

Nutrition and health of fish¹

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ABSTRACT: Research on nutrition and immune function of fish is slowly expanding to define the role of specific nutrients in disease resistance in fish. The potential impact of certain vitamins (A, E and C), trace elements (iron and selenium), protein, carbohydrate and lipid on the immune response and the pathogenesis of deficiency diseases is briefly reviewed. Recent developments on the functional role of n-3 and n-6 polyunsaturated fatty acids (PUFA) on nonspecific and specific humoral and cellular immunity are summarized. In addition to cell membrane function (e.g. fluidity and permeability), the immunological effects of PUFAs are associated with the formation of eicosanoids such as leucotrienes (LT) and prostaglandins (PG). Dietary n-3 and n-6 PUFAs intake have a significant effect on LT and PG production by macrophage and leukocytes, which directly influence the piscine immune function. Although potential for disease prevention in fish by dietary changes exists, additional information is required on the specific effects of nutrients in pathogenesis of common diseases and how these effects are influenced by other physiological and environment factors.

KEY WORDS: Fish, nutrient, immune function.

INTRODUCTION

Interest in fish and shellfish nutrition has increased markedly over the past two decades, largely due to the global increase in aquaculture production. Although several cold water and warm water fish are cultured commercially, diet formulations for many of these species are based on limited information on their nutrient requirements. Nutritional status is considered one of the important factors that determine the ability of fish to resist diseases. Outbreaks of fish diseases commonly occur when fish are stressed due to a variety of factors including poor nutrition. The need for proper diets to improve health and prevent diseases of farmed aquatic animals is widely recognized. Nutritional and physical characteristics of diets can modulate susceptibility of fish to infectious diseases. In the most severe cases, diets that are inadequate with respect to essential nutrients (protein, amino acid, essential fatty acids, vitamins and minerals) lead to gross malnutrition and high disease susceptibility. In general, gross malnutrition is no longer a problem, however, we are now faced with the more challenging task of determining the more subtle effects that micronutrients, and their interactions with other dietary components have on the immune system of fish. Several reviews have dealt with the subject of nutrition and immune response in fish (Blazer, 1992; Lall and Olivier, 1993; Waagbo, 1997), however, we lack complete information on the quantitative nutrient requirements of most fish. In addition, our

¹ Lall, S.P., 2000. Nutrition and health of fish. In: Cruz -Suárez, L.E., Ricque-Marie, D., Tapia-Salazar, M., Olvera-Novoa, M.A. y Civera-Cerecedo, R., (Eds.). *Avances en Nutrición Acuícola V. Memorias del V Simposium Internacional de Nutrición Acuícola*. 19-22 Noviembre, 2000. Mérida, Yucatán, Mexico.

knowledge of how nutrition affects the fish immune system is limited by our lack of understanding of that system.

In the past two decades significant advances have been made in establishing the quantitative requirements of more than 40 essential nutrients for optimum growth and better feed utilization, as well as to prevent deficiency diseases of single or multiple nutrients (NRC, 1993). In many cases, however, it is not known whether these requirement values that maximize productivity in healthy, unchallenged fish are optimal for immunocompetence and disease resistance. A better understanding of the mechanisms through which nutrition influences the immune system is necessary to appreciate the many complex interactions between diet and susceptibility to infectious diseases. Like all vertebrates, fish possess a wide array of defense systems to protect themselves against disease-causing organisms. The immune system of fish like that of other animals is broadly categorized into specific or acquired immunity and nonspecific or innate immunity. Fish depend more heavily on nonspecific defense mechanisms than mammals. This is particularly true for cold water fish because the rate of development of specific immune responses is temperature dependent. Both systems use cellular and humoral mechanisms to provide protection against infection. The specific immune system is induced by an initial interaction between an antigen or antigens and the lymphocytes. This results in an initial production of antibodies against the antigen and the development of a memory response. The memory response enables a rapid secondary antibody response upon re-exposure to the antigen. Nonspecific immunity includes such generalized host defenses as physical barriers (skin and mucus), enzymes (lactoperoxidase in saliva, lysozyme in mucus and other secretions in gastric juice and tissues etc.), phagocytic cells (macrophages and neutrophils) and blood proteins (interferon, C-reactive protein, complement etc.).

Nutritional modulation of resistance to infectious diseases, based upon the information on fish and terrestrial animals, is divided into five major groups. In the first category, one must consider a proper balance of macro- and micronutrients, including amino acids, polyunsaturated fatty acids (PUFA), vitamins and trace elements, which are essential for the development of immune system starting at the larval stage. Deficiencies in these nutrients may impact several development events including the proper development of lymphoid organs. Marginal deficiencies may negatively affect the immune system at later stages of life. Severe deficiencies will increase susceptibility to disease and may result in the death of the animal.

The second point is to consider that adequate nutrition is essential for cells of the immune system to divide and synthesize effector molecules. The diet supplies the immune system with the amino acids, PUFA, enzyme co-factors and energy necessary to support lymphocyte proliferation and the synthesis of effector (e.g. immunoglobulins, lysozyme and complement) and communication molecules (e.g. cytokines and eicosanoids). The quantitative need for nutrients to maintain a normal immune function is relatively small compared to the requirements for growth and reproduction.

In the third category, it is important to consider that some nutrients provide essential substrates for the proliferation of pathogens (e.g. iron) and their presence at low concentrations in body fluids may limit the growth of pathogens within the fish. The fourth mechanism may include the indirect regulatory effects of diets on the immune system that are mediated through the endocrine system. The regulatory action of PUFA and other nutrients (vitamins A and E) on leucocytes has been demonstrated. Eicosanoids produced from PUFAs, especially arachidonic acid, are a major component of the humoral immune system. Finally, diet composition and physical characteristics of the diet may modify the microorganisms in the gastrointestinal tract and the integrity of intestinal epithelium. The presence of

oxidized lipids, plant anti-nutritional factors (e.g. lectins, protease inhibitors, and oligosaccharides) and fiber can affect the gut physiology along with the makeup and size of the gut microfloral population and thus aspects of the nonspecific immune response.

As discussed above, inadequate nutrition and/or the improper balance of nutrients within the diet can have a major impact on immune functions. Other factors such as environmental stress, altered gastrointestinal activity (e.g. due to parasite infection or other factors), disease state, higher physiological needs (e.g. reproduction), drug-induced anorexia, metabolic defects and food contaminants can also result in a low nutrient supply for metabolism and have detrimental effects on fish health (Fig. 1). It is important to emphasize that the magnitude of a specific nutrient deficiency is also affected by genetic and species differences, the ability of fish to adapt to limited food availability, and other factors related to nutrient utilization from the diet (bioavailability, interaction among nutrients etc.). In this paper, I have briefly reviewed the current understanding of the role of nutrients in immune response and disease resistance in fish with emphasis on dietary lipids.

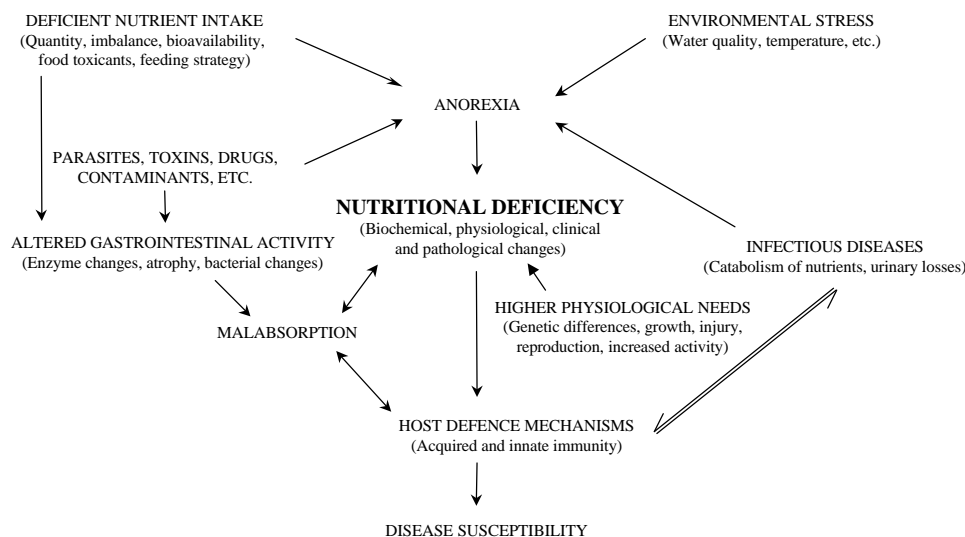


Figure 1. Factors influencing nutritional status, health and immune function of fish.

Lipid

Although, the relationship between dietary lipid and immunological functions in terrestrial animals has been studied extensively, only a few attempts have been made to investigate these interactions in aquatic animals. Fish tissues contain relatively higher concentrations of polyunsaturated fatty acids (PUFA) than found in mammals. PUFAs are important components of all cell membranes which makes fish tissue highly vulnerable to lipid peroxidation. Generally, essential fatty acids (EFA) requirements of freshwater fish can be met by the supply of 18:3n-3 and 18:2n-6 fatty acids in diets, whereas the EFA requirement of marine fish can only be met by supplying long-chain PUFA, 20:5n-3 and 22:6n-6 (NRC, 1993). Freshwater fish are able to elongate and desaturate 18:3n-3 to 22:6n-3, whereas marine fish, which lack or have a very low activity of 5-desaturase, require the long chain PUFA, eicosapentaenoic acid (20:5n-3; EPA), and docosahexaenoic acid (22:6n-3; DHA). The quantitative

requirements and deficiency signs of EFA in several freshwater and marine fish have been documented (NRC, 1993), however, the functional role of n-3 and n-6 PUFA in nonspecific and specific humoral and cellular immunity is not clearly defined (Bell *et al.* 1996; Secombes, 1996; Lall, 1998).

Twenty-carbon PUFAs derived from EFA are precursors of two groups of eicosanoids, prostaglandins, and leucotrienes with diverse pathophysiological actions including immune response and inflammatory processes. Eicosanoids are synthesized from di-homo gamma linolenic acid, 20:3 (n-6), arachidonic acid (AA; 20:4, n-6), and eicosapentaenoic acid (EPA; 20:5, n-3), by the action of two oxygenase enzymes, cyclooxygenase and lipoxygenase. Lipoxygenase yields a range of monohydroxy fatty acids (e.g. 5 (S)-hydroxy-eicosatetraenoic acid ; 5- HETE derived from AA) while di- and tri-hydroxy fatty acids, such as leucotrienes (LT), lipoxins (LX), are also formed via epoxy intermediates (Fig. 2). In the synthesis of leucotrienes, a highly unstable epoxide, LT_4 (5 (S), 6 (S)-*trans*-5,6 -oxido 7,9-*trans*-11, 14-*cis*-eicosatetraenoic acid) are formed from 5 (S)-hydroperoxy-6-*trans*-11, 14-*cis*-eicosatetraenoic acid; 5- HPETE). This epoxide is rapidly hydrolyzed enzymatically to LT_4 (5 (S), 12 (R) dihydroxy-6, 14-*cis*-8,10 -*trans*-eicosatetraenoic acid) or nonenzymatically to several dihydroxy-eicosatetraenoates (e.g.. 6-*trans*- LTB_4 , 6- *trans*-12-*epi*- LTB_4). Leucotriene A_4 can also converted to cysteinyl leucotrienes, LTC_4 , LTD_4 and LTE_4 .

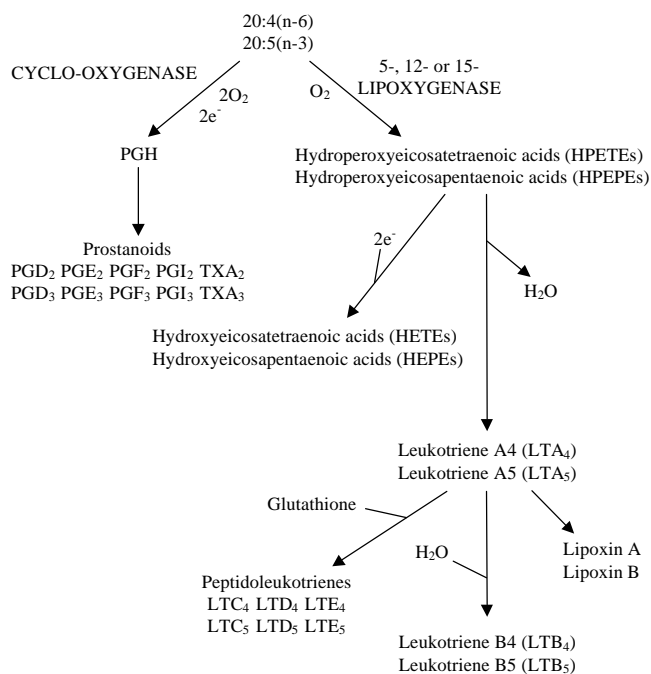


Figure 2. Pathways of conversion of 20:4(n-6) and 20:5(n-3) to eicosanoids.

Prostaglandins and leucotrienes constitute a group of extracellular mediator molecules that are part of an organisms defense system. They are formed during the inflammatory process, and if the inflammation is caused by invading bacteria, the formation of prostaglandin and leucotrienes will stimulate macrophages and other leucocytes to begin the process of destroying the bacteria.

Eicosanoids may be involved in the regulation of the immune system by their direct effects on cells such as macrophages and lymphocytes or their indirect effects via cytokines (Rowley, 1995). The nature of dietary lipids and the concentration of essential fatty acids have a direct effect on the eicosanoid metabolism and immune function.

Studies on laboratory animals have demonstrated that fatty acid composition of diet influences production of eicosanoid precursors and immune response. A diet high in n-6 PUFAs produces relatively high levels of the pro-inflammatory 2-series PGs and 4-series LTs and LXs derived from arachidonic acid (AA) whereas diets high in n-3 PUFAs produce the anti-inflammatory 3-series PGs and 5-series LTs and LXs derived from EPA. Generally, diets containing high levels of n-6 PUFAs enhance the immune response due to the high levels of pro-inflammatory AA-derived eicosanoids, and diets containing high levels of n-3 PUFA may be immunosuppressive due to the high levels of EPA-derived anti-inflammatory eicosanoids. However, the impact dietary fatty acids on the immune response is more complex and depends on several factors that influence eicosanoid production including competition between n-3 and n-6 fatty acid during metabolism for chain elongation and saturation, the cell type involved, and the source of fatty acids in the diet.

Recent studies conducted on fish show that diet containing different levels of n-3 and n-6 fatty acids from fish and vegetable oils can modify the fatty acid composition of cell phospholipid in turbot and Atlantic salmon (Bell *et al.* 1991a, 1993 and 1994). The changes in fatty acid composition of phospholipid affect the synthesis of eicosanoid precursors. When the intake of n-6 fatty acids increased, a higher level AA-derived eicosanoids was observed (Bell *et al.* 1993; Lall, 1998). However, reports on the effect of n-3 and n-6 fatty acids on immune response and eicosanoid production in fish are not conclusive and very often contradictory. Erdal *et al.* (1991) found decreased antibody titers and survival in Atlantic salmon fed diets with high n-3 PUFA levels. Channel catfish fed a diet containing high n-3 fatty acid content had decreased survival following a challenge with *Edwardsiella ictaluri*, compared to those fed a diet with high n-6 fatty acid content (Li *et al.* 1994). Moreover, Fracalossi and Lovell (1994) observed low disease resistance and immune functions such as phagocytic capacity and killing activity in channel catfish fed diets high in n-3 PUFAs. Li *et al.* (1994) suggested that immunosuppression caused by dietary n-3 fatty acids may be a possible mechanism for the decreased LBT4 and increased LTB-5 production by macrophages and neutrophils. Fracalossi and Lovell (1994) indicated that channel catfish require a carefully balanced dietary mixture of n-3 and n-6 fatty acids to optimize immune response in this species.

Other reports show positive effects of n-3 fatty acids on immune response of fish. The increased activity of head kidney macrophages has been associated with higher levels of dietary n-3 fatty acids in catfish (Blazer, 1991; Sheldon and Blazer, 1991). Atlantic salmon fed diets with (n-3):(n-6) PUFA ratios showed increased B lymphocyte response and survival following disease challenges with *Aeromonas salmonicida* and *Vibrio anguillarum*. Ashton *et al.* (1994) found that head kidney supernatants derived from rainbow trout fed a diet enriched with n-3 fatty acids had greater migration stimulating ability than supernatants originating from trout fed an n-6 fatty acid enriched diet.

Despite many conflicting reports on the effects of n-3 PUFAs on the immune response of fish, n-3 enriched diets improve the stability of cell membranes (Erdal *et al.* 1991; Klinger *et al.* 1996). This effect is particularly important for aquatic animals, where it is essential to maintain proper membrane function during the wide fluctuations in water temperatures. Channel catfish fed diets with high levels of n-3 fatty acids showed enhanced immune function (especially phagocytic capacity) at low temperatures, while fish fed high dietary levels of n-6 fatty acids had enhanced disease resistance

factors at high temperatures (Linge-felser *et al.* 1985). The physiological effects of water temperature may be due to the function of n-3 fatty acids in maintaining membrane fluidity, which is considered important during the ingestion stage of phagocytosis.

Essential fatty acid deficiency in rainbow trout reduces the *in vitro* killing of bacteria by macrophages and reduces antibody production (Kiron *et al.* 1995a). They also found that fish fed PUFA were more resistant to bacterial infections and excessive levels of n-3 PUFA did not enhance immunocompetence in fish. Montero *et al.* (1998) reported that adequate levels of n-3 PUFAs in the diet were necessary for the maintenance of alternative complement activity in gilthead seabream, *Sparus aurata*. Moreover, it is noteworthy that high dietary ratios of n-3 to n-6 fatty acids have been shown to prevent cardiomyopathy as well the susceptibility of Atlantic salmon to stress (Bell *et al.* 1991b). Therefore n-3 PUFAs are essential fatty acids in fish not only for optimal growth and feed efficiency, but also for immunological efficacy and cardiovascular function. Several biochemical abnormalities and diseases are also associated with rancid feeds where substantial loss of PUFA and micronutrients occurs due to lipid peroxidation. Some of the common fin erosion and skin inflammation problems in farmed fish have already been linked to lipid nutrition (Lall and Olivier, 1993).

Obviously, additional studies are needed to clearly establish the role of dietary lipid including marine fish and vegetable oils on immune response and disease resistance in fish. Potential exists to replace marine fish oils (MFO) with alternate lipids of plant and/or animal origin in feed of farmed fish because the global supply of MFO is becoming increasingly limited. In order to replace MFO with alternate lipid sources, it is important to establish that the dietary lipid supply is not only at the correct level with the proper balance of EFA for optimum growth and feed utilization but it can also maintain proper immune function and prevent infectious diseases in farmed fish.

Protein and carbohydrate

Although the protein requirements and their relationship to immunological function in mammals has been widely studied, only a few attempts have been made to study these interactions in fish. Marine and coldwater fish are carnivorous and the existing diets contain high levels of protein and a low amount of carbohydrate. Kiron *et al.* (1995b) found that lysozyme activity and C-reactive protein values were reduced in protein deficient rainbow trout. Coldwater fish have a limited ability to utilize carbohydrate for energy purposes and excess carbohydrates are known to produce pathological conditions in the liver and detrimentally affect the natural microbial population in the gut. To date, reports on the detrimental effects of carbohydrate on fish health and immune function are not conclusive.

Vitamins

Vitamin deficiency leads to aberrant biochemical functions and consequent cellular and organ dysfunction (clinical symptoms). Several gross morphological and functional changes have been reported in fish deprived of vitamins (NRC, 1993). Vitamin deficiencies may be caused by their low content in feeds, environmental or physiological stresses and by diseases especially those, which occur in the early stages of development. With respect to feed, losses of vitamins occur during processing and prolonged feed storage, often due to the oxidation of lipids caused by the addition of a sub-optimum level of antioxidant. Vitamin deficiencies result in depressed immune function and slow or no recovery from disease. This is especially true for early developmental stages in which the developing immune system requires an optimum level of vitamins. Vitamin demand can also be higher during

physiological conditions such as reproduction and stress. The demand also changes with changes in water temperature where higher levels of vitamins are normally required at higher temperatures (reviewed by Woodward, 1994).

Feeding of higher levels of vitamins is often reported to provide some protection against disease and to improve tissue regeneration following injury or tissue damage due to low temperatures. The prophylactic use of vitamins in animal nutrition is widely recognized and practiced. In assessing the vitamin status of aquatic animals, one must recognize that the storage capacity of vitamins is very limited (6-8 weeks) for water-soluble vitamins and a little higher for lipid-soluble vitamins A, D₃ and E. Increased intake of water-soluble vitamins often results in a sharp increase in their excretion. Therefore it is important to avoid excessive levels of these vitamins in feeds. The role of certain vitamins in health of fish is discussed in the following sections.

Vitamin C

Vitamin C is essential for collagen formation, wound healing, hematopoiesis, detoxification of compounds as well as for several metabolic functions including as part of the antioxidant system. In recent years, considerable research has been directed to determine the role of vitamin C in the immune function and disease resistance in fish. High doses of vitamin C intake (Table 1) increases the resistance to several bacterial and viral pathogens in fish (reviewed by Waagbo, 1997; Verlhac and Gabaudan, 1997). These diseases include: enteric redmouth disease, viral haemorrhagic septicemia, infectious hepatic necrosis, ichthyophthiriosis in rainbow trout; vibriosis and furunculosis in rainbow trout and Atlantic salmon; and enteric septicemia in channel catfish. The proposed mechanisms of disease resistance vary between species. Vitamin C has been shown to stimulate serum hemolytic complement activity, proliferation of immune cells, phagocytosis, the release of signal substances and antibody production (Verlhac and Gabaudan, 1997). However the immune response findings are not always consistent in all species (Lall *et al.* 1991; Leith and Kaattari, 1989).

Table 1. Effect of Vitamin C on resistance to various diseases and immune response in fish^{1,2}

Species	Immune parameters showing positive response to dietary Vitamin C ³	Disease	Vitamin C dose required to prevent disease (mg/kg of diet)
Atlantic salmon	Phagocytosis and oxidative burst by macrophage, iron metabolism, complement ⁴ , lysozyme, antibody response	Furunculosis	2000-4000
Rainbow trout	Phagocytosis, pinocytosis and oxidative burst by macrophage, complement ^{4,5} , lymphocyte proliferation, antibody production, iron binding capacity	Enteric redmouth disease	2000
		Vibriosis	500-2000
		Infectious hepatic necrosis	80-320
		Viral haemorrhagic septicaemia	2000
Channel catfish	Phagocytosis, complement ⁵ , antibody response to enteric septicaemia ⁶	Itch	2000
		Enteric septicaemia	1000-3000

¹See reviews by Lall and Olivier, 1993; Waagbo, 1997; Verlhac and Gabaudan, 1997

²Non-vaccinated fish

³Generally higher than 1g Vitamin C/kg of diet

⁴Alternative pathway

⁵Classical pathway of activation

⁶*Edwardsiella ictaluri*

Vitamin C has also been shown to be effective in reducing the negative impacts of environmental and husbandry induced stress on health and disease resistance. Fish fed diets that are low in vitamin C are more susceptible to stress caused by poor water quality such as high ammonia and low oxygen levels. Fish fed diets with high levels (> 300 mg/kg) of ascorbic acid have been demonstrated to be less effected by toxic levels of waterborne copper (Hilton, 1989) and nitrite (Wise *et al.* 1988). High levels of vitamin C in the diet has also been shown to protect rainbow trout against the adverse effects of organochlorine pesticides.

Vitamin E

Vitamin E and other antioxidant nutrients (ascorbic acid, $\hat{\alpha}$ -carotene and selenium) are required for optimum function of the immune system in terrestrial and aquatic animals. They decrease the production of lipid peroxides and reactive oxygen species which are considered toxic and destroy cells of the immune system and other tissues. Vitamin E, as a lipid-soluble biological antioxidant, protects the highly unsaturated fatty acids in cells against oxidative degeneration by terminating free-radical initiated chain reactions. Normally the production of free radicals is controlled by a complex biochemical mechanism involving manganese- and copper/zinc-dependent superoxide dismutases, the selenium-dependent enzyme, glutathione peroxidase and other enzymatic processes (Sies *et al.* 1992). However under certain conditions free-radical generation can proceed unchecked. This can lead to the free radicals initiating a chain reaction of lipid peroxidation of the polyunsaturated fatty acyl moieties of biological membrane phospholipids and a disruption of cellular function. Vitamin E acts as a second line of defense to prevent the proliferation of such chain reactions by scavenging fatty acyl peroxy radicals that are produced during/or before this chain reaction.

Recent findings on the effects of vitamin E on immune response of fish are not consistent. Hardie *et al.* (1990) reported that secretion of superoxide anion, serum lysozyme, lymphokine production and humoral immune response in Atlantic salmon were not affected by dietary vitamin E intake (7 to 880

mg vitamin E/kg) but the complement system was compromised in fish fed low levels of vitamin E. Other studies on the effect of vitamin E on immunostimulation and resistance to bacterial kidney disease and furunculosis infection have not demonstrated a clear effect on immune response and disease resistance (Leith and Kaattari, 1989; Lall and Olivier, 1993). Certain functions of vitamin E are also accomplished by selenium or some synthetic antioxidants, sulfur amino acids, methionine and cystine and ascorbic acid. Variations in their levels in the experimental diets used by various workers may have contributed to the differences observed in immune parameters. Most commercial feeds contain 150-400 mg of vitamin E per kg of diet, which seems adequate to maintain the immune function of salmonids, marine fish and catfish. When feeds are not stabilized with antioxidants, the high concentrations of PUFA and pro-oxidants (iron and copper, etc.) may further increase the requirement of vitamin E to protect the fish immune system.

Other vitamins

Vitamin A and other water-soluble B vitamins are also involved in cellular metabolism. The structurally diverse B vitamins act as enzyme activators and play a key role in carbohydrate, protein and lipid metabolism. Although studies on the relationship between low intake of B vitamins and change in immune function of experimental animals indicate that immunity can be severely compromised when tissue concentration is low, such information is lacking in fish and confined to a few vitamins (Waagbo, 1997). An extensive study to evaluate the role of folic acid, pyridoxine, riboflavin and panthothenic acid on the immune function and disease resistance in Chinook salmon suggested that dietary levels of these vitamins recommended by NRC (1981) for optimum growth were also adequate for optimum immune function (Leith and Kaattari, 1989). Several dietary factors and processing conditions affect the stability and bioavailability of B vitamins and their low intake can influence immune function. Obviously, additional studies are needed to determine the role these vitamins in immune response and disease resistance in fish. In order to ensure disease resistance we need to determine the optimal level of these vitamins in diets and how this level may differ between different species of fish.

Trace elements

Trace elements such as zinc, iron, copper and selenium are required as coenzymes for metalloenzymes and are vital for maintenance of cellular functions in the immune system of higher vertebrates. In fish little is known about the effects of trace elements on immune function. Iron is an essential nutrient for fish as well as microorganisms and the ability of pathogens to infect a host depends on its availability. Maintaining low concentrations of free iron in mucus membranes and in other tissues is thought to be one of the primary nonspecific host defenses against bacterial infections.

Iron deficiency causes microcytic anemia in several fish species (NRC, 1993). Levels of iron in fish during bacterial infection declines rapidly in the spleen, liver and kidney, particularly in fish a diet with a low iron content (Lall *et al.* 1996, unpublished results). Research on terrestrial animals suggests two different views. One proposes that an iron deficiency protects against infection by limiting the amount of iron available to bacteria. In this interpretation iron supplementation would increase susceptibility to infection. The second view implies that an iron deficiency predisposes animals to infection thus iron supplementation would increase disease resistance. Iron deficiency in fish is not a desirable means of controlling infection because iron deficiency makes the host more susceptible to infectious agents.

Generally, an iron deficiency is not a problem in aquatic systems because often water and feed ingredients in practical diets supply sufficient quantities of iron to meet the physiological needs of fish. Commercial fish feeds contain 150-800 mg iron/kg of diet. Feeds formulation based on blood and fish meal should be closely monitored because they supply high amounts of iron which may predispose fish to common bacterial pathogens. Recently, Naser and Lall (2000, unpublished results) observed that the utilization of dietary iron by *Aeromonas salmonicida* and *Vibrio anguillarum* differ and organic iron present in blood as heme compounds is readily available to fish and pathogens.

CONCLUSIONS

The subject of nutrition, immunological function and disease resistance in fish and other aquatic animals is an important area of research but clearly in its infancy. Investigations in this area holds great promise with respect to reducing the impact of diseases in aquatic animals. Recent reports on stimulatory effects of large doses of vitamin C and E are of practical interest for disease prevention, however, the cost of these vitamins and practical application of these results under farm conditions requires further evaluation. Diets formulated to match the nutrient requirements of fish could be used effectively with vaccines and chemotherapeutants to prevent and possibly eradicate infectious diseases. Use of high quality feed ingredients free from contaminants, proper nutrient balance in feed formulation, prevention of micronutrients loss during feed processing, better handling, storage and feed management also have good potential to improve health of aquatic animals.

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