Interrelationship of feeding with immunity and parasitic infection: a review

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ABSTRACT: Authors overlook the recent findings in the field of the complex interrelationship among nutrition, immune status and parasitic infestation. After summarizing the general characteristics of the active immune system, they describe the first period of the systemic immune response, the acute phase reaction. The cause of drastical decrease in serum zinc concentration is redistribution into the liver and lymphocyte metallothioneins. Immune deficiency correlates only indirectly with the nutrition. Ingestion of feed mycotoxins (e.g. T-2 toxin) and peroxides causes lymphocytes depletion in the lymphoid organs. Events of immunological stress are a special form of homeorrhetic control. Lack of energy and protein hardly damages the humoral immunity. Undernutrition fundamentally affects the cell-mediated immune response and the complement production. In animals, the lack of calcium, magnesium, iron, zinc, copper, iodine and selenium has been associated with signs of immunodeficiency. The concentrations of trace elements required for healthy animals are often below what is required for animals experiencing an immunological challenge. Zinc has both specific and aspecific role in the immune defence mechanism. Zinc regulates the maturation and function of immune cells, among others by protecting developing lymphocytes from apoptosis. As part of the zinc-finger proteins, may influence DNA transcription. The thymus synthesizes a 9-amino acid peptide hormone, the thymulin, which is activated after having bound zinc. Selenium has a vitamin E-independent immunostimulant effect in the marginally supplied animals. Active form of vitamin D_3 regulates transcription at cell level, acts as an immunomodulator and promotes phagocytosis. Lack of essential fatty acids in the diet of experimental animals caused atrophy of lymphoid organs and the reduction both the T-cell mediated and the independent immune response. Practical application of the new immunological findings is the segregated early weaning (SEW). Feed allergy results either in immediate hypersensitivity reaction within 1 to 2 hours or a T cell-mediated delayed hypersensitivity reaction within days. Under a certain number of worms ("threshold value") the host organism did not show detectable changes. Parasitic infection changes the body and skeletal composition: the water content increases, that of protein and fat drop; the calcium and phosphorus concentration of bones decreases. Helminths, developing in the animal, may cause serious local lesions; anaemia and the change of plasma proteins. Worms' toxins stimulate the production of gastrointestinal hormones, causing reduction in voluntary feed intake. Rabbits with biliary coccidiosis significantly decreased voluntary feed intake and the digestibility of the fats. The extent of infection and the oocyte excretion of *Eimeria maxima* in growing chickens showed a strong negative correlation with the plasma carotenoid level and strong positive correlation with the blood nitrogen oxide and γ-interferon concentration.

Keywords: acute phase; immunological stress; zinc-finger; thymulin; GALT; microbiota; feed allergy; minerals; Coxsackievirus B3; vitamins; gastrointestinal parasites; threshold values; feed intake; leak lesion

List of abbreviations

APR = acute phase reaction or response, **ESR** = erythrocyte sedimentation rate, **GALT** = gut-associated lymphoid tissue, **H_2O_2** = hydrogen peroxide, **IBR** = infectious bovine rhinotracheitis, **Ig** = immunoglobulin, **IL** = interleukin; **LEM** = lymphocyte endogenous mediator, **LPS** = lipopolysaccharide, **MØ** = mononuclear phagocyte, **MPO** = myeloperoxidase, **NADPH** = reduced nicotinic acid adenine dinucleotid phosphate, **NK** = natural killer, **NOS** = nitric oxide synthase, **PEM** = protein-energy malnutrition, **PMN** = polymorphonuclear leukocyte, **SAP** = serum-amyloid protein, **SEW** = segregated early weaning, **SOD** = superoxide dismutase, **TNF** = tumour necrosis factor, **VLDL** = very low density lipoprotein

Contents

1. Introduction

The immune system is one of the defence mechanisms of animals to keep the integrity of their body. The other types of protective mechanisms are the physico-chemical barrier of the skin, epithelium and mucous membranes. Functions of the healthy immune system comprise the natural and the acquired immune response. The natural or inherited immunity (activity of complement, macrophages, natural killer cells, cytokines etc.) develops quickly, has no antigen specificity and memory and is reinforced only linearly. On the contrary, the acquired or adaptive immunity (functioning of B- and T-lymphocytes, the antibodies and the T-cell receptors) is determined by the antigen and has an immunological memory (Gergely, 2006). The microflora in the gut (microbiota) plays an important role in the maintenance of "vigilance" level of the leukocytes by the lipopolysaccharide (LPS) and prostaglandin products. In case of a slight infection or stress the activated leukocytes excrete cytokines in low concentration, assuring the cellular and humoral protection and the integrity of organism without the development of acute systemic immune response. Notwithstanding, in case of severe infections, tissue damages and other stress factors, the number of activated cells dramatically increases. The latter cells release high amount of pro-inflammatory primary mediators (IL-1, TNFα and especially the IL-6) to the entire activation of the immune system. The acute phase reaction (APR) develops, in which the stimulating processes are dominant and systemic immune response is induced (Szigeti, 1991). The local immune systems, especially that of the gut (gut associated lymphoid tissue, GALT) has to respond to the intruder pathogens, without expressed response to feed antigens. In the distinction between commensal bacteria and pathogens the mammalian pattern recognition receptors, like the Toll-like receptors and the CD 14 receptors of macrophages and gut epithelium should be mentioned (MacDonald and Monteleone, 2005; Altorjay, 2006).

2. Nutrition and immunodeficiency

Immune deficiency may be congenital, genetic and acquired. The latter can be caused by virus infection (human and cat HIV), ingestion of certain mycotoxins (e.g. T-2 toxin, Fekete et al., 1989), peroxides of rancid feed (Fekete et al., 2007), long-lasting stress and corticosteroid treatment. Immune deficiency not only increases susceptibility against infections, but also is connected to some types of allergies and autoimmune diseases. At the same time, immune deficiency correlates only indirectly with the nutrition, namely if the primary cause of disease leads to chronic diarrhoea, malabsorption and therefore there are significant faecal blood, protein, mineral and vitamin losses. During designing the daily ration for these patients, the replacement of the lost substances should be taken into consideration.

3. The acute phase reaction

The non-specific immune response consists of many humoral factors, like compounds of the APR. The APR is especially sensitive to the nutritional status and reversely, the supply of organism by nutrients, minerals and vitamins may alter the processes of the APR. During the APR, starting with fever, anorexia and leukocytosis, the concen-

tration of some proteins (e.g. serum-amyloid-protein, the SAP; C-reactive proteins, coeruloplasmin) strikingly increases (Heegaard et al., 1998, 2000; Horadagoda et al., 1999), the complement system and the pro-inflammatory cytokines (IL-1, TNFα, IL-6), produced by the mononuclear phagocytes (MØ), as well as cellular factors like phagocytes, granulocytes and natural killer cells are activated. The biological role of the APR is to combat intruders, repair tissue damages and stimulate immune response. Owing to the adenohypophysis and the stimulated leukocytes, which in turn can also release ACTH and thyrotropin, the ACTH, corticosteroids and thyroxin level increases that of the retinol-binding protein and consequently, the vitamin A concentration, decrease. Mobilization of proteins leads to negative nitrogen balance. Owing to the effect of lymphocyte endogenous mediator (LEM) and the apolactoferrin, the plasma zinc, iron and copper level dramatically drops depriving bacteria from essential nutritional factors (Gruys et al., 1999). The causes of the drastical decrease in serum zinc concentration is partly redistribution into the liver and lymphocyte metallothioneins under the influence of LEM; partly the calprotectin, compound produced by the PMN (polymorphonuclear) leukocytes, binds part of the plasma zinc. The enhanced erythrocyte sedimentation rate (ESR) and the elevation of fibrinogen fraction get plasma more viscous, aggravating the survival and proliferation of infectious agents.

Owing to the specific immune response, animals get immune to the given antigen. In case of viral, bacterial, fungal or parasitic infections, the developed immunity is a desired result, because it helps in eliminating the infectious agent, with minimizing its damaging effect. However, if the antigen in question is of dietary origin, the immune response may be harmful to the organism. The protection against the pathogenic agents differs, according to the character of intruder, for example bacteria, acting extracellular (e.g. *Staphylococcus, Streptococcus, E. coli, clostridia* etc.), bacteria and fungi acting intracellular (e.g. *Listeria, Legionella, Candida*) or the viruses (Falus, 1996). However, there is a common mechanism, namely the active participation of natural killer cells (NK) by producing toxic oxygen metabolites. The process includes the so-called "respiratory burst", while the non-mitochondrial oxygen consumption abruptly increases. First, during phagocytosis the membrane receptors of granulocytes activate the intracellular NADPH-oxidase, which in turn, by reacting with molecular oxygen, produces superoxide anions. The latter, under the influence of superoxide-dismutase (SOD) enzyme transforms into hydrogen peroxide (H_2O_2). Then, from the H_2O_2 substrate the myeloperoxidase (MPO) is capable of producing of the extremely toxic hypochlorite anion, to kill the pathogens (Evans and Halliwell, 2001).

4. Metabolic consequences of immune response

The so-called "immunological stress" (Klansing et al., 1991), beginning with the acute phase reaction, has a variety of physiological and metabolic consequences, which are at many points different from stress states, caused by other stressors, like heat or crowding. Events of immunological stress are a special form of homeorrhetic control and have a significant influence on nutrient utilization and thereby requirements.

Metabolic changes are mediated by cytokines, produced by the activated macrophages (see above: TNF_α, IL-1 and IL-6). The intensity of immunological stress response is proportional to the antigen challenge, but even a vaccination or subclinical infection exert an important effect on nutrient partitioning, directed them to the synthesis of acute phase molecules and cells, instead of growth. The immune system may influence metabolism by three ways: using direct neural connections (Bellinger et al., 2001); by the classic endocrine system and by the released leukocytic cytokines (Rabson et al., 2005). These hormone-like peptides directly alter metabolic functions and reduce voluntary feed intake.

The physiological changes include an elevation in the basal metabolic rate, strikingly enhanced carbohydrate utilization and to support this, stimulated gluconeogenesis and glycogenolysis. Generally this degradation ends in lactic acid, which in turn, through the *Cori*-cycle returns to the liver for reutilization. There is a strong peripheral protein catabolism, to supply amino acids for the acute phase proteins synthesis in the liver and for the proliferation of new lymphocyte colonies. Moreover, amino acids, after deamination, may also serve as a source of energy. A high very low density lipoprotein (VLDL) blood level is characteristic, too. Starch supplementation has a beneficial effect on intermediary energy metabolism in monogastric animals during the immunological stress.

5. Influence of nutrient deficiency on the immunity

Not only the extremely insufficient feed intake (general energy and protein deficiency) alters immune functions, but also the ingestion of quantitatively sufficient, but unbalanced rations. However, the protein-energy malnutrition (PEM) is the primary factor in affecting immune response. Interpretation of the related data is difficult, because generally there is an accompanying vitamin and/or mineral deficiency, too (see human Kwasiorkor, Tanner and Taylor, 1965). Moreover, the commonly occurring secondary infection not only weakens the immune system further, but also worsens the general body condition. Most of the knowledge of this field derives from epidemiological studies, because results of the experiments, investigating the effect of a single nutritional factor on the immunity, are difficult to extrapolate to the complex situations of the real life.

5.1. Energy and protein deficiency

Lack of energy and protein hardly damages the humoral immunity: the number of B-lymphocytes in the blood is rather independent from the changes in feeding, the serum IgG and IgM level is stable and the IgA concentration generally is slightly increased (Chandra, 1990). However, the concentration of secretory IgA in the produced nasal, conjunctival, pulmonary discharges and intestinal secretions decreases. In the latter the species differences are great and for example a low lachrymal IgA level and the subsequent chromorhinodacryorrhea in rat is a very sensitive indicator of the protein deficiency or discomfort (Morton and Griffith, 1985; Meek et al., 2003; Zoukhri, 2006).

Undernutrition fundamentally affects the cell-mediated immune response and the complement production. Under the influence of juvenile malnutrition the lymphoid organs, like thymus, lymph nodes, tonsils and spleen become atrophied. Number and activity of circulatory T-lymphocytes decrease, which can be demonstrated by skin hypersensitivity reaction. Although the number of leukocytes does not change, their intracellular bacterial and fungal killing activity decreases. The susceptibility of the individual immune function is different and the manifestations are also individual according to the species. Obesity is a special form of malnutrition. Leptin acts as a cytokine-like immune regulator that has complex effects in both overnutrition and in the inflammatory response in malnutrition (Cunningham-Rundles et al., 2005). Dietary fat is capable of activating cholinergic anti-inflammatory pathway, which may explain the failure of immune system to react feed antigens and commensal bacteria (Tracey, 2005).

The role of individual amino acids is also peculiar in immune response. Provision of arginine (Lewis and Langkamp-Henken, 2000), glutamine and branched-chain fatty acids (leucin, isoleucin, valin) are essential in the in the APR (Calder, 2006). Dietary methionine is a precursor of the anti-inflammatory glutathione and taurine, but also of the pro-inflammatory homocysteine. Because the predominance of actual metabolic pathway depends also on the genetic background of the individuals, the methionine overdosage may prove harmful (Grimble, 2006). The injury of the immune system depends not only on the degree of malnutrition, but also on the presence of other metabolic troubles and also on the age. Thus, the malnutrition is only an important member of the factors, besides infective agents, stress, surgical intervention, tumours, endocrine and metabolic troubles debilitating the patient's immune system. At the same time, improvement in feeding supports the appropriate immune response and decreases susceptibility against infections.

5.2. Deficiency or surplus of minerals

Harmonious functioning of the immune system requires the presence of several macro- and microelements. In experimental animals, the lack of calcium, magnesium, iron, zinc, copper, iodine and selenium has been associated with signs of immunodeficiency. Mortality of mice, experimentally infected by *Listeria monocytogenes* strongly depends on their zinc status (Chandra et al., 1991). The excess of minerals may also be harmful to the immune system; even a slight exposure to heavy metals (lead, mercury and cadmium) alters immunocompetance, although the exact mode of action is not known in each cases.

There is increasing evidence that the concentrations of trace elements required for healthy animals are often below what is required for animals experiencing an immunological challenge. In the past few years there has been a great deal of research published showing the key role of trace minerals in maximizing immunological function. Copper level in the diet has been shown to affect the resistance of

sheep to bacterial infections. An excess of copper antagonists like sulphur and molybdenum may also cause a secondary copper deficiency. Ward et al. (1993) reported that prolonged exposure to molybdenum (10 ppm) and sulphur (0.2%) decreased *in vivo* cell-mediated immune function in feeder cattle. The lower *in vitro* viability of lymphocytes collected from steers receiving the molybdenum and sulphur suggests that these cells are more fragile. Either a deficiency or an excess of iron can compromise the immune system. It has been well documented that serum iron falls early in response to bacterial and viral infections and rebounds quickly with recovery. This hypoferraemia is believed to be an important protective component of the APR to infection. Anaemic animals are much more susceptible to infections than those with adequate iron supply (Oppenheimer, 2001). Once the infection is established, iron supplementation has been shown to increase the bactericidal activity of liver and splenic marcrophages. For example, chicks inoculated with *S. gallinarum* had increased survival when iron (100 ppm of diet or more) was added to a basal diet containing 200 ppm of iron.

Substantial evidence has been reported that adding zinc above the supposed requirement enhances disease resistance (Shankar and Prasad, 1998). However, excessive zinc (150 ppm) also depressed immunocompetence. Zinc has both specific and aspecific role in the immune defence mechanism. As aspecific function, it protects integrity of skin and mucous membranes (mucosal barrier). Besides copper and manganese, it is indispensable to the functioning of SOD and thereby to the NK activity. Zinc enhances the chemotaxic sensitivity and intensity of phagocytosis of PMN neutrophils, monocytes and macrophages, moreover, supports complement activity. In its specific role, zinc regulates the maturation and function of immune cells, among others by protecting developing lymphocytes from apoptosis (Fraker et al., 2000). Zinc counterbalances the glucocorticoid-induced thymocyte apoptosis; by means of the protein kinase contributes to the activation of lymphocytes, included NK cells. As part of the zinc-finger proteins, zinc may influence DNA transcription (Lepage et al., 1999). The thymus synthesizes a 9-amino acid peptide hormone, the thymulin, which is activated after having bound zinc (Frandson et al., 2003). The function of the thymulin includes the maturation and activation of the T-lymphocytes and the stimulation of the IL-2 production. It also functions as a transmitter between the neuroendocrin and immune systems. Its degree of saturation with zinc is an excellent indicator of the zinc supply of the organism.

Selenium is recognized as an immonostimulant in swine, poultry and ruminants. Often selenium and vitamin E are supplemented together. Colnago et al. (1984) challenged broiler cockerels with *E. tenella* oocysts; graded selenium levels from 0.1 to 1.0 ppm or 100 ppm of vitamin E/kg were added to the diet from day one of age. Dietary supplementation of at least 0.25 ppm selenium or vitamin E reduced mortality and increased weight gain. These authors showed that feeding 0.25 ppm selenium or more, increased leukocyte number in the blood after infection with coccidia, which may explain the immune enhancement. Boyne and Arthur (1981) reported that neutrophils from selenium-deficient calves had a decreased ability to kill ingested *Candida albicans*, compared to neutrophils from selenium supplemented calves. These authors linked the decreased effectiveness of the neutrophils to a reduced glutathione peroxidase activity resulting from selenium deficiency. When glutathione peroxidase activity is reduced, peroxides and lipid hydroperoxides tend to accumulate to toxic levels in the neutrophils. Rate of clinical mastitis was negatively correlated to plasma selenium concentration in well-managed dairy herds (Weiss et al., 1990).

The main function of the selenium is the neutralisation of the free radicals. It interferes to the findings that lack of selenium both alone and combined with vitamin E deficiency affects immunocompetance. Until the near past, epidemiologists used to explain the effect of insufficient nutrients and active ingredients upon the resistance against the infections solely by the debilitation of the host organism. According to this approach, the malnutrition interacts with several physical and chemical barriers and immune response, getting human and animal more susceptible to pathogenic agents. The idea, that the host organism may have a direct effect on the pathogens, too, has not ever emerged. On the contrary, recently it has been proved this possibility in rodents, infected by enterovirus. The definitive evidence has been provided for this change of paradigm by Beck (1997). Benign Coxsackievirus B3 has been inoculated into selenium or vitamin E deficient mice. The virulence of the virus increased, which could be demonstrated also by the change of its genetic material. In other words, the benign Coxsackievirus B3, by means of mutation, became capable of inducing

heart lesions and the virus retains its virulent state when passaged into a well-nourished host (Beck and Levander, 2000). Using this knowledge, by peroral selenium application the manifestation of human cardyomyopathy (*Keshan*-disease) could have been prevented in a selenium-poor territory of China. Consequently, the traditional model of nutrition-infection interaction should be modified and include the possibility of the direct influence of the host organism on the virulence of pathogenic agents.

Selenium has a vitamin E-independent immunostimulant effect (Turner and Finch, 1991), for example in the marginally supplied (0.03 mg/kg of feed) calves. The protection could be demonstrated by the increased plasma gluthathion-peroxidase and IgM level after artificial IBR (infectious bovine rhinotracheitis) infection. There are evidences about the increase in total IgG concentration, neutrophyl and lymphocyte function after selenium application and about the stimulation of the agglutination after vitamin E supplementation. Both selenium and vitamin E are able to stimulate immune response and to decrease mortality caused by natural and artificial infections (Broome et al., 2004; Pinelli-Saavedra, 2003).

Added chromium is mostly beneficial in the periods of high-stress. Moonsie-Shageer and Mowat (1993) fed 0, 0.2, 0.5, and 1 ppm supplemental chromium from high-chromium yeast, to Charolais-crossed feeder cattle stressed due to shipment. Chromium supplementation decreased morbidity and rectal temperature at Day 2 and 5 after arrival. In dairy cows chromium caused increased anti-ovalbumin response but did not affect the immune response to the red blood cells. These data suggest that chromium supplementation may enhance resistance to mastitis in dairy cows (Burton et al., 1993). Chromium reduced serum cortisol levels. Glucocorticods, which include cortisol, are known to suppress the immune system. Cobalt deficiency rendered sheep more susceptible to bacterial infections. Reductions in candidacidal activity of ovine neutrophils have been reported as a result of cobalt deficiency. These authors noted that the changes in the health of the neutrophils became evident before vitamin B_{12} status altered.

5.3. Lack of vitamins and essential fatty acids

In the circle of production or companion animals the occurrence of extreme vitamin deficiency or overdosage is uncommon. Therefore, data concerning the effect of the individual vitamins on immune function mostly derive from animal trials. From the group of fat soluble vitamins, the role of vitamin A and E is essential. Lack of vitamin A frequently accompanies PEM. Vitamin A deficiency decreases resistance against infections. This is partly due to the injury of skin and mucous membranes, partly to the impairment of humoral and cell-mediated immune response. Deficient vitamin A supply of growing chicken induced atrophy (lower organ weight, compared to the control) of bursa *Fabricii*, thymus and spleen (West et al., 1991). On the contrary, vitamin A supply increases two-three times the number of IgG-producing cells in the mesenterial lymph nodes and in the spleen of mice with *Trichinella spiralis* infection. Combined effect of supplementary vitamin A and β-carotene was able to decrease somatic cell count in milk of dairy cow. To elucidate the independent carotenoid effect from the role as a vitamin A precursor, rats were fed on β-carotene and canthaxantine containing diets. The latter compound is effective against the free radicals, but cannot serve as a vitamin A precursor. At the end of the 20-week trial, it could be stated that on mitogen stimulation by concanavalin, phytohaemagglutinin A and LPS, the T- and B-cells of carotenoid-pre-treated animals reacted more intensively (Bendich and Saphiro, 1986). Carotenoids, included β-carotene, cryptoxanthin, canthaxanthin, lycopene have immunostimulant effect not only by quenching of free radicals but also stimulate lymphocytes, macrophages and natural killer cells. Production and secretion of tumour cytotoxic factors by the immune system are also induced by carotenoids (Bendich, 1991). Active form of vitamin D_3 regulates transcription at cell level, acts as an immunomodulator and promotes phagocytosis. Insufficient vitamin E provision reduces both humoral and cell-mediated immune response (Kelleher, 1991). On the other hand, extra large dosages of tocopherols are immunostimulant. Members of vitamin B group (thiamine, riboflavin, pyridoxine, pantothenic acid and biotin) promote antibody production. Folic acid and vitamin B_{12} are involved in antibody and nucleic acid synthesis.

Lack of essential fatty acids in the diet of experimental animals caused atrophy of lymphoid organs and the reduction both the T-cell mediated and the independent immune response (Halas et al., 2006). Therefore, ω-3 and ω-6 fatty acids are essential in the membrane composition of white

blood cells and in the release of prostaglandins and leukotriens. The ratio of triens to tetraens (three and four double bonds fatty acids) and that of ω-3 to ω-6 fatty acids proved to be also important in relation to the immune response. Feeding fish oil of high concentration in ω-3 fatty acids attenuates many T cell-mediated inflammative processes (Calder et al., 2002). Using murine *in vivo* and *in vitro* models it was elucidated that dietary fish oil reduced number of Th1 cell by means of suppression of clonal expansion, but not by stimulating their apoptosis (Zhang et al., 2006). It is logical to cite hereby that the lack of carotenoids (e.g. lutein) has also a systemic pro-inflammatory influence in poultry (Koutsos et al., 2006). Feeding a conjugated linoleic acid-enriched diet, the inflammatory effect of LPSs in weaned piglets can be attenuated (Changhua et al., 2005).

Among the water-soluble vitamins the insufficient intake of vitamin B_6 (pyridoxine), the pantothenic acid and folic acid may disturb both humoral and cell-mediated immune response. Vitamin C increases the phagocytic activity of macrophages. Huge amount of peroral intake of vitamin C (2 g/day) increased the ascorbic acid concentration of leukocytes, granulocytes and blood plasma in human (Evans, 1982). Higher lymphocyte proliferation, measured by ^{3}H-thymidine incorporation in DNA of human lymphocytes over 18 hours after previous incubation for 2 days with concanavalin A at varying ascorbic acid concentration, proved the dose-related immunostimulant effect of vitamin C (Kolb, 1997). Effect of minerals and vitamins on the immune status is linked in many points. For example, vitamin B_6, in form of pyridoxal kinase, carrying magnesium and zinc, helps the free radical production in the NK cells.

Although, most of the described data came from animal experiments, the occurrence of diet-induced immunodeficiency is not uncommon in the practice, either. If newborn calf delays in receiving the first colostrum portion, becomes susceptible to the slight mineral deficiency in the cow's milk. Subclinical B_{12} deficiency of ewes (established by the serum B_{12} and methyl-malonic acid level), caused by insufficient cobalt intake, had no effect on the live weight of newborn lambs, but the perinatal mortality of offspring increased. The latter can be explained by the impaired immune system of dams and the insufficient passive immunity, given to the lambs. If pregnant sows of average vitamin supply were provided by 5 mg sodium selenium and/or by 1 000 mg DL-tocopherol on day 100 of gestation, the amount of transmitted antibodies to the offspring increased. Another practical application of the new immunological finding is the segregated early weaning (SEW), which serves the protection of young piglets from the antigenic challenges from the dam, weaning them in the age of 10 to 14 days (Williams et al., 1997). At that time the passive immunity of piglet is on the peak and lacking the above described immunological stress, their weight gain and feed conversion significantly improve.

6. Feed intolerance, allergy and aversion

Feed intolerance is a reproducible phenomenon, related to an actual chemical component of the diet (Young, 1990). The common manifestation is dyspepsia, abdominal discomfort or pain with or without diarrhoea. In the background, the lack of a digestive enzyme (e.g. lactose or fructose intolerance; Cox, 1991), a special pharmacological effect (e.g. caffeine stimulated peristalsis) or a non-immunological histamine release (ingestion of certain seafoods like mollusc, octopus, squid, scallop, oyster, crab, lobster etc.) may stand. Frequently and unjustified the latter is also named as allergy or sensitivity.

Feed allergy (or sensitivity) is an abnormal immunological reaction, while the organism tuned to one of the feed proteins, like milk casein, wheat gluten, soy protein and others (McAdam and Sollid, 2000). Feed antigens represent a continuous challenge, giving chance to the development of a hypersensitivity reaction (Young, 1991). The latter may be an acute, IgE-mediated (reagin or reaginic antibodies) immediate hypersensitivity reaction within 1 to 2 hours or a T cell-mediated delayed hypersensitivity reaction within days, resulting in bronchospasmus (see sudden cot death in human medicine), severe scour or even death. The chronic hypersensitivity, in turn, can be characterized by increased protein secretion, like secretory immune globulin A, mucus and epithelial cells in the gut lumen, changes in peristalsis and disturbed permeability of intestinal wall, caused by histological damages (Peakman and Vergani, 1997). The specific antibodies are present in the blood, because there is a possibility for antigen uptake when the protein digestion is incomplete and macromolecules may remain intact. Another ways of getting antigen in the bloodstream include the non-specific

absorption by the M-cells in the ileum, defects in mucosal barrier (subchronic enteritis), IgA immunodeficiency or very high concentration of antigens in the intestinal lumen (Walker, 1987). There are other than intestinal ways (through conjunctivae or lungs) of intact dietary antigen intake, too. The plasmacytic colitis with diarrhoea and increased histamine release accompanying by itching wheals on skin are the common signs of manifestation (Guaguere, 1995).

Feed aversion is a learned, psychological process, based on conditioned reflex, which cannot be triggered unless the questionable feed is offered in the same physical form (Royal College of Physicians and The British Nutrition Foundation, Joint Report, 1984).

7. Nutrition and parasitic infection

7.1. General effect of gastroenteral parasites

The interaction between the presence of parasites in the host organism and nutrition can be well demonstrated on the example of gastro-intestinal worms. The following data derive mainly from experiments using the following animal models: *Obeliscoides cuniculi* in the rabbit stomach; *Ostertagia circumcincta* in the abomasum of sheep and goat; *Ostertagia ostertagi* in the cattle abomasum; *Trichostrongylus axei* in the cattle abomasum; *Haemonchus contortus* in abomasum of sheep and goat; *Trichostrongylus columbriformis* and the *Trichostrongylus vitrinus* in the sheep small intestine; *Chabertia ovina*, in sheep large intestine; *Oesophagostomum columbianum* in the large intestine of sheep and goat. Laboratory rodent models have also been used (Koski and Scott, 2001).

Presence of each of the enumerated helminths decreased the average daily gain of growing animals; moreover, in many cases they caused loss of weight. The characteristic localization of the worms showed no correlation with the extent of the reduction in live weight, but the gravity of infection did. Under a certain number of worms ("threshold value") the host organism did not show detectable changes (Titchen and Anderson, 1977). The main reason for the harmful effect is a decreased feed intake, but the feed utilization is also worsened. Owing to the increased heat production part of the metabolisable energy is lost. The described state is reversible, even some adaptation could be observed.

Parasitic infection changed the body and skeletal composition: the water content increased that of protein and fat dropped; the calcium and phosphorus concentration of bones decreased by 15 to 45%. The wool consists mainly of protein. This is the reason why even a moderate gastro-intestinal helminthiasis decreased the length and diameter of the wool fibres. Against the PEM the sequence of tissue susceptibility is as follows: wool, fat depots, muscle, blood, liver, spleen, heart and the more resistant are the nerves and the brain (Hammond, 1952). PEM decreased the resistance against the new infections, but had no influence on the already present worms, included their egg production. Initial establishment and short-term survival of *Nippostrongylus brasiliensis* were the same in protein-deficient (5 to 10%) or protein-rich (30%) fed rats, but the long-term worm survival increased in protein-deficient animals (Bolin et al., 1977). Resistance to internal parasites is also compromised by copper deficiency. Copper deficient lambs inoculated with *Taenia axei* and *Taenia colubriformis* had maximum faecal egg counts 2 weeks sooner and became more hypoalbuminaemic than lambs receiving supplemental copper. Ingestion of tanniferous plant by grazing animal may attenuate gravity of gastrointestinal parasitosis (Athanasiadou et al., 2006).

Helminths, developing in the animal, may cause serious local lesions: for example *Ostertagia circumcincta* is capable of destroying glands of abomasal wall, causing haemorrhage. In small intestine the flattening and atrophy of villi, in turn, in the large intestine ulcer and haemorrhage are typical signs of worm damages. After the appropriate anthelmintic treatment regeneration took up approximately three weeks. Devastated intestinal cells are replaced by functionally undifferentiated cells; in the mucous membrane hyperplasia and inflammation develop and the wall becomes thick. The functionally immature cells, covering the secretory and absorptive surfaces have a higher permeability to the macromolecules ("leak lesion"), which results in pathological alterations (Bilkslager and Roberts, 1997). In the abomasum the pH may change; in the small intestine the production of brush-border enzymes declines.

Anaemia and the change of plasma proteins are frequent concomitant of the gastro-intestinal parasitosis. Generally the albumin level drops, that of globulin and total protein increases. In case of serious infection the concentration of the latter drops, too (Anderson and Bremner, 1983). Infection is frequently manifested also in oedema, diarrhoea,

lower blood pepsinogen level and change in activity of some liver enzymes.

7.2. Effects of worms on digestion

Under the influence of intestinal parasites the gut motility modifies: the peristalsis generally slows down, unless diarrhoea occurs at the same time. Worms' toxins stimulate the production of gastrointestinal hormones, like gastrin and cholecystokinin, causing reduction in voluntary feed intake. The production of hydrochloric acid in the abdomen, except the immediate vicinity of helminths, decreases (Gay et al., 2000). Digestion and absorption of nutrients are also reduced and the endogenous nitrogen excretion elevates. To replace the amount of plasma proteins excreted into the gut lumen, the protein synthesis in blood and liver is enhanced, in turn that in the muscles, is lowered. The described alterations in the postabsorptive metabolism can be mitigated and shortened by benzimidazol treatment.

As a consequence of reduced feed intake, less volatile fatty acid and ammonia are produced in the rumen. Part of the amino acids in the gut lumen undergoes deamination; the released ammonia is absorbed, transforms into urea, in turn, and is excreted by the urine. Consequently the higher urinary urea and methyl-histidin from the muscle mobilization reflects increased protein losses. Higher turnover of the urea cycle involves a higher need to arginine and vitamin B_6. Extra protein synthesis (to replace the plasma proteins) uses part of the available metabolisable energy. Summarizing, both energy and protein balance become negative. As a consequence, the body composition changes and the percentage of protein in the carcass decline. Gastro-enteral helminthiasis alters the utilisation of calcium, phosphorus and magnesium. Thereby, the measure and density of bone (poor mineralization) decrease in growing animals. Blood level of the mentioned minerals generally does not change, except phosphorus, which in case of a serious infection may drop, too.

7.3. Nutrition and the other parasitic infections

The leading symptoms of the ruminants' gastrointestinal helminthiasis, namely the negative energy and protein balance and the changes in the body composition have also been found in wild boars, infected with stomach (*Physocephalus sexalatus* and *Ascarops strongylina*), as well as with lung worms (*Metastrongylus* spp.*).* Basically similar results have been received, after the artificial infection of poultry with intestinal coccidia or pigs with different helminths (*Strongyloides ransomi, Stephanurus dentatus, Ascaris suum, Oesophagostomum* spp. and *Trichuris suis*). Infection of rabbits with *Eimeria stiedai*, causing biliary coccidiosis (or hepatic coccidiosis), significantly decreased voluntary feed intake (possibly owing to TNFα-release) and the digestibility of nutrients, especially that of the fats (Yvore and Guillaume, 1976). The latter finding is traceable to the hepatomegalia, liver lesions and chronic jaundice, caused by the coccidia.

Zhu et al., (2000) investigated the effect of *Eimeria maxima* in growing chickens. The extent of infection and the oocyte excretion showed a strong negative correlation with the plasma carotenoid level and strong positive correlation with the blood nitrogen oxide and γ-interferon concentration, as signs of protection. Coccidiosis may alter carotenoid metabolism in many points: only an indirect effect at the ingestion (minor change in feed consumption), a direct alteration in the intestinal absorption of carotenoids, due to the altered permeability. There are no data about the digestive liberation of carotenoids in the gut lumen); coocidia effect transport process into the liver; they also directly modify the tissue storage (included eggs) and the faeces elimination of the carotenoids by speeding the transit time. As possible consequences, the tissues and the egg-yolk looses colour and generally the carotenoid requirements will increase. At the same time, higher dosages (≥ 5%) of omega-3-fatty acids are able to counterbalance harmful effects of *Eimeria tenella* infection. Interestingly enough, the recovery of intestinal epithelium damages requires the presence of otherwise harmful biogenic amine, the putrescine (1,4-diaminobutane) in the gut lumen (Girdhar et al., 2006).

7.4. Effect of nutritional status and age on the nematode survival

According to recent evidences, the malnutrition-supported prolonged nematode survival is developed by the alterations of immune functions: PEM and vitamin A deficiency down-regulate the expression of protective Th2 cytokines. Shortage in

zinc supply caused a down-regulation of IL-4 in the spleen (Scott and Koski, 2000): the dysregulation of Th1 and Th2 phenotypes disturb the GALT specific and aspecific functions resulting reduced defence and expulsion mechanism (Kassai et al., 1980; Koski et al., 1999). The age-related rise of dehydroepiandrosterone sulphate (DHEAS) decreased the susceptibility and improved the nutritional status in *Schistosoma japonicum* infected human adolescents by downregulating the proinflammatory immune response (Coutinho et al., 2007).

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9. REFERENCES

Altorjay I. (2006): Food allergies (in Hungarian). Magyar Orvos, 14, 41–44.

Anderson N., Bremner K.C. (1983): Lifecycle and pathogenesis of helminths of major economic importance. In: Anderson N., Woller P.J. (eds): The Epidemiology and Control of Gastrointestinal Parasites of Cattle in Australia. Commonwealth Scientific and Industrial Research Organization, Australia. 23–34.

Athanasiadou S., Kyriazakis I., Jackson F. (2006): Can plant secondary metabolites have a role in controlling gastrointestinal nematode parasitism in small ruminants? In: Sandoval-Castro C.A., Hovell F.D.DeB., Torres-Acosta J.F.J., Ayala-Burgos A. (eds.): Herbivores: Assessment of Intake, Digestibility and the Roles of Secondary Compounds. BSAS Publication 34. Nottingham University Press, Nottingham. 197–205.

Beck M.A. (1997): Increased virulence of Coxackievirus B3 in mice due to vitamin E or selenium deficiency. The Journal of Nutrition, 127, 966S–972S

Beck M.A., Levander O.A. (2000): Host nutritional status and its effect on a viral pathogen. Journal of Infectious Diseases, 182 (Suppl.), 93–96.

Bellinger D.L., Lorton D., Lubhhn C., Felten D.L. (2001): Innervation of lymphoid organs: association of nerves with cells of the immune system and their implications in diseases. In: Ader R., Fleten D.L., Cohen N. (eds): Psychoneuroimmunology. Vol. 1. 3rd ed. Academic Press. San Diego, CA. 55–112.

Bendich A. (1991): β-carotene and immune response. Proceedings of Nutrition Society, 50, 263–274.

Bendich A., Saphiro S.S. (1986): Effect of beta-carotene and canthaxanthin on the immune responses of the rat. The Journal of Nutrition, 116, 2254–2262.

Bilkslager A.T., Roberts M.C. (1997): Mechanisms of intestinal mucosal repair. Journal of American Veterinary Medical Association, 211, 1437–1441.

Bolin T.D., Davis A.E., Cummings A.G., Duncombe V. M., Kelly J.D. (1977): Effect of iron and protein deficiency on the expulsion of *Nippostrongylus brasiliensis* from the small intestine of the rat. Gut, 18, 182–186.

Boyne R, Arthur J.R. (1981): Effects of copper and selenium deficiency on neutrophil function in cattle. Journal of Comparative Pathology, 91, 271.276.

Broome C.S., McArdle F., Kyle J.A., Andrew F., Lowe N.M., Hart C.A., Arthur J.R., Jackson M.J. (2004): An increase in selenium intake improves immune function and poliovirus handling in adults with marginal selenium status. American Journal of Clinical Nutrition, 80, 154–162.

Burton J.L., Mallard B.A., Mowat D.N. (1993): Effects of supplemental chromium on immune response of periparturient and early lactation dairy cows. Journal of Animal Science, 71, 1532–1539.

Calder P.C. (2006): Branched-chain amino acids and immunity. The Journal of Nutrition, 136, 288S–293S.

Calder P.C., Yaqoob P., Thies F., Wallace F.A., Miles E.A. (2002): Fatty acids and lymphoid functions. British Journal of Nutrition, 87 (Suppl.1), S31–S48.

Chandra R.K. (1990): Nutrition and immunity. American Journal of Clinical Nutrition, 53, 1087–1101.

Chandra R.K., Baker M., Whang S. (1991): Effect of two feeding formulas on immune responses and mortality in mice challenged with *Listeria monocytogenes*. Immunological Letters, 27(1), 45–48.

Changhua L., Jindong Y., Defa L., Lidan Z., Shu Q., Jianjun X. (2005): Conjugated linoleic acid attenuates the production and gene expression of proinflammatory cytokines in weaned pigs challenged with lipopolysaccharid. The Journal of Nutrition, 135, 239–244.

Colnago G.L., Jensen L.S., Long P.L. (1984): Effect of selenium and vitamin E on the development of immunity to coccidiosis in chickens. Poultry Science, 63, 1136–1143.

Coutinho H.M., Leenstra T., Acosta L.P., Olveda R.M., McGarvey S.T., Friedman J.F., Kurtis J.D. (2007): Higher serum concentrations of DHEAS predict improved nutritional status in helminth-infected children, adolescents, and young adults in Leyto, the Philippines. The Journal of Nutrition, 137, 433–437.

Cox T.M. (1991): Fructose intolerance: diet and inheritance. Proceedings of the Nutrition Society, 50, 305–309.

Cunningham-Rundles S., McNeeley D.F., Moon A. (2005): Mechanisms of nutrient modulation of the immune response. Journal of Allergy and Clinical Immunology, 115, 1119–1128.

Evans R.M. (1982): Effect of short-term high ascorbic acid intake on its plasma, leukocytes and granulocyte concentration. British Journal of Nutrition, 47, 471–482.

Evans P., Halliwell B. (2001): Micronutrients: oxidant/antioxidant status. British Journal of Nutrition, 85 (Suppl. 2), S67–S74.

Falus A. (1996): Physiological and Molecular Basics of Immunology (in Hungarian). Semmelweis Kiado, Budapest. 201–208.

Fekete S.,Tamas J.,Vanyi A., Glavits R., Bata A. (1989): Effect of T-2 toxin on feed intake, digestion and pathology of rabbits. Laboratory Animal Science, 39, 603–606.

Fekete S.Gy., Fodor K., Andrasofszky E., Glavits R. (2007): Effect of rancid feed on rat's performance, protein utilization and pathological findings. Journal of Animal Physiology and Animal Nutrition: submitted for publication

Fraker P.J., King L.E., Laakkoo T., Volimer T.L. (2000): The dynamic link between the integrity of the immune system and zinc status. The Journal of Nutrition, 130, 1399S–1406S.

Frandson R.D., Wilke W.L., Fails A.D. (2003): Anatomy and Physiology of Farm Animals. 6th ed. Lippincott Williams & Wilkins, Philadelphia, Baltimore, New York, London, Buenos Aires, Hong Kong, Sidney, Tokyo. 246–257.

Gay J., Fioramonti J., Garcia-Villar R., Bueno L. (2000): Development and sequels of intestinal inflammation in nematode-infected rats. Role of mast cells and capsaicin-sensitive afferents. Neuroimmunomodulation, 8, 171–178.

Gergely J. (2006): Introduction to the immunology. In: Gergely J., Erdei A. (eds.): Immunobiology (in Hungarian). Medicina Konyvkiado Rt., Budapest. 15–17.

Girdhar S.R., Barta J.R., Santoyo F.A. Smith T.K. (2006): Dietary putrescine (1,4-diaminobutane) influences recovery of turkey poults challanged with mixed coccidial infection. The Journal of Nutrition, 136, 2319–2324.

Grimble R.F. (2006): The effect of sulfur amino acid intake on immune function in human. The Journal of Nutrition, 136, 1660S–1665S.

Gruys E., Toussaint M.J.M., Landman W.J.M., Tivapasi M., Chamanza R., van Veen L. (1999): Infection, inflammation and stress inhibit growth. Mechanism and non-specific assessment of the processes by acute phase proteins. In: Wensing Th. (ed.): Production Diseases in Farm Animals. In: 10th International Conference, 1998, Wageningen Pers, Wageningen, The Netherlands, 72–87.

Guaguere E. (1995): Food intolerance in cats with cutaneous manifestations: A review of 17 cases. European Journal of Companion Animal Practice, 5, 27–35.

Halas V., Kovacs M., Babinszky L. (2006): Impact of nutrient supply on the immune functions in pig. Literature review (in Hungarian with English abstract). Magyar Allatorvosok Lapja, 128, 535–543.

Hammond J. 1952): Farm Animals. Their breeding, growth and inheritance. Edward Arnold & Co., London. p. 99.

Heegaard P.M., Klausen J., Nielsen J.P. (1998): The porcine acute phase response to infection with *Actinobacillus pleuropneumoniae*: Haptoglobin, C-reactive protein, major acute phase protein and serum amyloid. Comparative Biochemistry and Physiology (B), 119, 365–373.

Heegaard P.M., Godson D.L., Toussaint M.J. (2000): The acute phase response of haptoglobin and serum amyloid A (SAA) in cattle undergoing experimental infection with bovine respiratory syncytial virus. Veterinary Immunology and Immunopathology, 77, 151–159.

Horadagoda N.U., Knox K.M., Gibbs H.A. (1999): Acute phase proteins in cattle: Discrimination between acute and chronic inflammation. Veterinary Record, 144, 437–441.

Kassai T., Redl P., Jecsai G., Balla E., Harangozo E. (1980): Studies on the involvement of prostaglandisns and their precursors in the rejection of *Nippostrongylus brasiliensis* from rat. International Journal of Parasitology, 10, 115–120.

Kelleher J. (1991): Vitamin E and the immune response. Proceeding of the Nutrition Society, 50, 245–249.

Klansing K.C., Johnstone B.J., Benson B.N. (1991): Implication of an immune response on growth and nutrient requirement of chicks. In: Haresign W., Cole D. J.A. (eds): Recent Advances in Animal Nutrition. Butterworth/Heinemann Ltd. Linacre House, Jordan Hill, Oxford. 135–146.

Kolb E. (1997): Vitamins and the Immune System. F. Hoffmann-La Roche Ltd., Basel. 46–50.

Koski K.G., Scott M.E. (2001): Gastrointestinal nematodes, nutrition and immunity: Breaking the negative spiral. Annual Reviews of Nutrition, 21, 297–321.

Koski K.G., Su Z., Scott M.E. (1999): Energy deficits suppress both systemic and gut immunity during infection. Biochemical and Biophysical Research Communications, 264, 796–801.

Koutsos E.A., Lopez J.C.G., Klansing K.C. (2006): Carotenoids from in ovo or dietary sources blunt systemic indices of the inflammatory response in growing chicks (*Gallus gallus domesticus*). The Journal of Nutrition, 136, 1027–1031.

Lepage L.M., Giesbrecht J-A.C., Taylor C.G. (1999): Expression of T lymphocyte p56lck, a zinc-finger signal transduction protein, is elevated by dietary zinc deficiency and diet restriction in mice. The Journal of Nutrition, 129, 620–627.

Lewis B., Langkamp-Henken B. (2000): Arginine enhances *in vivo* immune responses in young, adult and aged mice. The Journal of Nutrition, 130, 1827–1830.

MacDonald T.T., Monteleone G. (2005): Immunity, inflammation, and allergy in the gut. Science, 307, 1920–1925.

McAdam S.N., Sollid L.M. (2000): Getting to grips with gluten. Gut, 47, 743–745.

Meek B., Speijer D., de Jong P.T.V.M., de Smet M.D., Peek R. (2003): The ocular humoral immune response in health and disease. Progress in Retinal and Eye Research, 22, 391–415.

Moonsie-Shageer S., Mowat D.N. (1993): Effect of level of supplemental chromium on performance, serum constituents, and immune status of stressed feeder calves. Journal of Animal Science, 71, 232–238.

Morton D.E., Griffith P.H.M. (1985): Guidelines on the recognition of pain, distress and discomfort in experimental animals and an hypothesis for assessment. Veterinary Record, 116, 431–436.

Oppenheimer S.J. (2001): Iron and its relations to immunity and infectious diseases. The Journal of Nutrition, 131, 616S–635S.

Peakman M., Vergani D. (1997): Basic and Clinical Immunology. Churchill Livingstone, Edinburgh. 205–213.

Pinelli-Saavedra A. (2003): Vitamin E in immunity and reproductive performance in pig. Reproduction and Nutrition Development, 43, 397–408.

Rabson A., Roitt I.M., Delves P.J. (2005): Really essential medical immunology. Blackwell Publishing, Malden, Oxford, Carlton. 1–16.

Royal College of Physicians and The British Nutrition Foundation (1984): Food intolerance and food aversion. Joint Report. Journal of the Royal College of Physicians of London, 18, 83–123.

Scott M.E., Koski K.G. (2000): Zinc deficiency impairs immune responses agains parasitic nematode infections at intestinal and systemic sites. The Journal of Nutrition, 130, 1412S–1412S.

Shankar A.H., Prasad A.S. (1998): Zinc and immune function: the biological basis of altered resistance to infection. American Journal of Clinical Nutrition, 68 (Suppl.), 447S–463S.

Szigeti G. (1991): Interactions of host organism, feed and gut flora (in Hungarian with English summary). Magyar Allatorvosok Lapja, 46, 391–394.

Tanner J.M., Taylor G.R. (1965): Growth. Time Life Books, New York. 188 pp.

Titchen D.A., Anderson N. (1977): Aspects of the physico-pathology of parasitic gastritis in the sheep. Australian Veterinary Journal, 53, 369–373.

Tracey K.J. (2005): Fat meets the cholinergic antiinflammatory pathway. Journal of Experimental Medicine, 202, 1017–1021.

Turner R.T., Finch J.M. (1991): Selenium and immune response. Proceedings of the Nutrition Society, 50. 275–285.

Walker W.A. (1987): Pathophysiology of intestinal uptake and absorption of antigens in food allergy. Annals of Allergy, 59, 7–16.

Ward J.D., Spears J.W., Kegley E.B. (1993): Effect of copper level and source (copper lysine *vs* copper sulfate) on copper status, performance, and immune response in growing steers fed diets with or without supplemental molybdenum and sulfur. Journal of Animal Science, 71, 2748–2755.

Weiss W.P., Hogan J.S., Smith K.L., Hoblet K.H. (1990): Relationship among selenium, vitamin E, and mammary gland health in commercial dairy herds. Journal of Dairy Science, 73, 381–390.

West C.E., Rombout J.H.W., Van der Zijpp A.J., Sitsma S.R. (1991): Vitamin A and immune function. Proceedings of the Nutrition Society, 50, 251–262.

Williams N.H., Stahhly T.S., Zimmerman D.R. (1997): Effect of level of chronic immune system activation on the growth and dietary lysine needs of pigs from 6 to 112 kg. Journal of Animal Science, 75, 2481–2496.

Young E. (1990): Allergic responses to diets in humans. In: Haresign W., Cole D.J.A. (eds.): Recent Advances in Animal Nutrition. Butterworth, London, Boston, Singapore, Sydney, Toronto, Wellington. 3–6.

Young E. (1991): Atopy, allergy and alimentary canal. Proceedings of the Nutrition Society, 50, 299–303.

Yvore P., Guillaume J. (1976): The effect in rabbit, of hepatic coccidiosis on digestibility of fat and energy. Annales de la Recherche Veterinaire, 7, 343–348.

Zhang P., Kim W., Zhou L., Whang N., Ly L.H., McMurray D.N., Chapkin R.S. (2006): Dietary fish oil inhibits antigen-specific murine Th1 cell development by suppression of clonal expansion. The Journal of Nutrition, 136, 2391–2398.

Zhu J.J., Lillehoj H.S., Allen P.C., Yun C.H., Pollock D., Sadjadi M., Emara M.G. (2000): Analysis of disease

resistance-associated parameters in broiler chickens challenged with *Eimeria maxima*. Poultry Science, 79, 619–625.

Zoukhri D. (2006): Effect of inflammation on lacrimal gland function. Experimental Eye Research, 82, 885–898.

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