Happy Bodies

References

(1) A chemical compound foreign to a given biological system. Xenobiotics include drugs, drug metabolites and environmental pollutants that are not produced by the body. In the environment, xenobiotics include pesticides, herbicides, tobacco smoke, phthalates, toxic metals and many other pollutants. ***Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health,*** **Seventh Edition. © 2003 by Saunders, an imprint of Elsevier, Inc.**

(2) The body's elimination of xenobiotics such as drugs and toxins is an essential process designed to protect against potential toxicity. Food broken down in the stomach is absorbed by the small intestine and transported directly to the liver via the portal vein. This process allows the liver time to detoxify compounds before they are distributed through the circulatory system. In the liver, there are two main types of metabolism that deal with xenobiotics. The first, the Phase I detoxification pathway, results in small chemical changes that make a compound more hydrophilic, so it can be effectively eliminated by the kidneys. Cytochrome P450 enzymes ("CYP enzymes") are responsible for most Phase I reactions. In mammals, these enzymes are found primarily in liver cells (hepatocytes). CYP enzymes oxidize molecules, often making them more water-soluble for clearance. Mammalian CYP enzymes can oxidize both xenobiotics and endogenous compounds, and are important for detoxification of foreign substances, as well as for controlling the level of endogenous compounds, such as hormone synthesis and breakdown, cholesterol synthesis and vitamin D metabolism. **McDowall J. Cytochrome P450. *European Bioinformatics Institute*.**

(3) Any molecular species capable of independent existence that contains an unpaired electron in an atomic orbital. Many radicals are unstable and highly reactive. They can either donate an electron to or accept an electron from other molecules, therefore behaving as oxidants or reductants. The most important oxygen-containing free radicals in many disease states are hydroxyl radical, superoxide anion radical, hydrogen peroxide, oxygen singlet, hypochlorite, nitric oxide radical and peroxynitrite radical. These are highly reactive species capable of damaging biologically relevant molecules such as DNA, proteins, carbohydrates and lipids. **Young IS, Woodside JV. Antioxidants in health and disease. *J Clin Pathol*. 2001;54:176–86.**

(4) The basic principle of drug metabolism is to convert a lipophilic drug or xenobiotic to hydrophilic metabolites that can be more readily excreted from the body. Sometimes during this process of biotransformation some of the drug or xenobiotic may be activated to chemically reactive species. This biotransformation of relatively inert chemicals to highly reactive intermediary metabolites is commonly referred to as bioactivation, and it is known to be the initial event in many chemically induced toxicities. **Attia SM. Deleterious Effects of Reactive Metabolites. *Oxidative Medicine and Cellular Longevity*. 2010 Jul-Aug; 3(4): 238–253.**

(5) Reactive oxygen species (ROS) exert a multitude of biological effects covering a spectrum that ranges from physiological regulatory functions to damaging alterations participating in the pathogenesis of an increasing number of diseases. Most studies have linked ROS to disease states such as cancer, insulin resistance, diabetes mellitus, cardiovascular diseases, atherosclerosis and aging. **Alfadda AA. Reactive Oxygen Species in Health and Disease. *Journal of Biomedicine and Biotechnology*. 2012; 2012: 936486.**

(6) Secondary tissue damage, also known as oxidative stress, is physiological stress on the body that is caused by the cumulative damage done by free radicals inadequately neutralized by antioxidants and that is held to be associated with aging and various diseases. ***Merriam-Webster Medical Dictinary.***

(7) The Phase II detoxification pathway is activated if Phase I is insufficient to clear a compound from circulation, or if Phase I generates a reactive metabolite. These reactions usually involve adding a large polar group (conjugation reaction), such as glucuronide, to further increase the compound's solubility. Often, the functional groups generated in Phase I reactions are required for attachment of the Phase II polar groups (though in some cases Phase II reactions can occur on their own). Transferase enzymes are responsible for most Phase II reactions, e.g. uridine diphosphoglucuronosyl transferase (UGT), N-acetyl transferase (NAT), glutathione S-transferase (GST) and sulphotransferase (ST). **McDowall J. Cytochrome P450. *European Bioinformatics Institute*.**

(8) Numerous sources, including: **(i) Liska D, Quinn S, Lukaczer D, Jones DS, Lerman RH. *Clinical Nutrition – A Functional Approach*. 2004; 243-261 and (ii) Hodges RE, Minich DM. Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review and Clinical Application. *Journal of Nutrition and Metabolism*. 2015; 2015-760689.**