ROLE OF NUTRITION IN RELATION TO IMMUNE SYSTEM - A REVIEW

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ABSTRACT
Most nutritional research on various nutrient requirements for animals is carried out under strict sanitation and pathogen free state that cannot be applicable in real field conditions. For this reason, the minimum nutrient requirements prescribed by various feeding standards (NRC, ARC, BIS) may not be relevant to on-farm conditions. The immune system must compete with production for nutrients. When the immune system is engaged in defense against a particular pathogen, its actual nutrients demand might be increased manifolds because of anabolic components of the immune system i.e. clonal proliferation of lymphocytes, production of immunoglobins, recruitment of new myloid cells, synthesis of mineral content enzymes and metallo-proteins, chaperones, hepatic secretion of acute phase proteins including complement components, thousands types of receptor proteins, transcription factors etc. Many effector mechanisms used by the immune system generate large amount of reactive oxygen intermediates. Nutrient antioxidants can successfully protect bio-molecules against damage from these reactive oxygen intermediates. For instance, vitamin E exerts its action on the immune system by lowering of the prostaglandin synthesis and by preventing the oxidation of PUFA in the cell membrane. Nutritional manipulation might affect not only the development of immune system but also the immune defense to pathogen.

An immune reaction can be triggered by using nutrition in several aspects. Nutritional status of the developing embryo through dam has profound effects on the development of its immune system as well as degree of immune response to a specific disease. Only dietary nutrients can provide the substrates for proliferation and adequate action of immune cells and effectors molecule. Based on this view, the nutritional status of an animal can dramatically affect the degree of immune cell proliferation and/or defensive molecules production. Productive farm animals require all kind of dietary nutrients in right proportion and in right amount for invading pathogens rely on the host by supplying the nutrients. For this reason, deficiency, excess and/or imbalance of protein, amino acids, energy, vitamins, minerals or anti-nutritional factors etc. can be affected, the ability of a pathogen to replicate and expand in vivo. In addition, most of the nutrient can be effective as substrate for inter-cellular and intra-cellular signal transduction of the immune cells and their bioavailability may be extremely critical for a purposeful immunocompetent. Pattern of nutrient intakes and their availabilities may also affect the endocrine system which enhances magnitude, type and/or duration of the immune functions. The immune system can act to recognize the presence of macromolecules of non-self origin. Immune cells can respond even more effectively on second exposure to the same protein antigens through their cell receptors e.g. membrane bound immunoglobulin, while phagocytic cells such as neutrophil, eosinophil, macrophages, dendritic cells and its modification forms specially recognize lipid and carbohydrate complex molecules through their complex surface pattern receptors. Antigen recognition results in leukocyte activation, revive complement system, cytokine secretion and the engagement of defensive mechanisms directed at removal of the pathogen. Bearing in mind, this review discusses development of recent concepts and literature on role of nutrition and its importance in immune response.
Overview of cytokines networks in relation to immune reaction

Cells of the immune system secrete a puzzling variety of proteins that regulate the immune responses by signalling between cells. The generic term for these regulatory proteins is cytokine. When cytokines bind to specific receptors on the cell membrane of target cells and signal transduction pathways, ultimately, they can have a difference of effects on the behaviour of the cells. Cytokine may induce the target cell to divide or differentiate, or may stimulate the production of new receptors and/or other protein products by altering gene expression in target cells (Paludan, 2000; Singh and Pachauri, 2001). Alternatively, cytokines may inhibit these effects, inhibiting division, differentiation, or new protein synthesis. The activities of cytokine can be regulated by regulation of receptor expression, by receptor antagonists, by specific binding proteins and/or by other cytokines that exert opposite effects (Callard and Gearing, 1994). The response of T cells to IL-2 (interleukin-2) is largely determined by the level of IL-2R expression in target cells. Resting T cells (T-lymphocyte) express very little receptor but begin its synthesis and expression when activated. The actions of IL-1 have been generated by the activation of receptor antagonist (IL-1RA). This is a form of IL-1, which binds to the IL-1 receptor but does not stimulate signal transduction. For that reason, it blocks the activities of active- IL-1 (Akira et al., 1990). Macrophages produce four major cytokines, namely IL-1, IL-6, IL-12 and TNF-α. Their production has triggered by many different stimuli, including bacteria and their products such as endotoxin, leukotrienes, activated complement components, immune complexes, TNF (tumor necrosis factor) and IL-1 itself (Paludan, 2000; Sharma et al., 2002). There are three subtypes of IL-1 i.e. IL-1α, IL-1β and IL-1RA. The interleukin-1 has also produced by langerhans-cells, T cells, B cells, NK cells, vascular endothelium, fibroblasts and keratinocytes. Interleukin-1 acts on T cells, B cells, NK cells, neutrophils, eosinophils, dendritic cells, fibroblasts, endothelial cells, hepatocytes and monocytes. IL-1α and IL-1β are the major co-stimulators of helper T lymphocyte-2 (Th-2 cells). The IL-1RA, in contrast, is biologically inert and binds to the type 1 IL-1R (target cell) but does not trigger signals. For that reason, it acts as a receptor antagonist (Myers and Muttaugh, 1995). IL-6 has produced not only by macrophages but also by T- and B- cells, bone marrow-stromal cells, vascular endothelial cells, fibroblasts, keratinocytes and mesenchimal cells. IL-6 acts on T cells, B cells, hepatocytes and bone marrow-stromal cells. Interleukin-6 enhances IL-2 and IL-2R production and T cell differentiation. It acts as a cofactor with IL-1 in IgM synthesis and with IL-5 in IgA synthesis. It also stimulates the production of acute phase proteins (APP) by hepatocytes and acts as a pyrogen (a fever producing substance) (Downing and Miyan, 2000). The tumor necrosis factor-alpha (TNF-α) is secreted by macrophages, T cells, B cells and fibroblasts and can act on almost all nucleated cells. The TNF-α is a mediator of many immune and inflammatory functions and regulates the growth of many cell types. It also activates macrophages and can trigger apoptosis in some tumor cells. The TNF-β type (lymphotoxin) has produced by Th-1 cells and activated CD8+ T cells (cluster of differentiation 8-plus expressed T lymphocytes). The TNF-β may be secreted in a soluble form or remain associated with another protein, lymphotoxin-β (LTB) in the T cell membrane. TNF-β also causes apoptosis of tumor cells and activates neutrophils, macrophages, endothelial cells and B cells (Callard and Gearing, 1994). The interleukin-16 has secreted by CD8+ and which suppresses the replication of immunodeficiency viruses. The interferon (INF) is a family of glycoprotein with molecular weight of 20-34
KDa secreted by viral infected cells that protect other cells against virus, bacterial and protozoan invasion. Interferon (IFN) are classified into two major classes i.e. class-I includes IFN-γ, IFN-β and IFN-ω, and the class II is IFN-α. The IFN-α is produced by lymphocytes, monocytes and macrophages whereas the IFN-β is produced by fibroblasts. The embryonic trophoblast cells produce the IFN-ω. All types of interferon probably act on virus-infected cells to inhibit viral growth and activate macrophage. A cytokine derived from antigen stimulated T cells i.e. Th-1 cells, CD8 + T cells and NK cells mainly produce IFN-γ (Roitt et al., 1997; Singh and Pachauri, 2001). The IFN-γ acts on B cells, T cells, NK cells and macrophages. IFN-γ stimulates B cell for production of Ig2a and lower production of IgG3, IgG1, IgG2b and IgE. It enhances T cell production of MHC class I. The IFN-γ induces Th-1 cells to produce both IL-2 and IL-2R and acts on Th-2 cells to inhibit the production of IL-4 and as a result, blocks IgE production (Henderson and Black, 1992). IFN-γ activates macrophages secretion of IL-1, IL-6 and TNF-α (but all of which are inhibited by IL-4 derived from activated Th-2 cells) and greatly increases their ability to destroy ingested pathogenic microorganisms. It promotes antibody mediated phagocytosis as well as antibody dependent cell mediated cytotoxicity reactions.

The binding of antigen in TCR (T-cell receptor) must send a signal to the T cell and trigger an appropriate response. For this reason, the two antigen-binding chains of TCR are always associated with a set of glycoproteins collectively called CD3. The CD3 complex is required to transfer a signal from the TCR module to the cell. CD3 consists of 4 peptide chains (γ, δ and 2ζ). The TCR β chain has directly linked to CD3γ, and the TCRα chain linked to CD3ζ. Both the TCR chains are linked to CD3ε. In addition to there are two additional peptide chains associated with TCR and CD3. These are called ζ (zeta) and η (eta) and are structurally and genetically distinct from the CD3 chains (Kabelitz, 1990). About 90% of α/β TCRs have a ζ-ζ homodimer, so that the complete complex consists of α/β - γδεζζ. The remaining 10% have - heterodimers i.e. α/β - γδεζη. The ζ-ζ and ζ-η dimers also play an important role in signal transduction (Tizard, 1997; Goldsby et al., 2000). Two other peptides (CD4 and CD8) are found in association with TCR. The CD4 is a single chain glycoprotein of 55 KDa, and CD8 is a dimer of 68 KDa. The presence of CD4 or CD8 determines the class of the MHC molecule that is recognised by a T cell. Thus, CD4 is found on helper T cells and which binds to MHC class II molecules on an antigen-presenting cell and helps trigger a helper response. The CD8, in contrast, is found on cytotoxic T cell (Tc cell) and which binds to MHC class I molecule on an antigen-presenting cell on an antigen-presenting cell (particularly endogenous antigen) and triggers a cytotoxic response (by destroying foreign or altered cells such as virus infected cells and foreign organ graft). Stimulation of T cell by APC is potentiated about 100 folds when CD4 or CD8 is associated with TCR (Seder and Le Gross, 1995; Sharma et al., 2002). The Tc cell receives two signals. The first is IL-2 secreted by Th-1 cells. The regulatory protein molecule, IL-2 binds to receptors on CD8+ T cells, triggering them to make more IL-2 receptors. The second signal comes from the endogenous antigen-MHC class I complex of the abnormal cell binding to the TCR- CD8 complex of the T cells. The combination of signals initiates DNA synthesis and mitosis. Responding T cells, as they divide, eventually differentiate into memory T cell populations. Once fully activated, Tc cells trigger apoptosis in their targets through either perforin (found in the type I granules of Tc cells and NK cells) or fas (CD95) pathways (Roitt et al., 1997).
Nutrients on cytokine system of immune response

The major proinflammatory cytokines such as interleukin 1 (IL-1), IL-6, IL-8, tumor necrosis factor- alpha (TNF-α), interferon-gamma (IFN-γ) etc. act as communication molecules between the cells of the immune system and control the movement of lymphocytes in, or between tissues and other cells of the body (Ling et al., 1997; Chang and Bistrian, 1998). Secretion of these regulatory proteins occurs rapidly after an infectious challenge with suitable nutrients environment and they act locally to regulate the immune response. The proinflammatory cytokines reach systematically relevant levels within a few hours of a challenge (Taga and Kishimoto, 1993).

Quantitatively, their production is regulated by a complex network of costimulatory and feedback loops that respond to various stimuli (Roitt et al., 1997; Singh and Pachauri, 2001). Among the mediators that counterbalance the proinflammatory cytokines are glucocorticoids, transforming growth factor (TGF), receptor antagonists, soluble receptors, acute phase protein components. The acute phase proteins are C-reactive protein (CRP), serum amyloid protein (SAP) and serum amyloid A (SAA). The levels of these proteins in the blood may rise a thousandfold following bacterial invasion and tissue damage. In addition, some dietary factors can regulate the initiation of proinflammatory cytokines synthesis and anti-inflammatory molecules production. Vital protective cytokines are essential for coordination of the various biochemical, cellular and endocrine responses that enhance immune function and act as substrate to the immune reaction and other protective pathways (Table 1). In a homeorhetic response driven by elevated systemic levels of proinflammatory cytokines, nutrients are redirected from anabolic pathways related to growth, skeletal muscle accretion or reproduction towards pathways that bolster defence against pathogens. Nutrient repartitioning results in an increased rate of protein turnover, which leads to increased body temperature and basal metabolic rate. In addition, accelerated protein degradation may augment host defence by increasing the activities of proteasome, which is a complex cytoplasmic structure consisting of different proteases and it can act on proteins to cleave them into multiple fragments and for this reason enhancing expression of peptide fragments from intra cellular proteins on MHC class-I or MHC class-II molecules (Tizard, 1997). This process permits greater detection of intra cellular pathogens and is illustrative of the heightened vigilance and activities of the immune system induced by a generalized stress condition. In some tissues such as skeletal muscle, increased proteolysis is not matched by augmented protein synthesis causing decreased tissue accretion i.e. manifested as growth in young animals or negative nitrogen balance in matured adult animals. Nutrient repartitioning occurs not only with protein and amino acids but also with virtually every other essential nutrients.

Most cells have receptors for some of cytokines and can respond directly to these messenger molecules when their levels are sufficiently high in blood and/or gastro-intestinal fluids. Cytokines can also stimulate neurons that innervate immune tissues such as lymph nodes, spleen, thymus, skin, hemolymph nodes, bone marrow, bursa fabricus in poultry, payer patch, or liver permitting communication with areas of the brain that regulate important processes such as body temperature, appetite and behaviour (Downing and Miyan, 2000). Stimulation of local neural networks modifies vascular tone in specific tissues and in some cases decreases gastro-intestinal motility which affects voluntary food intake. Cytokines can also exert their actions via the endocrine system either by modifying the release of hormones, affecting hormone receptors or impinging on
Table 1. Effects of cytokines on metabolism and immune response

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Metabolic effect</th>
<th>Immune effect</th>
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<tbody>
<tr>
<td>IL-1</td>
<td>Increase glucose-oxidation</td>
<td>Increase acute phase protein production.</td>
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<td></td>
<td>Increase gluconeogenesis</td>
<td>Increase intestinal mucous production.</td>
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<td></td>
<td>Increase body temperature</td>
<td>Increase mediator production (IL-2, PGE-2, histamine etc.)</td>
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<td></td>
<td>Increase collagen synthesis</td>
<td>Increase lumphocyte chemotaxis.</td>
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<td></td>
<td>Increase bone resorption</td>
<td>Increase proliferation of vascular smooth muscle</td>
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<td></td>
<td>Increase live weight loss</td>
<td>Increase expression of adherence molecules.</td>
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<tr>
<td></td>
<td>Decrease voluntary food intake</td>
<td>Increase growth of fibroblasts, keratinocytes, glial cells etc.</td>
</tr>
<tr>
<td>IL-6</td>
<td>Increase metallo-thionein production</td>
<td>Increase growth/differentiation stem cells, neurons, macrophages</td>
</tr>
<tr>
<td></td>
<td>Increase body temperature</td>
<td>Increase acute phase protein production</td>
</tr>
<tr>
<td></td>
<td>Decrease voluntary food intake</td>
<td>Increase IL-2 production</td>
</tr>
<tr>
<td>IFNγ</td>
<td>Decrease growth of neoplastic cells</td>
<td>Increase IL-2, IL-2R production</td>
</tr>
<tr>
<td></td>
<td>Decrease growth of normal cells</td>
<td>Increase antigen presenting cells</td>
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<tr>
<td>TNFα</td>
<td>Increase osteoclast activity</td>
<td>Increase cytotoxicity of macrophages</td>
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<tr>
<td></td>
<td>Increase body temperature</td>
<td>Increase cytokine production by vascular endothelial cells</td>
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<td></td>
<td>Increase resting energy expenditure</td>
<td>Increase B cell growth/differentiation</td>
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<tr>
<td></td>
<td>Increase catabolism in skeletal muscle</td>
<td>Increase phagocytosis by neutrophils</td>
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<tr>
<td></td>
<td>Increase lipid release by adipocytes</td>
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<td></td>
<td>Increase live weight loss</td>
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<td></td>
<td>Increase hepatic cholesterol and TG synthesis</td>
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<td></td>
<td>Increase collagenase gene transcription</td>
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<td></td>
<td>Decrease fatty acid uptake by adipocytes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decrease voluntary food intake</td>
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Adapted from Ling et al. (1997); Chang and Bistrian (1998).

the second messenger pathways. For instance, the anabolic drive induced by IGF-I and insulin is sluggish by cytokines (Elsasser et al., 1995). The cytokines have their own set of unique activities as well as a large number of actions that overlap synergistically with their cytokines (Paludan, 2000). The specific milieu of pro-inflammatory cytokines released during an infectious challenge depends upon the type of challenging pathogen and its portal of entry. Most of bacterial pathogens tend to stimulate secretion of IL-1, IL-6 and TNF-α while viral infections tend to stimulate the production of different interferons (Fossam, 1998; Sharma et al., 2002). The immune responses cause an overall change in the metabolism, hormone production and behaviour of an animal. Effect of cytokine secretion reduces in feed intake (Johnson, 1998) and subsequently reduces in live weight gain in growing animals (Table 1). An immune response can effectively reduce growth rates and performance of reproduction by changing the hormonal status of an animal (Mc Cann et al., 1998). Anterior pituitary cells have specific binding sites for TNFα when they bind with cytokines resulted in a decrease in responsiveness to GHRF, TRF etc. These hormones normally regulate metabolism, growth and their related organs. Feed may contain a number of immunomodulators such as β-glucans and arabino galactans of plant, fungal, yeast or microbial origin, saponins and
phenolic derivates. B-glucans are taken up by cells in the gut and stimulate macrophages as well as complement system. Thus, selected feed ingredients as well as herbal extracts may enhance or modulate immune responses (Wills et al., 2000). During the immune response, the macrophages are activated to destroy invading pathogens. The macrophage responds to interleukin and other effector molecules by producing bactericidal factors including hydrogen peroxide, super-oxide anion, protease etc. (Tizard, 1997). These mediators effectively destroy invading microorganisms. Even though host cells are susceptible to these mediators, host pathology inevitable results as a consequence of disease. Dietary manipulation can modulate the production of cytokines and effector molecules and thus affects on the level of macrophage activity and tissue pathology. 

**Nutrients demand in response to immune reaction**

When the immune system is engaged in defense against a pathogen its actual nutrient demands would be increased. The nutrients are to be used as substrates for clonal production of lymphocytes, antibody synthesis, cytokines, complement components (C2, C3, C4, C5, factor-B, C3-inhibitor, C1-inhibitor, C4 binding protein, etc.), recruitment of new myeloid cells, chaperones, hepatic secretion of acute phase proteins including metallo-proteins, haptoglobin, ceruloplasmin, transmembrane receptors, communicator enzymes such as phospholipase-C, protein kinase-C, transcription factors - leucine zipper, c-fos, c-jun, RNA-polymerase, for DNA synthesis - DNA polymerase, methionine synthetase, type-I iodothyronine deiodinase, glutathione peroxidase, tyrosine kinase, thymulin hormone, NADPH-oxidase, superoxide dismutase etc. contain one or more elements as prosthetic moiety in their structures (O’Dell and Sunde, 1997). Among these processes, the production of acute phase proteins quantitatively appears to be the most nutritionally demanding process. Consequently, the development, maintenance and use of the immune system need almost all nutrients in varying levels that must ultimately originate only from the dietary substances.

The immune response to a pathogen can be affected the nutrition of animal by altering digestion, absorption, metabolism and excretion of nutrients, thus affecting substrate availability and dietary requirement. An immune response can increase the need for some substrates in some cases. For instance, an energetic expenditure for fever has proposed due to used up in increasing body temperature, increased rate of bio chemical reactions because of increased body temperature and increased cellular utilization of ATP due to useless cycling. Some nutrients are metabolised in greater amounts during an immune reaction, which may increase dietary requirements during a disease state. Many effector mechanisms used by the immune system generate large amount of reactive oxygen intermediates. Antioxidant nutrients such as vitamins (ascorbic acid- vitamin C, carotenoids-vitamin A, tocopherol-vitamin E), trace elements (zinc-ions, copper-ions, selenium, manganese etc.) and antioxidant enzymes ( glutathion peroxidase, superoxide dismutase, catalase etc.) have an important role in health of animals. These nutrients may be components of proteins, carbohydrates or any other macromolecules performing essential activities in the immune cells or other tissues. Antioxidant properties substances protect macromolecules against the damage from these reactive oxygen intermediates (Mebel et al., 1998; Sandhu and Singh, 2002). Therefore, antioxidant nutrients require to be increased during the immune reaction than that of normal healthy animals. The level of voluntary feed intake in the animals is decreased during immune reaction. For that reason, it may be necessary to increase nutrient offer prior to a
The time period in which immune cells differentiate and populate the tissues of the body is relatively long compared to other developmental processes and extends well beyond birth. The high rate of cell proliferation in combination with complexity of regulatory control over the developmental events is unmatched in any other tissues of the neonate. These developmental processes require a complex series of highly regulated cellular differentiation steps followed by deletion of self-reacting clones of lymphocytes that might cause a disease called autoimmunity. For this reason, a chronic deficiency of any required nutrient during the period of immune system development has negative impacts on immunocompetence. In general, those required nutrients that function in regulating cell differentiation specifically vitamin A and vitamin D, and particularly detrimental to the development of immunocompetence cells. Nutritional status affects not only the development of the immune system, but also the immune response to disease (Calder and Jackson, 2000). Many nutrients modulate the immune system, by mechanisms related to the provision of substrates. For instance, supplementation of chromium (Cr) in the diets of animal enhances immune system and lymphocyte blastogenic response that Cr reduces serum cortisol levels by inhibiting the synthesis of IKβα. Glucocorticoids, which include cortisole, are well known to suppress the immune system. Shipping stress or other stress condition causes increased glucose mobilization, which subsequently increases mobilization of Cr from body stores (chromodulins). The probable mechanism of Cr in glucose or insulin metabolism that chromium-transferrin in blood stream shifted the Cr ions into the Cr-sensitive cells. When insulin binds to receptor stimulates, which in turn react apo-chromodulin with Cr to form holo-chromodulin (4 Cr3+ : 4 aa). The holo-chromodulin binds to the cytoplasmic receptor site of insulin, which further activates the receptor-kinase activity. The activated insulin potentiates the conversion of glucose into CO₂ or lipid into adipocytes. The resting immune system is probably not very nutritionally demanding, as it contains some of the most inactive cells of the body i.e. resting B- and T-lymphocytes. Activation of immune system results in some of the most metabolically active and rapidly proliferating cells of the body. This sudden burst of activity may be regulated and critical decision to make at this time regarding the threshold for a response, the magnitude of the immune response and the type of the cells recruited for the response. Nutrients are important in supplying the substrates needed for this rapid rate of cell proliferation and the secretion of the effectors molecules. The cytokine response orchestrates metabolic changes such as skeletal muscle catabolism, which provides a source of energy or nutrients for these processes even when dietary intake is insufficient or undernutrition.

Just as the immune system is capable of repartitioning nutrients for immune cell proliferation and effectors molecule production, repartitioning of some nutrients occurs as a defence mechanism against the invading pathogens. However, some nutrients have directly served as substrate for microorganisms and support their proliferation and degree of virulence. For instance, iron is the limiting nutrient in the plasma and extra cellular fluids of animals. The cytokines released during a pathogen challenge mediate a shift in iron from transferring (extra-cellular fluids) to ferritin located in intracellular locations (Weinberg, 1998) and for motion of other iron binding proteins such as haptoglobin, hemopexin and lactoferrin in production animals. By this process, iron make unavailable to invading bacteria. In this way, they inhibit,
bacterial proliferation and invasion. Haptoglobin also reduces iron availability for RBC production; so that anemia in the host is commonly associated with severe infection. In neonatal pigs, an excessive amount of iron, provided through diet or via injection, enhances the proliferation of several types of pathogens (Kadis et al., 1984). In addition, increased pathogenicity due to nutrient excess, a nutrient deficiency may also directly affect pathogens. In mice, a selenium deficiency has demonstrated to provide a host environment in which a non-virulent strain of coxsackie virus may mutate and become virulent (Beck, 2000). The mechanism for this change in the viral genome seems to be related to antioxidant status, as vitamin E deficiency resulted in similar observations. The major role of selenium in immune reaction is through mainly enzymes, catalyzing biological oxidation-reduction reactions, which detoxify the free radicals in the system. The molecules of free radical have produced in the body during complex-biological reactions involved in the growth, reproduction and maintenance of the cells. Free radicals have unpaired electrons of mostly oxygen molecules. These free radicals are highly reactive ions and easily react with other molecules making them inactive. These free radicals damaged bio molecules and subsequently the bio molecules cannot perform their normal physiological functions. Hence, they are assumed as harmful molecules in the system; glutathione peroxidase- a seleno-enzyme is an important free radical scavenging enzyme. Many nutrients are indirectly involved in regulation of intra- and extra cellular environmental communication of immune cells. Dietary polyunsaturated fatty acid (PUFA) has reflected in the PUFA content of cellular membranes. Therefore, the PUFA is the precursor for eicosanoid synthesis including prostaglandin, leukotriene - B4, C4, D4 and - E4, thromboxanes etc. The PUFA content in the cellular membranes affects the type and amounts of eicosanoids released during an immune response. This change in regulatory environment has reflected in the type of immune response that predominates during an infectious challenge and in the outcome of the infection (Harbige, 1998). There are two classes of the PUFA i.e. the n-6 series found primarily in vegetable oils and the n-3 series found in fish oils and also in certain vegetable oils such as soya, linseed, canola etc. The ratio of n-6 to n-3 PUFA may be more important than that the absolute amount each of these classes of fatty acids in the diet. The ideal ratio of n-6 to n-3 PUFA is actually unknown, but estimates range from 5:1 to 10:1. Specifically, feeding n-3 PUFAs of marine fish origin, primarily eicosa-pentaenoic acid (EPA; 20:5 n-3) and docosa-hexaenoic acid (DHA; 22:6 n-3), results in decreased production of PGE2. Supplementation of EPA results in increased production of PGE3, a less biologically active molecule than the PGE2, while enrichment with DHA causes suppression of PGE, formation via cyclo-oxygenase inhibition (Chapkin et al., 2000). In addition, n-3 PUFAs from marine fish sources have shown to reduce IL-12 and IFN-α release causing a shift from Th-1 towards Th-2 responses. This modulation of the immune response causes increased susceptibility to infection that are controlled by a strong Th-1 response, such as Listeria sp, but an increase in resistance controlled by an activated Th-2 response, such as E. coli (Fritshe et al., 2000). In an experiment of poultry, a diet supplemented with n-3 fatty acids significantly decreased the incidence of septicaemia by 25%, but resulted in a 24% increase in the incidence of tumor (Klasing and Leshchinsky, 2000). Other nutrients that modulate the communication networks within the immune system include vitamins such as A, D and E, minerals such as iron and volatile fatty acids like butyrate. (Klasing and Leshchinsky, 2000; Weinberg, 2000). Carotenoids or vitamin A deficiency is rare in animal nutrition except in
poultry but which increases specific subsets of lymphocytes, enhances the activity of NK cells, stimulates the production of cytokines and activates phagocytic cells (Kim et al., 2000). Vitamin C is a water-soluble antioxidant and found in body fluids rather than in cellular lipid and membranes. Vitamin C acts as a major antioxidant in the aqueous phase and which reinforces the effects of other antioxidants, such as vitamin E, by regenerating their active forms after they have reacted with free radicals. Vitamin C level is very high absolutely in the organ of thymus. Vitamin C plays an important role in the function of phagocytes. High doses of vitamin C have often applied in an attempt to prevent respiratory infections. It is unclear whether this is effectively reducing common cold and flu. Antioxidant nutrients, such as vitamin E also modulate an immune response. Reactive oxygen species are responsible for promoting transcription factors such as NF-KB, which are involved in the regulation of viral gene expression, cytokine synthesis and the acute inflammatory reactions (Lander, 1997). Vitamin E and other antioxidants can inhibit the activation of these transcription factors, thus affecting the magnitude of the immune response. In addition to these roles, vitamin E can affect arachidonic acid metabolism, thereby affecting the immune response in a similar manner to PUFAs. Finally, the amount of ration fed, the pattern of feeding i.e. restricted versus ad-libitum, and the ratio between protein and energy density in the ration influenced the hormonal milieu. The hormonal profile in turn modulates the immune response via leukocytes, which have receptors for hormones produced by the classical endocrine system, including glucocorticoids, insulin, glucagons, growth factor hormone and thyroxin (Berezi et al., 1998).

CONCLUSION

The immune system is one of the most complex and intricate cellular and molecular interactions known in all of biology. Well-balanced quality nutrition is of the utmost importance for disease resistance and act as keys, which unlock the ability of the immune system towards off invaders. Proper supplementation of nutrients such as energy, protein, amino acids, minerals and vitamins will not eliminate disease, but it will allow the animal’s immune system to respond with peak efficacy to minimize the risk of significant economic losses.

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