2018): 2763-2813.

42. Celi P., *et al*. "Gastrointestinal functionality in animal nutrition and health: New opportunities for sustainable animal production". *Animal Feed Science and Technology* 234 (2017): 88-100.

43. Kogut MH and RJ Arsenault. "Editorial: gut health: the new paradigm in food animal production". *Frontiers in Veterinary Science* 3 (2016).

44. Sahoo A. "Pre- and pro-biotics translating gut microbiota and host health". In: Proceeding National Seminar on "Opportunities and Challenges of Translational Research in the Frontier Areas of Animal Biotechnology". OUAT, Bhubaneswar, India (2017).

45. van der Meer Y., *et al*. "Performance of pigs kept under different sanitary conditions affected by protein intake and amino acid supplementation". *Journal of Animal Science* 94 (2016): 4704-4719.

46. Cottrell JJ., *et al*. "Nutritional strategies to alleviate heat stress in pigs" *Animal Production Science* 55 (2015): 1391-1402.

47. Rist VT., *et al*. "Impact of dietary protein on microbiota composition and activity in the gastrointestinal tract of piglets in relation to gut health: a review". *Animal* 7 (2013): 1067-1078.

48. de Lange CFM., *et al*. "Strategic use of feed ingredients and feed additives to stimulate gut health and development in young pigs". *Livestock Science* 134 (2010): 124-134.

49. Zoran D. "Nutritional management of gastrointestinal disease". *Clinical Techniques in Small Animal Practice* 18 (2003): 211-217.

50. Singh B and A Sahoo. "Newer concepts, implications and approaches in the use of unconventional feeds to improve animal production". In: Proceeding, V^{th} Biennial Conference of ANA. NIANP, Bengaluru (2004): 1-14.

51. Sahoo A. "A review on nutrition and gastro-intestinal nematode parasitism: interaction and implications in ruminant livestock". *Indian Journal of Small Ruminants* 17 (2011): 1-20.

52. Waller PJ and SM Thamsborg. "Nematode control in 'green' ruminant production systems". *Trends in Parasitology* 20 (2004): 493-497.

53. Coop RL and I Kyriazakis. "Influence of host nutrition on the development and consequences of nematode parasitism in ruminants". *Trends in Parasitology* 17 (2001): 325-330.

54. van Houtert MFJ and AR Sykes. "Implication of nutrition for the ability of ruminants to withstand gastrointestinal nematode infections". *International Journal for Parasitology* 26 (1996): 1151-1167.

55. Sykes AR. "Manipulating host immunity to improve nematode parasite control - Quo vadit". *Parasite Immunology* 30 (2008): 71-77.

56. Colditz IG. "Metabolic effects of host defence responses during gastrointestinal parasitism in sheep". *Australian Journal of Experimental Agriculture* 43 (2003): 1437-1443.

57. Colditz IG. "Some mechanisms regulating nutrient utilization in livestock during immune activation". *Australian Journal of Experimental Agriculture* 44 (2004): 453-457.

58. Kahn LP., *et al*. "Regulation of the resistance to nematode parasites of single- and twin-bearing Merino ewes through nutrition and genetic selection". *Veterinary Parasitology* 114 (2003): 15-31.

59. Murdoch BM., *et al*. "Nutritional influence on epigenetic marks and effect on livestock production". *Frontier Genetics* 7 (2016): 182.

60. Sejian V., *et al*. "Effect of mineral mixture and antioxidant supplementation on growth, reproductive performance and adaptive capability of Malpura ewes subjected to heat stress". *Journal of Animal Nutrition and Animal Physiology* 98 (2013): 72-83.

61. De Kalyan., *et al*. "Effect of selenium-yeast feeding on amelioration of simulated heat stress and reproductive performance in Malpura ewe under semi-arid tropical environment". *Indian Journal of Animal Sciences* 87 (2017): 163-167.

62. Pierre JF., *et al*. "Pharmaconutrition review: physiological mechanisms". *JPEN Journal of Parenteral and Enteral Nutritio*n 37 (2013): 51S-65S.

63. Sahoo A., *et al*. "Immuno-biochemical status of sheep exposed to periods of experimental protein deficit and re-alimentation". *Journal of Animal Science* 87 (2009): 2664-2673.

64. Jones NE and DK Heyland. "Pharmaconutrition: a new emerging paradigm". *Current Opinion in Gastroenterology* 24 (2008): 215-222.

65. Sahoo A. "Drug bioavailability in animals: Impact of feeding and nutrition". *INTAS Polivet* 7 (2006): 1-7.

66. Gow S., *et al*. "The effect of treatment duration on weaning weights in a cow-calf herd with a protracted severe outbreak of diarrhea in calves". *Canadian Veterinary Journal* 46 (2005): 425-426.

67. Hodges RE and DM Minich. "Modulation of metabolic detoxification pathways using foods and food-derived components: a scientific review with clinical application". *Journal of Nutrition and Metabolism* (2015).

68. Ralston SL. "Fudge factors for estimating caloric needs of clinically ill animals". *Journal of Equine Veterinary Science* 5 (1985): 336.

69. Keusch GT. "Malnutrition and the thymus gland". In: Cunningharm RS (Eds) Nutrient modulation of immune response. New York, Marcel Dekker, Inc. 9 (1993): 283-299.

70. Patra RC and A Sahoo. "Nutritional therapy in hepatopathy". *Livestock International* 6 (2002): 14-16.

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