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FREE RADICALS AND CARES FOR AGING PETS

I. Ivanov

Department of Veterinary Microbiology, Inefectiouse and Parasitics diseases,
Faculty of Veterinary Medicine, Trakia University, Stara Zagora, Bulgaria

In the normal human and animal organism, metabolic processes for defence from external and internal harmful cellular agents (bacteria, viruses, toxins, dead somatic cells etc.) are in course. Those processes are performed with the participation of various enzymes, vitamins, hormones, oxidative products and especially, free radicals. Recently, there is a lot of information about the role of free radicals in the process of aging, in cancerogenesis, in immune defence mechanisms etc. In order to improve the care for aged animals, it is interesting to detect the sources of free radicals, their mechanisms of action, the means for their inhibition and elimination.

Free radicals(FR) are atoms or molecules that possess one unpaired electron on their outer orbital. They are very unstable and can react with other molecules by taking or giving an electron.

Superoxide anion ($O_2^{\cdot-}$) is the most widely produced free radical. It is negativily charged from the reduction of molecular oxygen. It is produced enzymatically in phagocytosis (NADPH oxidase), in cell respiration (mitochondrial cytochrome oxydase), in oxidative metabolisms of xenobiotics (liver cytochrom P-450), in ischemia reperfusion (xanthin-oxidase). In the presence of protons its dismutation leads to oxygen and to hydrogen peroxide. Oxigen-generated free radicals damage chromosomes (Lieber, 2002).

Hydroxyl radical ($^{\cdot}OH$) is also produced in tissues and is more times reactive than O_2 which leads to the formation of new free radicals. It can be formed from hydrogen peroxide in the presence of ferrous ions. Hydrogen peroxide (H_2O_2) is not a free radical, but has a high oxidant capacity via the hydroxyl radical ($^{\cdot}OH$). Hydrogen peroxide is able to cross biologic membranes and to induce cellular damage, resulting in the formation of hydroxyl free radical.

Peroxyl ($ROO^{\cdot}$) free radical is also synthesized, essentially from polyunsaturated fatty acids which results from the action of hydroxyl radical. This is the initiation phase of lipid peroxidation. Proteins are also very sensitive to free radical attacks; there is a rise of oxidized proteins as a function of age, which is due to free radical induced damages and to the decreased elimination of these proteins.

Ribo- and deoxyribonucleic acids (RNA, DNA) are also favored targets for free radicals. Some studies show a relationship between radical-induced damages in both nuclear and mitochondrial DNA and aging.

Some hypothesis and data imply that longer-lived species have a higher degree of protection against by-products of oxygen metabolisms. Some results show a clear positive correlation of the life span with plasma α-tocopherol and carotenoid. At the same time in the controversy it has been shown that mitochondria isolated from animals with the lowest life span produced the highest contents of superoxide anion (O_2) and hydrogen peroxide (H_2O_2).

A free radical with a superoxidative effect is the hypochloric acid (HOCL $^{\cdot-}$). It is stable and possesses a very powerful oxidative activity.

One of the sources of free radicals is liver, where the harmful substances are rendered harmless and eliminated. As end products of this elimination, FR (O_2, $OH^{\cdot}$, H_2O_2) are created and accumulated.

Another source of free radicals is

phagocytosis (process of ingestion, digestion and elimination of bacteria, parts of erythrocytes, foreign mechanical particles etc.). For elimiination of foreigh bodies, phagocytes (blood monocytes and neutrophil leukocytes; tissue histiocytes or macrophages) use a broad arsenal of lysosomal enzymes, proteases for DNA degradation and especially oxidases, that mediate the creation of FR. Those FR are normally destroying foreign bodies in the healthy organism. In fact, this is a normal mechanism for systemic defence. Those processes are energy-independent and occur with the participation of glucose and glycogen.

Sometimes, FR could act as pathogenic factors. This occurs when liver disorders are available (glycogen deficiency, cirrhosis, dystrophy, infections, intoxications etc.). Ionized radiations increase FR as well. The intracellular level of FR is also elevated in mitochondrial hypoxia and ischemia.

Free radicals inhibit enzymes and enhance the process of aging of the organism. The accumulated free radicals break down the DNA chain and impair the cellular genome, that could later result in a cancerogenic effect.

Free radicals influence the permeability of cellular membranes. In smooth muscle cells this leads to impaired skin and blood vessel elasticity, retarded intestinal peristaltics etc. This effect is manifested by haemorrhages in endothelial blood vessel cells.

Free radicals impair the K(potassium)-Na(sodium) cellular pump, resulting in a K outflow and Na inflow. Thus, the intracellular osmotic pressure is changed and the cell is damaged.

In fact, toxins, infectious agents and ionized radiation are the principal prerequisites for FR increase. Accumulation of FR is observed in aging as well.

The involvement of radical attacks in aging and in some pathologies leading to an accelerated aging (atherosclerosis, diabetes, weakness of immunity, cancerogenesis, heart weakness) is highly probable. Approches that inhibit these factors could be thus applied to slow down the aging process and to avoid and to prevent geriartric pathologies. Such role may play the antioxidants like vit C, vit E, vit A, and selenium(Se).. An antioxidant cocktail has been used to reduce oxidative stress in trained and untrained dogs (Waldrion et al., 2007).

For decrease of FR production and their elimination, the so-called antioxidants are recommended. In the practice, vit C, vit E, vit A, selenium etc. are widely used.(Philips, 2007;) Antioxidant factors have been identified in S.cerevisiae which may effectively remove the free radical moieties circulating in the body of chicken (Raju et al., 2005).

Vitamin C (ascorbinic acid) as an antioxidant decreases the FR level. This is the most active antioxidant, ingested with food. Its effect is manifested primarily upon the cellular membrane. Vitamic C takes part in oxidization and reduction processes within the cell and maintains the entity and the strength of connective tissue and blood vessel walls. This vitamin decreases the risk of neoplasms and increases the resistance towards infections. It aids the immune system and combined with calcium renders thicker the blood vessels, acting antihaemorrhagically, antiallergically and antiinflammatorily.

Vitamin E (tocopherol) is a powerful antioxidant, that delays cellular aging, due to FR, aldehyde or ketone oxidative activities. Mixed tocopherols are still the best natural antioxidant preservative that we have at present (Aldrich, 2005).This vitamin inhibits the oxidation of unsaturated fatty acids (oleic, linolic, linolenic, arachidonic), participating in biological membranes. Vitamin E as an antioxidant catches oxygen and thus, preserves the lipids from oxidation (going rancid). Vitamin E preserves from the action of peroxidase upon the cellular membrane, i.e. saves the unsaturated links of fatty acids in the cellular wall. The antioxidative effect of vitamin E is the most apparent in muscles, skin and sexual glands, where it maintains the tone, the turgor and the functional activity. His combination with S- (sulfur)-containing amino acids (methionine, lysine, cystein) and Se, that potentiates the muscular activity and turgor contributes further in this connection.

Vitamin A (retinol) as an antioxidant inhibits the oxidation of unsaturated fatty acids. This vitamin strengthens the epithelial lining of skin and muscles. It stimulates and enhances immunity, has an antiinfectious activity and decreases the risk of neoplasms. Vitamin A delays the systemic aging processes and maintains the skin and muscle turgor and tone.

It could be emphasized that the biliary acids are necessary for the absorption of fat-soluble vitamins (A, E) in intestines. The

obstruction of bliary ducts (stones, neoplasms, parasites) and liver inflammations influences negatively this process.

Selenium has also an antioxidative effect against free radicals. It stimulates the immune system. The selenium deficiency (under 75 microgrammes/daily) aids the cancerogenesis. The selenium deficiency is encountered more frequently in aging organisms. The addition of selenium to the diet of the dog or cat help to overcome the oxidative stress resulting from free radicals. The selenium acts favourably against skin decoloration (white cutaneous spots, vitiligo). As an antioxidant, it interferes with the formation of peroxides from unsaturated fatty acids. The selenium enhances the effect of vitamin E.

Against FR the organisms possess several defence systems. The first line of this system includes easily oxidable compounds, which are present in the cytosil (ascorbinic acid, vit C) and in membranes (vit E, α-tocopherol). The second -line defence systems are constituted of repair systems for biomolecules that have been damaged by free radical attacks.

The normal physiological level of hormones (tyroxine, estrogens, androgens) impairs the excessive formation and accumulation of free radicals. The maintainance of the hormonal balance retards the process of aging. In some cases, the hormonal therapy leads to mammary tumours in bitches and pyometra in queens.

The good health condition in aged dogs and cats requires paying attention to free radicals and the administration of antioxidants. Thus, the aging would be retarded and the immunity – rendered stronger. The risk of tumour growth, diabetes, obesity, alopecia, hypercholesterolemia, atherosclerosis, would be reduced. Vitamin C is provided by the lemons and fresh salads in the diet or by drug formulations (pills, ampules) in daily doses of 100-300 mg per animal. Vitamin E is provided by fresh liver or fresh minced meat or by drugs (ampules, tablets) in a daily dose of 10 mg/animal. Vitamin A is included in the diet via carrots, red peppers, tomatoes, pumpkins, liver, cod-liver oil or capsules containing 100-200 IU per animal. Aged dogs and cats should be provided also with fresh air, walks for lung ventilation with good blood oxidation and strengthening of muscles and the heart. Thus, the natural reactivity (the olfaction and the habit to mix in dogs; bird chase or tree climbing in cats) would be maintained. As an antioxidant, selenium (selenic acid, sodium selenite) shoud be added to the diet in a dose of 1 mg per dog or cat once weekly.

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