

Preface



Lester Mandelker, DVM

Guest Editor

I am honored to have the opportunity to address an important aspect of medicine: oxidative stress. This issue addresses conditions of oxidative stress in relation to free radical damage, cellular inflammation, and disease, and it especially pertains to specific organs such as the heart, liver, kidney, brain, and even the eye. Most of us are familiar with the effects of oxygen and free radicals and the damage they can cause. This issue presents these effects and shows how they relate to each organ system. Each author presents his/her view of oxidative stress and discusses just how antioxidants can be beneficial.

Oxidative stress is a physiological condition that occurs when there is a significant imbalance between production of reactive oxygen species and antioxidant defenses. Since oxidative stress occurs in almost every disease, one may ask, is it part of the disease process or a disease in itself? Inflammation is also an important aspect of free radical damage and plays a very significant part in oxidative stress. Inflammatory mediators, such as reactive oxygen species and tumor necrosis factor-alpha, activate inflammation. This occurs through transcription factors like nuclear protein kappa B (NF- κ B) that transcribe genes in the nucleus of the cell to produce inflammatory cells. The transcription factor NF- κ B is a very important part of the inflammatory cascade, is very sensitive to changes in oxidative stress, and is termed redox sensitive (oxidants to antioxidant/ratio). There is an in-depth article on free radicals and the inflammatory process in this issue.

We know oxygenation and oxygen free radicals are needed to fight off invading organisms. We know oxygen free radicals (reactive oxygen species) are even produced daily during normal respiration by the mitochondrial

respiratory chain and during the production of energy by each and every mitochondrion. Therefore, one may consider oxidative stress a necessary outcome of physiological functions such as respiration, digestion, and metabolism.

Therefore, not all forms of oxidative stress are bad. Oxidative stress also has its benefits. Without some form of oxidative stress, living cells would not survive. Oxidative stress drives many of our most important signaling pathways that produce new tissues, heal wounds, promote growth, and allow our bodies to adapt to stress and disease. So oxidative stress is commonplace and occurs in almost every cell. Only when oxidative stress is excessive and inappropriate is it of more concern to our health. Excessive oxidative stress can damage proteins, cell membranes, DNA, lipids, and various tissues throughout our body. If oxidative stress causes tissue damage and mitochondrial dysfunction, shouldn't we then treat this as part of our medical therapy? Clinical medicine today does not adequately approach the concept of treating for excessive oxidative stress that occurs with diseases. This issue will address that concept.

Organ dysfunction begins at the cell level primarily with the mitochondria and this will be an important focus of this issue. The mitochondria are the most important organelle in the cell, not only because they produce the energy for life, but also because they determine whether cells live or die. In addition, they contain their own DNA (mtDNA), which allows them to be self-replicating. Mitochondria are also both the major producer of free radical species and a major target of oxidative damage. With this in mind, it follows that oxidative damage, which leads to disturbances of mitochondrial function, can lead to disruption of cell function. This disruption often is expressed as mitochondrial disease and can have far reaching effects to all aspects of health.

In this issue, there are very prominent, well-respected veterinarians and physicians more knowledgeable than myself that believe oxidative stress is an important part of the disease process. I am very grateful for their input and expertise in explaining how each organ system (ie, heart, kidney, eye, liver, and brain) is involved in oxidative stress. Each author presents the science and available research and interprets the means through evidence based medicine of the application of antioxidants and pharmaceuticals to treat oxidative stress. This is mainstream medicine. There are also numerous pharmaceuticals that treat oxidative stress. For example, beta-blockers work to reduce cardiac contractions and slow heart rates. This specific action reduces the production of energy by the mitochondria in the heart, and in doing so, reduces the production of free radicals, which in turn reduces oxidative stress. High blood pressure therapies also reduce oxidative stress to tissues by lowering blood pressure. There are numerous other indications where pharmaceuticals and nutraceuticals reduce oxidative stress, and we, as practitioners, deserve to utilize more of these specific therapies when

appropriate for the benefit of our patients. This issue will offer advice to you (as clinical practitioners) on understanding oxidative stress mechanisms and the therapies that are available to us for such use. Enjoy!

Lester Mandelker, DVM
Community Veterinary Hospital
1631 W. Bay Drive
Largo, FL 33770, USA

E-mail address: lestervet2@aol.com