DOWNLOAD PDF OXIDATIVE STRESS RADICALS

Chapter 1 : Alcohol, Oxidative Stress, and Free Radical Damage

Oxidative stress is an imbalance between free radicals and antioxidants in your body. Free radicals are oxygen-containing molecules with an uneven number of electrons.

The resulting damage caused by singlet oxygen reduces the photosynthetic efficiency of chloroplasts. In plants exposed to excess light, the increased production of singlet oxygen can result in cell death. In addition to direct toxicity, singlet oxygen acts a signaling molecule. Levels of jasmonate play a key role in the decision between cell acclimation or cell death in response to elevated levels of this reactive oxygen species. These include not only roles in apoptosis programmed cell death but also positive effects such as the induction of host defence [12] [13] genes and mobilization of ion transport systems. In particular, platelets involved in wound repair and blood homeostasis release ROS to recruit additional platelets to sites of injury. These also provide a link to the adaptive immune system via the recruitment of leukocytes. They may also be involved in hearing impairment via cochlear damage induced by elevated sound levels , in ototoxicity of drugs such as cisplatin , and in congenital deafness in both animals and humans. Specific examples include stroke and heart attack. This prevents the spread of the pathogen to other parts of the plant, essentially forming a net around the pathogen to restrict movement and reproduction. In the mammalian host, ROS is induced as an antimicrobial defense. To highlight the importance of this defense, individuals with chronic granulomatous disease who have deficiencies in generating ROS, are highly susceptible to infection by a broad range of microbes including Salmonella enterica, Staphylococcus aureus, Serratia marcescens, and Aspergillus spp. The exact manner in which ROS defends the host from invading microbe is not fully understood. One of the more likely modes of defense is damage to microbial DNA. More recently, a role for ROS in antiviral defense mechanisms has been demonstrated via Rig-like helicase-1 and mitochondrial antiviral signaling protein. This induction of ROS led to the induction of type III interferon and the induction of an antiviral state, limiting viral replication. In addition to energy, reactive oxygen species ROS with the potential to cause cellular damage are produced. ROS are produced as a normal product of cellular metabolism. In particular, one major contributor to oxidative damage is hydrogen peroxide H2O2 , which is converted from superoxide that leaks from the mitochondria. Catalase and superoxide dismutase ameliorate the damaging effects of hydrogen peroxide and superoxide, respectively, by converting these compounds into oxygen and hydrogen peroxide which is later converted to water , resulting in the production of benign molecules. While ROS are produced as a product of normal cellular functioning, excessive amounts can cause deleterious effects. In particular, the accumulation of oxidative damage may lead to cognitive dysfunction, as demonstrated in a study in which old rats were given mitochondrial metabolites and then given cognitive tests. Results showed that the rats performed better after receiving the metabolites, suggesting that the metabolites reduced oxidative damage and improved mitochondrial function. Additional experimental results suggest that oxidative damage is responsible for age-related decline in brain functioning. Older gerbils were found to have higher levels of oxidized protein in comparison to younger gerbils. Treatment of old and young mice with a spin trapping compound caused a decrease in the level of oxidized proteins in older gerbils but did not have an effect on younger gerbils. In addition, older gerbils performed cognitive tasks better during treatment but ceased functional capacity when treatment was discontinued, causing oxidized protein levels to increase. This led researchers to conclude that oxidation of cellular proteins is potentially important for brain function. While studies in invertebrate models indicate that animals genetically engineered to lack specific antioxidant enzymes such as SOD , in general, show a shortened lifespan as one would expect from the theory , the converse manipulation, increasing the levels of antioxidant enzymes, has yielded inconsistent effects on lifespan though some studies in Drosophila do show that lifespan can be increased by the overexpression of MnSOD or glutathione biosynthesizing enzymes. Also contrary to this theory, deletion of mitochondrial SOD2 can extend lifespan in Caenorhabditis elegans. Deleting antioxidant enzymes, in general, yields shorter lifespan, though overexpression studies have not with some recent exceptions consistently extended lifespan. Numerous studies have shown that 8-OHdG increases in different mammalian organs with age [26] see DNA damage theory of aging. Male infertility[edit

] Exposure of spermatozoa to oxidative stress is a major causative agent of male infertility. But under oxidative stress conditions, excessive ROS can damage cellular proteins, lipids and DNA, leading to fatal lesions in cell that contribute to carcinogenesis. Cancer cells exhibit greater ROS stress than normal cells do, partly due to oncogenic stimulation, increased metabolic activity and mitochondrial malfunction. ROS is a double-edged sword. On one hand, at low levels, ROS facilitates cancer cell survival since cell-cycle progression driven by growth factors and receptor tyrosine kinases RTK require ROS for activation [31] and chronic inflammation, a major mediator of cancer, is regulated by ROS. On the other hand, a high level of ROS can suppress tumor growth through the sustained activation of cell-cycle inhibitor [32] [33] and induction of cell death as well as senescence by damaging macromolecules. In fact, most of the chemotherapeutic and radiotherapeutic agents kill cancer cells by augmenting ROS stress. Modest levels of ROS are required for cancer cells to survive, whereas excessive levels kill them. As a result, production of NADPH is greatly enhanced, which functions as a cofactor to provide reducing power in many enzymatic reactions for macromolecular biosynthesis and at the same time rescuing the cells from excessive ROS produced during rapid proliferation. The resulting genomic instability directly contributes to carcinogenesis. Both exogenous and endogenous ROS have been shown to enhance proliferation of cancer cells. The role of ROS in promoting tumor proliferation is further supported by the observation that agents with potential to inhibit ROS generation can also inhibit cancer cell proliferation. Excessive ROS can induce apoptosis through both the extrinsic and intrinsic pathways. DNA damage, oxidative stress, and loss of mitochondrial membrane potential lead to the release of the pro-apoptotic proteins mentioned above stimulating apoptosis. Autophagy can be induced by ROS levels through many different pathways in the cell in an attempt to dispose of harmful organelles and prevent damage, such as carcinogens, without inducing apoptosis. When this type of cell death occurs, an increase or loss of control of autophagy regulating genes is commonly co-observed. Autophagy and apoptosis are two different cell death mechanisms brought on by high levels of ROS in the cells, however; autophagy and apoptosis rarely act through strictly independent pathways. There is a clear connection between ROS and autophagy and a correlation seen between excessive amounts of ROS leading to apoptosis. When mitochondria are damaged and begin to release ROS, autophagy is initiated to dispose of the damaging organelle. If a drug targets mitochondria and creates ROS, autophagy may dispose of so many mitochondria and other damaged organelles that the cell is no longer viable. The extensive amount of ROS and mitochondrial damage may also signal for apoptosis. This crosstalk and connection between autophagy and apoptosis could be a mechanism targeted by cancer therapies or used in combination therapies for highly resistant cancers. Cancer cells with elevated ROS levels depend heavily on the antioxidant defense system. The result is an overall increase in endogenous ROS, which when above a cellular tolerability threshold, may induce cell death. Radiotherapy also relies on ROS toxicity to eradicate tumor cells. However, modulation of ROS signaling alone seems not to be an ideal approach due to adaptation of cancer cells to ROS stress, redundant pathways for supporting cancer growth and toxicity from ROS-generating anticancer drugs. Combinations of ROS-generating drugs with pharmaceuticals that can break the redox adaptation could be a better strategy for enhancing cancer cell cytotoxicity.

Chapter 2 : 3 Ways to Treat Oxidative Stress | Our Everyday Life

Oxidative stress reflects an imbalance between the systemic manifestation of reactive oxygen species and a biological system's ability to readily detoxify the reactive intermediates or to repair the resulting damage.

Most articles written about them are highly technical, very scientific and often boring and confusing. One purpose of inflammation is to protect the site of an injury. Most people are familiar with the kind of painful inflammation that occurs due to accidents and athletic injuries. Some of the above conditions are very serious and if not halted, cause death. While in the short term this is not a problem, in the long term it causes progressive damage. Chronic systemic inflammation is not confined to a particular tissue, but involves the lining of blood vessels and many internal organs and systems. This inflammatory process is often associated with free radical damage and oxidative stress and may not cause pain, as some internal organs do not relay pain. Because there is no pain, you may not be aware of the serious damage systemic inflammation is causing, often leading to chronic, debilitating and even life-threatening diseases, some of which are listed above. Your body constantly interacts with oxygen as you breathe and your cells produce energy. Free radicals are unstable, highly reactive molecules that lose an electron as a result of this activity. In other words â€” in simple unscientific terms, free radicals are molecules that are missing an electron. Molecules are made up of atoms, and atoms are made up of protons, neutrons and electrons. If your body is unable to stop the spiraling free radical chain reaction a molecule stealing an electron from another molecule, causing that molecule to steal an electron from another molecule, causing this molecule to steal an electron, etc. Oxidative stress damages cellular proteins, membranes and genes and leads to systemic inflammation. Antioxidants are vitamins and other substances that supply missing electrons for unstable molecules in order to prevent free radical damage from external and internal sources. Antioxidants include vitamins A, C and E, grapeseed extract, pycogenol, alpha-lipoic acid and others. It is a vital component of every cell in your body and is manufactured by your body, in the cells of your body. In so doing, it recycles the antioxidants, thus keeping them in an active state longer. In the last 30 years, however, due to the ever-increasing environmental toxins and mental and emotional stresses, the amount of free radicals we are being bombarded with is increasing at an alarming rate. As you probably know, nutritionists, holistic doctors and even some medical doctors recommend that we eat antioxidant rich foods and take antioxidant supplements. Most health-conscious people do this, but the numbers of devastating, life- threatening diseases have not diminished. To learn about the one of a kind, proven natural supplement that raises glutathione levels in your body, and how to order it at a discount, call me:

Chapter 3 : Explained: Oxidative Stress, Free Radicals, Reactive Oxygen Species - Healthy Eating Harbor

Oxidative stress is the total burden placed on organisms by the constant production of free radicals in the normal course of metabolism plus whatever other pressures the environment brings to bear (natural and artificial radiation, toxins in air, food and water; and miscellaneous sources of oxidizing activity, such as tobacco smoke).

Formed by radical reactions with cellular components such as lipids and nucleobases. Lipid forms participate in lipid peroxidation reactions. Produced in the presence of oxygen by radical addition to double bonds or hydrogen abstraction. Formed from H 2O 2 by myeloperoxidase. Lipid-soluble and highly reactive. Will readily oxidize protein constituents, including thiol groups , amino groups and methionine. Lipid-soluble and similar in reactivity to hypochlorous acid. Protonation forms peroxynitrous acid, which can undergo homolytic cleavage to form hydroxyl radical and nitrogen dioxide. Hydrogen peroxide is produced by a wide variety of enzymes including several oxidases. Reactive oxygen species play important roles in cell signalling, a process termed redox signaling. Thus, to maintain proper cellular homeostasis , a balance must be struck between reactive oxygen production and consumption. The best studied cellular antioxidants are the enzymes superoxide dismutase SOD , catalase , and glutathione peroxidase. Less well studied but probably just as important enzymatic antioxidants are the peroxiredoxins and the recently discovered sulfiredoxin. Other enzymes that have antioxidant properties though this is not their primary role include paraoxonase, glutathione-S transferases, and aldehyde dehydrogenases. The amino acid methionine is prone to oxidation, but oxidized methionine can be reversible. Oxidative stress also plays a role in the ischemic cascade due to oxygen reperfusion injury following hypoxia. This cascade includes both strokes and heart attacks. Oxidative stress has also been implicated in chronic fatigue syndrome. Oxidative stress is likely to be involved in age-related development of cancer. The reactive species produced in oxidative stress can cause direct damage to the DNA and are therefore mutagenic , and it may also suppress apoptosis and promote proliferation, invasiveness and metastasis. The American Heart Association therefore recommends the consumption of food rich in antioxidant vitamins and other nutrients, but does not recommend the use of vitamin E supplements to prevent cardiovascular disease. This action catalyzes production of reactive radicals and reactive oxygen species. These metals are thought to induce Fenton reactions and the Haber-Weiss reaction, in which hydroxyl radical is generated from hydrogen peroxide. The hydroxyl radical then can modify amino acids. For example, meta- tyrosine and ortho- tyrosine form by hydroxylation of phenylalanine. Other reactions include lipid peroxidation and oxidation of nucleobases. Metal catalyzed oxidations also lead to irreversible modification of R Arg , K Lys , P Pro and T Thr Excessive oxidative-damage leads to protein degradation or aggregation. One of the most important classes of these are the quinones. Quinones can redox cycle with their conjugate semiquinones and hydroquinones , in some cases catalyzing the production of superoxide from dioxygen or hydrogen peroxide from superoxide. Immune defense[edit] The immune system uses the lethal effects of oxidants by making production of oxidizing species a central part of its mechanism of killing pathogens; with activated phagocytes producing both ROS and reactive nitrogen species. Male infertility[edit] Sperm DNA fragmentation appears to be an important factor in the aetiology of male infertility , since men with high DNA fragmentation levels have significantly lower odds of conceiving. However, it was recently shown that the fluoroquinolone antibiotic enoxacin can diminish aging signals and promote lifespan extension in nematodes C. The rise of oxygen levels due to cyanobacterial photosynthesis in ancient microenvironments was probably highly toxic to the surrounding biota. Under these conditions, the selective pressure of oxidative stress is thought to have driven the evolutionary transformation of an archaeal lineage into the first eukaryotes. Selective pressure for efficient repair of oxidative DNA damages may have promoted the evolution of eukaryotic sex involving such features as cell- cell fusions , cytoskeleton -mediated chromosome movements and emergence of the nuclear membrane.

Chapter 4 : 5 Signs of Oxidative Stress and 7 Ways You Can Stop It - Doctor Doni

Oxidative stress is essentially an imbalance between the production of free radicals and the ability of the body to counteract or detoxify their harmful effects through neutralization by antioxidants.

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They also contain a very high concentration of antioxidants called polyphenols that have been shown to have cancer-fighting properties. Herbs and spicesâ€" These include things like cinnamon, oregano, ginger, turmeric and rosemary. Additionally, essential oils made from the same plants can also be a great source of antioxidant, anti-inflammatory compounds. While eating more antioxidant foods is a big step in the right direction, you also benefit from limiting intake of pesticide- and herbicide-laden foods those that are not organically grown and by avoiding too much sugar, refined oil or refined grains. And be sure to limit intake of antibiotic- and hormone-laden foods, such as farm-raised meat or fish. Avoid Toxin or Pollutant Exposure Besides improving your diet, here are other ways to start reducing free radical damage: Keep in mind that while being sedentary is definitely not helping you to age any slower, either is overworking yourself. Exhaustion, mental fatigue and burnout also cause the immune system and body more damage. According to some experts, there are literally thousands of different antioxidants in the human diet, and they exist in many different forms. Because of the complexities of how antioxidants work in the body to combat free radicals, some scientists believe that only in food form do phytonutrients or antioxidants interact beneficially with our bodies. Surveys shows that about 30 percent of Americans are taking some form of antioxidant supplement. Hensrud points out that most foods with high ORAC scores like cocoa, green tea or acai berries, for example offer great benefits beyond just supplying antioxidants, such as containing fiber, protein, vitamins and minerals. Variety and interaction of many different antioxidants as they exist in food seem to be most beneficial for longevity and optimal health. Final Thought on Free Radicals Our bodies produce free radicals as byproducts of ordinary cellular reactions like breathing or other vital functions, in addition to exposure to pollutants, a poor diet, radiation, high amounts of stress and other toxins. Antioxidants help slow down the effects of free radicals and protect us from disease or signs of early aging. Antioxidant sources include plant foods like fruits or veggies, green or white teas, cocoa, red wine, spices, and herbs. The best way to reduce free radical damage is through a healthy diet and lifestyle, rather than taking supplements. Antioxidant supplements can sometimes cause unwanted effects and are not as beneficial as eating whole plant foods. Top 10 High Antioxidant Foods From the sound of it, you might think leaky gut only affects the digestive system, but in reality it can affect more. Click here to learn more about the webinar.

Chapter 5 : Inflammation, Free Radical Damage, Oxidative Stress, Hydrogen and Cancer

Free Radicals and Oxidative Stress - Getting Into the Details Free radicals also have beneficial effects on the organisms. 1 That is perhaps one reason why balance of oxidation is so important. Nitric oxide (NO) is a free radical and is an important signaling molecule that has a role in regulating vascular tone and hemodynamics. 2.

Can you guess why this is so? Extensive research during last two decades has revealed the mechanism by which continued oxidative stress leads to chronic inflammation, which in turn mediates most chronic diseases including cancer. Oxidative stress, caused by rivers of free radicals, is a plague on modern man. Imagine a patient, newly in remission from cancer, being exposed every three months to CAT or PET scans, which dramatically increase oxidative stress, just begging for the cancer to come back or a new cancer to emerge so they can treat the patient again. Oxidative stress, directly or indirectly caused by chemotherapeutics is one of the underlying mechanisms of the toxicity of anticancer drugs in noncancerous tissues, including the heart and brain. Reactive metabolites formed during this process cause oxidative stress and can impair the function of drug metabolizing enzymes leading to toxicity. According to its recent report, one in four deaths among children aged under five are now due to environmental hazards such as air pollution and contaminated water. It is simple; poisons in our air and water create oxidative stress, which leads to disease, cancer and death. Epidemiological studies have shown a clear association between cardiovascular morbidity, decreased lung function, increased hospital admissions, mortality, and airborne concentrations of photochemical and particulate pollutants. Cellular exposure to ionizing radiation leads to oxidizing events that alter the molecular structures of macromolecules through direct interactions of radiation that target the macromolecules, or via products of water radiolysis. Further, the oxidative damage may spread from the targeted to neighboring, non-targeted bystander cells through redox-modulated intercellular communication mechanisms. People who started using cell phones at an earlier age have a greater chance of developing a brain tumor when compared to people who started late during their adult years. Learn to diagnose yourself so you can treat yourself and your loved ones! Learn More When certain chemicals in the body have their electron configuration changed, they become very reactive and are called "free radicals" or "oxidants". These chemicals roam freely through the rest of the body stealing electrons from other cells. Free radicals damage cellular DNA. The majority of modern science has come to the conclusion that free radical damage in the human body is an important cause of aging. This oxidation is due to the lack of antioxidants that are available to stop free radical damage. Reactive oxygen species ROS are a byproduct of normal metabolism. Even under pristine conditions when our cells use glucose to make energy we create a cascade of free radicals that cause oxidative stress. The more sugar we consume to greater our oxidative stress. When our immune system is fighting off bacteria and creating inflammation we suffer from increased oxidative stress. When our bodies detoxify pesticides, herbicides, fungicides and cigarette smoke we create oxidative stress. Pancreatic cancer cells use the sugar fructose to help tumors grow more quickly. Tumor cells fed both glucose and fructose used the two sugars in two different ways, a team at the University of California Los Angeles found. Their findings, published in the journal Cancer Research, helps explain other studies that have linked fructose intake with pancreatic cancer, one of the deadliest cancer types. Researchers concluded that anyone wishing to curb their cancer risk should start by reducing the amount of sugar they eat. However, as long as we have enough anti-oxidants, a careful balance is maintained and damage is prevented. Oxidative stress happens when the amount of free radicals exceeds the amount of antioxidants. Hydrogen as Key Antioxidant against Oxidative Stress and Cancer Oxidative stress is closely related to all aspects of cancer, from carcinogenesis to the tumor-bearing state, from treatment to prevention. The human body is constantly under oxidative stress arising from many sources. Active oxygen species are involved in carcinogenesis through two mechanisms: Molecular hydrogen is a new medical gas that can be dissolved in water and administered through drinking, inhalation, baths, intravenous drip IV , and has been shown to suppress VEGF Vascular Endothelial Growth Factor , a key mediator of tumor angiogenesis the development of new blood vessels , by the reduction of excessive ROS oxidative stress and through the down regulation of ERK key growth factor needed for cellular division. It is interesting to

note, however, that only three papers addressed effects on cancers. First, molecular hydrogen caused growth inhibition of human tongue carcinoma cells HSC-4 and human fibrosarcoma cells HT but did not compromise growth of normal human tongue epithelial-like cells DOK. Second, hydrogen suppressed the expression of vascular endothelial growth factor VEGF , a key mediator of tumor angiogenesis, in human lung adenocarcinoma cells A, which was mediated by downregulation of extracellular signal-regulated kinase ERK. Elimination of radical oxygen species by hydrogen should reduce a probability of introducing somatic mutations. It has been shown that cancerous cells have a higher expression of MMP genes leading to tumor invasion and tumor angiogenesis. H2 has been shown to reduce tumor invasion and tumor growth and because of this effect, H2 has been shown to have anti-tumor effects. Hydrogen has potential for improving the quality of life of patients during chemotherapy by efficiently mitigating the side effects of cisplatin. For example, it was demonstrated that molecular hydrogen may protect and retard the development of thymic lymphoma in mice. On the base of my skull is a 2cm tumor. Understanding the severity of the situation I took a long shot and recommended not only hydrogen water but also a hydrogen inhaler. Eat like crazy, gained 10 pounds, and feel better every day. Have not thrown up. Feel stronger ever day! Just hope to keep going! My readers will have to excuse my reporting on this case as it is happening but it is too exciting and too important. We Know Cancer Can Be Cured Two years ago, before I even had heard about the miracles of molecular hydrogen I got a letter from another patient also on the verge of death. Sircus when I was completely healed and tell him my story. My PSA is now 2. If his protocol plus my work and the grace of God could get me off my death bed, and dancing all night with my family well maybe people should consider this wonderful protocol and try it. Both of these patients showed extraordinary will successfully and willfully doing the most difficult part of the Natural Allopathic protocol , which is breathing retraining. Another famous case written up in my bestselling book Sodium Bicarbonate was Vernon Johnston , who breathed his way back to life by using sodium bicarbonate perfectly while breathing consciously four hours a day. Hydrogen is new in medical science and even newer in relationship to the treatment of cancer. Hydrogen is safe, easily administered, a potent antioxidant-effect, and gets everywhere it is needed because of its small size. I do not know of anyone reporting anything close to a case like this. There is nothing to lose administering high dosages of hydrogen and everything to gain for cancer patients. Some common substances with antioxidant properties are vitamin C, vitamin E, beta-carotene, selenium, manganese, glutathione, lipoic acid, flavonoids, phenols, polyphenols, phytoestrogen, and many more. According to Tyler W. We actually require some free radicals, and because H2 is a stable molecule, it unlike conventional antioxidants, H2 will not react with these. However, it is clear from animal and human studies that H2 can decrease oxidative stress via its cell-modulating effects. Antioxidants are nutrients vitamins and minerals as well as enzymes proteins in your body that assist in chemical reactions. Hydrogen just happens to be the smallest and as it does its work it promotes full hydration. It also just happens to be the icing on the cake in terms of my protocol. Please note that I never promote a single agent for the treatment of cancer or any other disease. Hydrogen should always be used in the context of a rational protocol. Ionizing radiation-induced metabolic oxidative stress and prolonged cell injury [2] International Journal of Cell Biology. Oxidative Stress in Nontargeted Tissues. PubMed [4] Integr Cancer Ther. Molecular hydrogen protects chondrocytes from oxidative stress and indirectly alters gene expressions through reducing peroxynitrite derived from nitric oxide [8] Oxid Med Cell Longev. Suppressive effects of electrochemically reduced water on matrix metalloproteinase-2 activities and in vitro invasion of human fibrosarcoma HT cells [12] PeerJ. Hydrogenâ€”water enhances 5-fluorouracil-induced inhibition of colon cancer [13] Cancer Chemotherapy and Pharmacology. Molecular hydrogen alleviates nephrotoxicity induced by an anti-cancer drug cisplatin without compromising anti-tumor activity in mice.

Chapter 6 : Reactive oxygen species - Wikipedia

Oxidative stress happens when the amount of free radicals exceeds the amount of antioxidants. That's when oxidation damages our cells, proteins and our DNA (genes). How Do You Know If You Have Oxidative Stress?

Electrons are like serial monogamists: They always like to have partners, so they generally stick together in pairs. When an electron loses its partner, it frantically searches for a new one like any good serial monogamist after a breakup. And in its search for a new mate, it sets off a chain reaction by stealing an electron from the nearest stable atom or molecule a group of two or more atoms. Good news for bachelor number one, but bad news for bachelor number two, which now starts its own frantic search for a new electron. These atoms and molecules that are missing an electron are called free radicals. And as they maraud through the body causing breakup after breakup, they can do some serious damage. How Are Free Radicals Formed? This loss of electrons is actually a completely normal biological process. It can happen during metabolism or as part of an appropriate immune response. And under normal circumstances, the body can actually neutralize the effects of these free radicals with antioxidants. Antioxidants basically show up like a chaperone at a dance and tell all those desperate bachelors to pack it up and go home. Really, they offer up one of their own electrons, putting electron-stealing chain reactions to an end. And that can happen for all sorts of reasonsâ€”such as smoking, exposure to environmental toxins, intense exercise, and even aging. This imbalance is called oxidative stress. Oxidative stress can damage every component of cellsâ€”proteins, enzymes, and even DNA. This damage can be measured through various tests. Nitric oxide NO is a free radical and is an important signaling molecule that has a role in regulating vascular tone and hemodynamics. Oxygen-related free radicals superoxide and hydroxyl radicals and reactive species hydrogen peroxide, nitric oxide, peroxynitrile, and hypochlorous acid , are produced in the body, primarily as a result of aerobic metabolism. Reactive oxidative species are particularly active in the brain and neuronal tissue as the excitatory amino acids and neurotransmitters, whose metabolism produces large amounts of reactive oxidative species, which are unique to the brain and serve as sources of oxidative stress. For the past 40 years or so, oxidative stress has been increasingly recognized in research topics in health and medicine. Superoxides are powerful free radicals. The cytoplasm is where all important cellular metabolic processes happen. In normal circumstances, it is thus reliably protected from oxidative damage. Rather than remaining in the cytoplasm, oxidized glutathione gets locked up in the vacuole. A transcription factor called nuclear factor erythroid-derived 2 -like 2, or Nrf2 is of interest in this new understanding. Nrf2 modulate the expression of hundreds of genes, including not only the familiar enzymes, but large numbers of genes that could affect seemingly disparate processes. The chemical concepts are rather straight forward but when you apply that concept to a complex system of human biology, some of the simplicity falls away. As science progresses, we learn about redundancies in the systems, so that if one particular pathway or route cannot take on the workload, additional systems are in place to support basic health unless that burden is too excessive or lasts too long. While the nitty gritty of oxidative stress may be overwhelming, what to do about it is rather simple. Minimize your exposure to toxins, skip the processed foods, reduce stress, and eat lots of brightly colored vegetables or fruits. She believes in the science, art, and mystery of healing and has a heartfelt passion for the individual wellness of all people. Built on this foundational belief, she uses the magnificence of multiple media platforms to truly make a difference and empower people to heal. He is a certified nutrition specialist, licensed nutritionist, and chiropractic physician board-certified in clinical nutrition. He has earned degrees in nursing and phytotherapeutics, and has a private integrative medicine practice in Hudson, Wisconsin. He is on the board of directors for the International Probiotics Association andan advisor to Functional Medicine University. The evolution of free radicals and oxidative stress. Zheng M, Storz G. Redox sensing by prokaryotic transcription factors. Free radicals, antioxidants, and human â€¦: Role of oxidative DNA damage in â€¦ initiation and promotion. Oxidative stress induced-neurodegenerative â€¦: Multiple glutathione disulfide removal pathways mediate cytosolic redox homeostasis. Nature Chemical Biology, ; doi: Giudice A, Montella M. Activation of the Nrf2-ARE signaling pathway: Subscribe to receive the latest blog updates via email.

Chapter 7 : Oxidative stress - Wikipedia

the excessive generation of molecules and oxidative stress in alcohol toxicity. of Pharmacology and Biological Chemistry, called free radicals, which can result in This article summarizes some of these Mount Sinai School of Medicine, New.

Luckily for you, this article discusses all three of them. It also dives into their relationship and explains how it affects you through your food choices. Moreover, their implications in chronic inflammation will become clearer to you. Reactive oxygen species ROS Reactive oxygen species are highly reactive molecules which contain oxygen. Two examples of ROS are oxygen ions and peroxides, compounds containing an oxygen-oxygen single bond. ROS are created when we breathe; we spend oxygen from the environment and our cells start to produce energy. During this process a group of ROS, called free radicals, become synthesized. ROS are usually a part of the natural defenses of our immune system. They are also produced during our everyday metabolic functioning. One must know, ROS have important roles in our homeostasis and normal cell signaling. However, there are also non-radicals. Ozone is considered a ROS as well! Free radicals, the bad guy? Free radicals are atoms, ions, or molecules that have at least one unpaired electron in their structure, with certain ions and complexes being an exception. They usually target different victims, among which we can find: Lipids They cause lipid peroxidation, a degradation of lipids where their structure and function are affected. Free radicals basically steal an electron from the lipid cell membrane which, as you might imagine, negatively affects it with them mentioned changes. Interestingly, polyunsaturated fatty acids are the group of fats most prone to this process, as a consequence of their chemical bonds. They also like to target the peptide chain, a chain linking multiple amino acids â€" the building blocks of protein. A similar thing happens in proteins as does with lipids â€" the structure and function of proteins is affected in a negative way. The involved changes can cause mutations, they are also cancerous and teratogenous. Neither of these changes is pleasant. When they are produced, oxidative stress occurs through the mentioned targets. An increase in oxidation of these molecules is associated with an important number of diseases, including inflammation. Under normal conditions, our body is well adapted to scavenge remaining ROS, thus maintaining their numbers at an ideal and manageable level. They can suppress the growth of tumors. Moreover, chemotherapy often kills cancer cells by increasing ROS stress. But generally, higher levels of oxidative stress are considered undesirable for healthy cells. This is where the antioxidant capabilities of our body come in. This protein-controlled response is vital to maintain a enough balance of ROS in our bodies. Namely, oxidative damage is the result of a higher oxidative stress baseline. By now you might be wondering what causes oxidative stress. However, another important source is cigarette smoke. And not only active smoking, passive smoking causes significant increases in oxidation of the mentioned molecules as well. Physical stress working out causes an increase in ROS too. Are you advocating not to be physically active? There is a slight and short-term increase in free radicals. It is believed this increase is a triggering mechanism or signal which allows our body to up regulate its natural antioxidant production. To put it in simple terms, you have an increase in free radicals which send a message to your body to increase the production of antioxidants. These counter the increase again and homeostasis reigns once more. There is one more thing that needs mentioning in this mix â€" antioxidants. Antioxidants As their name suggests antioxidants, are molecules which inhibit oxidation of other molecules. They are comprised of endogenous, produced by our body, and exogenous, we get them through our diet, antioxidants. In the past it was believed food containing antioxidants are the Holy Grail against cancer. However, large clinical trials with limited numbers of antioxidants, by that I mean few antioxidants out of all available ones, suggested that supplementing with a few antioxidants in large numbers may actually be harmful. They have a synergistic effect You need to eat a variety of antioxidants for them to work correctly. Increasing amounts of antioxidants through supplementation of isolated antioxidants can be harmful for your body Clinical trials which have used synthetic antioxidants for longer periods of time noted potential disturbances in the redox network of the bodies of participants. I suggest reading it completely, as this is an important topic. Before you go away If you

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Chapter 8 : Inflammation, Free Radicals, Oxidative Stress and Antioxidants

Oxidative stress occurs when there is an imbalance of free radicals and antioxidants (too many free radicals and too few antioxidants), according to the Pharmacognosy Review. Antioxidants can be.

For example, alcohol breakdown in the liver results in the formation of molecules whose further metabolism in the cell leads to ROS production. Alcohol also stimulates the activity of enzymes called cytochrome Ps, which contribute to ROS production. Further, alcohol can alter the levels of certain metals in the body, thereby facilitating ROS production. Finally, alcohol reduces the levels of agents that can eliminate ROS i. The resulting state of the cell, known as oxidative stress, can lead to cell injury. ROS production and oxidative stress in liver cells play a central role in the development of alcoholic liver disease. One factor that has been suggested as playing a central role in many pathways of alcoholâ€"induced damage, and which has been the focus of much research, is the excessive generation of molecules called free radicals, which can result in a state called oxidative stress. These terms and concepts will be defined and explained in more detail in the following sections. Particularly important are the actions of a class of oxygenâ€"containing free radicals known as reactive oxygen species ROS. ROS can damage or cause complete degradation i. Both acute and chronic alcohol exposure can increase production of ROS and enhance peroxidation of lipids, protein, and DNA, as has been demonstrated in a variety of systems, cells, and species, including humans. Researchers have learned much about alcohol metabolism and the various enzymes and pathways involved, as well as about the role of lipid peroxidation and oxidative stress in alcohol toxicity. This article summarizes some of these findings. A detailed description of free radicals, ROS, and oxidative stress is followed by a review of the alcoholâ€"related cellular systems involved in ROS production. Next, the article explains why ROS are toxic to cells and what systems have evolved to help cells protect themselves against ROS. Finally, the role of ROS and oxidative stress in alcoholâ€"induced cell injury is discussed, with suggestions about future directions for research in this field. Although this discussion focuses on the role of oxidative stress in alcoholic liver disease, alcoholâ€"induced oxidative stress also occurs in and damages other tissues e. A free radical is an atom, molecule, or compound that is highly unstable because of its atomic or molecular structure i. As a result, free radicals are very reactive as they attempt to pair up with other molecules, atoms, or even individual electrons to create a stable compound. The four primary types of chemical reactions that free radicals undergo are: Hydrogen abstraction, in which a radical interacts with another molecule that has a free hydrogen atom i. As a result, the radical binds to the hydrogen atom and becomes stable, whereas the hydrogen donor is converted to a free radical. Addition, in which the radical binds to another, originally stable molecule, converting the combined molecule into a radical. Termination, in which two radicals react with each other to form a stable compound. Disproportionation, in which two identical radicals react with each other, with one of the radicals donating an electron to the other so that two different molecules are formed, each of which is stable. Molecular oxygen O2 is essential for cell function because it plays a pivotal role in a series of biochemical reactions occurring in the respiratory chain, which is responsible for most of the production of adenosine triphosphate ATP , which provides the energy required for a multitude of cellular reactions and functions. For more information on the respiratory chain and ATP production, see the article by Cunningham and Van Horn in this issue. The electron is transferred to the first component of the respiratory chain, and the proton is released into the surrounding fluid. The reverse reactions [i. The reduced respiratory chain component, in turn, passes the electron on to other molecules in the respiratory chain until it is finally transferred to O2, which then interacts with protons in cells to generate water. This series of electron transfer reactions generates sufficient energy to produce several molecules of ATP for each electron that passes through the respiratory chain. Molecular oxygen can accept a total of four electrons, one at a time, and the corresponding number of protons to generate two molecules of water. Superoxide, peroxide, and the hydroxyl radical are considered the primary ROS and have sparked major research on the role of free radicals in biology and medicine. Thus, systems producing superoxide also will result in formation of H2O2. However, because they are unstable and rapidly react with additional electrons and protons, most of these ROS are converted to water before they can

damage cells. It has been estimated that only about 2 to 3 percent of the O2 consumed by the respiratory chain is converted to ROS Chance et al. Nevertheless, the toxic effects of oxygen in biological systemsâ€”such as the breakdown i. What Is Oxidative Stress? The resulting stateâ€”which is characterized by a disturbance in the balance between ROS production on one hand and ROS removal and repair of damaged complex molecules such as proteins or DNA on the otherâ€”is called oxidative stress Halliwell Oxidative stress is associated with numerous deleterious consequences for the cell e. Many processes and factors are involved in causing alcoholâ€”induced oxidative stress, including: Alcohol is metabolized in two steps. First, the enzyme alcohol dehydrogenase converts alcohol to acetaldehyde, a toxic and reactive molecule. Next, the enzyme aldehyde dehydrogenase converts the acetaldehyde to acetate. Each of these reactions leads to formation of one molecule of NADH, thereby providing more starting material and thus enhanced activity of the respiratory chain, including heightened O2 use and ROS formation. Production of acetaldehyde during alcohol metabolism, which through its interactions with proteins and lipids also can lead to radical formation and cell damage. For information on acetaldehyde and its detrimental effects, see the article in this issue by Tuma and Casey. Damage to the mitochondria resulting in decreased ATP production. Effects on cell structure e. Alcoholâ€”induced oxygen deficiency i. For more information on alcoholâ€”induced hypoxia in the liver and its consequences, see the article by Cunningham and Van Horn in this issue. Alcoholâ€”induced increase in the ability of the bacterial molecule endotoxin to enter the bloodstream and liver, where it can activate certain immune cells. For more information on the role of endotoxin in liver damage, see the article by Wheeler in this issue. Alcoholâ€”induced increases in the levels of free iron in the cell i. Conversion of the enzyme xanthine dehydrogenase into a form called xanthine oxidase, which can generate ROS. Many of these processes operate concurrently, and it is likely that several, indeed many, systems contribute to the ability of alcohol to induce a state of oxidative stress. The major source of ROS production in the cell is the mitochondrial respiratory chain, which, as described earlier, utilizes approximately 80 to 90 percent of the O2 a person consumes. Thus, even though only a small percentage of that oxygen is converted to ROS, the mitochondrial respiratory chain in all cells generates most of the ROS produced in the body. Another major source of ROS, especially in the liver, is a group of enzymes called the cytochrome P mixedâ€”function oxidases. Many different variants of these ironâ€”containing enzymes exist, some of which are responsible for removing or detoxifying a variety of compounds present in our environment and ingested e. Some cytochrome P enzymes also are important for metabolizing substances that naturally occur in the body, such as fatty acids, cholesterol, steroids, or bile acids. The biochemical reactions spurred i. The extent of ROS generation may vary considerably depending on the compound to be degraded and on the cytochrome P molecule involved. This enzyme is of particular interest when investigating alcoholâ€”induced oxidative stress because its activity increases after heavy alcohol exposure and because CYP2E1 itself also metabolizes alcohol Lieber ROS also are produced by a variety of oxidative enzymes present in cells, such as the previously mentioned xanthine oxidase. Under normal physiological conditions, xanthine oxidase acts as a dehydrogenaseâ€”that is, it removes hydrogen from xanthine or hypoxanthine and attaches it to NAD, thereby generating NADH. However, under certain conditions, such as the disruption of blood flow to a tissue, xanthine dehydrogenase is converted to a ROSâ€”producing oxidase form. Alcohol consumption also may promote the conversion of xanthine dehydrogenase to xanthine oxidase Sultatos , which can generate ROS, thereby enhancing oxidative stress. Other sources of ROS in the body are two types of immune cells called macrophages and neutrophils, which help defend the body against invading microorganisms. In this case, however, ROS production is beneficial and even essential to the organism because it plays a central role in destroying foreign pathogens Rosen et al. Macrophages and neutrophils contain a group of enzymes called the NADPH oxidase complex, which, when activated, generates superoxide radicals and hydrogen peroxide. Hydrogen peroxide then interacts with chloride ions present in the cells to produce hypochlorite the active ingredient in bleach , which in turn destroys the pathogen. Patients with this condition are highly sensitive to infections and usually die at an early age. Besides the ROS generation that occurs naturally in the body, humans are constantly exposed to environmental free radicals, including ROS, in the form of radiation, UV light, smog, tobacco smoke, and certain compounds referred to as redox cycling agents, which include some pesticides, but also certain

medications used for cancer treatment. The toxicity of these medications against tumor cells as well as normal body cells results from the fact that the compounds are modified by cellular enzymes to an unstable intermediate, which then reacts with molecular oxygen to produce the original product plus a superoxide radical. Thus, a vicious cycle of chemical reactions involving these compounds continually produces ROS. Role of Metals Most of the systems for the production of ROS described above produce superoxide radicals or hydrogen peroxide. Under normal physiological conditions, direct interaction between these two radicals is not likely to play a significant role in generating hydroxyl radicals. However, in the presence of certain metals, particularly free iron or copper ions, a sequence of two reaction steps can occur that results in hydroxyl radical generation. In the first step, hydrogen peroxide can produce the hydroxyl radical by removing an electron from the participating metal ion. This combination of two chemical reactions appears to account for most of the hydroxyl radical production in biological systems and explains, at least in part, why metals such as iron and copper produce oxidative stress and ROSâ€"induced injury in cells. Similarly, adding iron to alcoholâ€"containing diets has been shown to exacerbate liver injury in animal studies Tsukamoto et al. ROS are toxic to cells because they can react with most cellular macromolecules, including proteins, lipids, and DNA. Proteins perform numerous crucial functions in the cell, primarily in the form of enzymes that mediate most biochemical reactions required for cellular functions. Proteins are made up of approximately 20 different building blocks called amino acids, which differ in their sensitivity to interactions with ROS. For example, the amino acids cysteine, methionine, and histidine are especially sensitive to attack and oxidation by the hydroxyl radical. Finally, protein oxidation often will make the marked protein more susceptible to degradation by cellular systems responsible for eliminating damaged proteins from the cell. Lipids that contain phosphate groups i. Consequently, damage to the phospholipids will compromise the viability of the cells. The complete degradation i. These double bonds can easily be opened in chemical reactions and interact with other substances. Fatty acids containing only one such double bond are called monounsaturated; fatty acids with two or more double bonds are called polyunsaturated. A single hydroxyl radical can result in the peroxidation of many polyunsaturated fatty acid molecules because the reactions involved in this process are part of a cyclic chain reaction. In addition to damaging cells by destroying membranes, lipid peroxidation can result in the formation of reactive products that themselves can react with and damage proteins and DNA. For more information regarding the actions of such reactive products, see the article by Tuma and Casey in this issue. Thus it is essential for the viability of individual cells or even the entire organism that the DNA remain intact. The building blocks of DNA molecules are called nucleotides; they consist of a sugar component and an organic base. Each DNA molecule consists of two strands of nucleotides held together by weak chemical bonds. Changes in the nucleotides in one strand can result in mismatches with the nucleotides in the other strand, yielding subsequent mutations.

Chapter 9 : Fighting Free Radicals & Free Radical Damage - Dr. Axe

If free radicals overwhelm the body's ability to regulate them, a condition known as oxidative stress ensues. Free radicals thus adversely alter lipids, proteins, and DNA and trigger a number of human diseases.

Received Mar 26; Accepted May 5. This article has been cited by other articles in PMC. Abstract Free radicals and oxidants play a dual role as both toxic and beneficial compounds, since they can be either harmful or helpful to the body. They are produced either from normal cell metabolisms in situ or from external sources pollution, cigarette smoke, radiation, medication. When an overload of free radicals cannot gradually be destroyed, their accumulation in the body generates a phenomenon called oxidative stress. This process plays a major part in the development of chronic and degenerative illness such as cancer, autoimmune disorders, aging, cataract, rheumatoid arthritis, cardiovascular and neurodegenerative diseases. This mini-review deals with the taxonomy, the mechanisms of formation and catabolism of the free radicals, it examines their beneficial and deleterious effects on cellular activities, it highlights the potential role of the antioxidants in preventing and repairing damages caused by oxidative stress, and it discusses the antioxidant supplementation in health maintenance. When cells use oxygen to generate energy, free radicals are created as a consequence of ATP adenosine triphosphate production by the mitochondria. These by-products are generally reactive oxygen species ROS as well as reactive nitrogen species RNS that result from the cellular redox process. These species play a dual role as both toxic and beneficial compounds. The delicate balance between their two antagonistic effects is clearly an important aspect of life. At high concentrations, they generate oxidative stress, a deleterious process that can damage all cell structures 1 - Oxidative stress plays a major part in the development of chronic and degenerative ailments such as cancer, arthritis, aging, autoimmune disorders, cardiovascular and neurodegenerative diseases. The theory of oxygen-free radicals has been known about fifty years ago 4. However, only within the last two decades, has there been an explosive discovery of their roles in the development of diseases, and also of the health protective effects of antioxidants. This mini-review deals with the taxonomy, the mechanisms of formation and catabolism of the free radicals, it examines their beneficial and deleterious effects on cellular activities, it highlights the potential role of the antioxidants in preventing and repairing damages caused by oxidative stress, and it discusses the advantages and inconveniences of the antioxidant supplementation in health maintenance. Radicals are less stable than non-radical species, although their reactivity is generally stronger. A molecule with one or more unpaired electron in its outer shell is called a free radical 1 - 5. Free radicals are formed from molecules via the breakage of a chemical bond such that each fragment keeps one electron, by cleavage of a radical to give another radical and, also via redox reactions 1 , 2. Biological free radicals are thus highly unstable molecules that have electrons available to react with various organic substrates such as lipids, proteins, DNA. Enzymatic reactions generating free radicals include those involved in the respiratory chain, the phagocytosis, the prostaglandin synthesis and the cytochrome P system 1 - 9. H2O2 a non radical is produced by the action of several oxidase enzymes, including aminoacid oxidase and xanthine oxidase. The last one catalyses the oxidation of hypoxanthine to xanthine, and of xanthine to uric acid. This reaction is known as the Fenton reaction 3 - 8. Hypochlorous acid HOCl is produced by the neutrophil-derived enzyme, myeloperoxidase, which oxidizes chloride ions in the presence of H2O2. Free radicals can be produced from non-enzymatic reactions of oxygen with organic compounds as well as those initiated by ionizing radiations. The nonenzymatic process can also occur during oxidative phosphorylation i. Endogenous free radicals are generated from immune cell activation, inflammation, mental stress, excessive exercise, ischemia, infection, cancer, aging. After penetration into the body by different routes, these exogenous compounds are decomposed or metabolized into free radicals. The importance of ROS production by the immune system is clearly exemplified by patients with granulomatous disease. Other beneficial effects of ROS and RNS involve their physiological roles in the function of a number of cellular signaling systems 7 - 9. Their production by nonphagocytic NADPH oxidase isoforms plays a key role in the regulation of intracellular signaling cascades in various types of nonphagocytic cells including fibroblasts, endothelial cells, vascular smooth muscle cells,

cardiac myocytes, and thyroid tissue. For example, nitric oxide NO is an intercellular messenger for modulating blood flow, thrombosis, and neural activity 7. NO is also important for nonspecific host defense, and for killing intracellular pathogens and tumors. Another beneficial activity of free radicals is the induction of a mitogenic response 7 , 8. Oxidative stress can arise when cells cannot adequately destroy the excess of free radicals formed. For example, hydroxyl radical and peroxynitrite in excess can damage cell membranes and lipoproteins by a process called lipid peroxidation. This reaction leads to the formation of malondialdehyde MDA and conjugated diene compounds, which are cytotoxic and mutagenic. Lipid peroxidation occurs by a radical chain reaction, i. If not regulated properly, oxidative stress can induce a variety of chronic and degenerative diseases as well as the aging process and some acute pathologies trauma, stroke. Cancer and oxidative stress The development of cancer in humans is a complex process including cellular and molecular changes mediated by diverse endogenous and exogenous stimuli. It is well established that oxidative DNA damage is responsible for cancer development. Cancer initiation and promotion are associated with chromosomal defects and oncogene activation induced by free radicals. A common form of damage is the formation of hydroxyled bases of DNA, which are considered an important event in chemical carcinogenesis 3 , 9. This adduct formation interferes with normal cell growth by causing genetic mutations and altering normal gene transcription. Oxidative DNA damage also produces a multiplicity of modifications in the DNA structure including base and sugar lesions, strand breaks, DNA-protein cross-links and base-free sites. For example, tobacco smoking and chronic inflammation resulting from noninfectious diseases like asbestos are sources of oxidative DNA damage that can contribute to the development of lung cancer and other tumors 3 , 6. The highly significant correlation between consumption of fats and death rates from leukemia and breast, ovary, rectum cancers among elderly people may be a reflection of greater lipid peroxidation 5 , Cardiovascular disease and oxidative stress Cardiovascular disease CVD is of multifactorial etiology associated with a variety of risk factors for its development including hypercholesterolaemia, hypertension, smoking, diabetes, poor diet, stress and physical inactivity amongst others 2 , 15 , Recently, research data has raised a passionate debate as to whether oxidative stress is a primary or secondary cause of many cardiovascular diseases Further in vivo and ex vivo studies have provided precious evidence supporting the role of oxidative stress in a number of CVDs such as atherosclerosis, ischemia, hypertension, cardiomyopathy, cardiac hypertrophy and congestive heart failure 2 , 5 , 15 , Pulmonary disease and oxidative stress There is now substantial evidence that inflammatory lung diseases such as asthma and chronic obstructive pulmonary disease COPD are characterized by systemic and local chronic inflammation and oxidative stress 21 - Oxidants may play a role in enhancing inflammation through the activation of different kinases and redox transcription factors such as NF-kappa B and AP-1 23 , Rheumatoid arthritis and oxidative stress Rheumatoid arthritis is an autoimmune disease characterized by chronic inflammation of the joints and tissue around the joints with infiltration of macrophages and activated T cells 4 , 25 , Oxidative damage and inflammation in various rheumatic diseases were proved by increased levels of isoprostanes and prostaglandins in serum and synovial fluid compared to controls Nephropathy and oxidative stress Oxidative stress plays a role in a variety of renal diseases such as glomerulonephritis and tubulointerstitial nephritis, chronic renal failure, proteinuria, uremia 5 , The nephrotoxicity of certain drugs such as cyclosporine, tacrolimus FK , gentamycin, bleomycin, vinblastine, is mainly due to oxidative stress via lipid peroxidation 27 - Heavy metals Cd, Hg, Pb, As and transition metals Fe, Cu, Co, Cr -induced different forms of nephropathy and carcinogenicity are strong free radical inducers in the body 11 , Ocular disease and oxidative stress Oxidative stress is implicated in age-related macular degeneration and cataracts by altering various cell types in the eye either photochemically or nonphotochemically Under the action of free radicals, the crystalline proteins in the lens can cross-link and aggregate, leading to the formation of cataracts In the retina, long-term exposure to radiation can inhibit mitosis in the retinal pigment epithelium and choroids, damage the photoreceptor outer segments, and has been associated with lipid peroxidation Fetus and oxidative stress Oxidative stress is involved in many mechanisms in the development of fetal growth restriction and pre-eclampsia in prenatal medicine 34 - In pregnancies complicated by pre-eclampsia, increased expression of NADPH oxidase 1 and 5 isoforms which are the major enzymatic sources of superoxide in the placenta is seen

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