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A Context of Translational Science Research

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The involvement of oxidative stress in the pathology of several diseases associated with overt inflammation is widely discussed. This includes diabetes from its associated cardiovascular dysfunctions, nephropathy, neuropathy, retinopathy (leading to blindness) and embryopathy or congenital malformations. In this issue of the Archives of Medical and Biomedical Research (AMBR), Sies reviews the context of oxidative stress and its impact on redox biology and medicine. The oxidation-reduction (redox) reactions in living cells are utilized in fundamental processes of redox regulation, collectively termed 'redox signalling' and 'redox control'. The *molecular redox switches* mechanism was opened by the discovery of phosphorylation/dephosphorylation reaction pathways. A bridge between phosphorylation and dephosphorylation and protein cysteine reduction/oxidation is given by the redox sensitivity of critical cysteinyl residues in protein phosphatases, opening the molecular pathway for signalling cascades as fundamental processes throughout biology. Viral and bacterial infections are often associated with deficiencies in micronutrients, including the essential trace element, selenium, and the redox-active moiety in selenoproteins. It was pointed out that selenium status may affect the function of cells in both adaptive and innate immunity. There needs to be continued focus on research addressing the micronutrients and minerals but on molecular mechanisms of action of extracts and/or the biofactors flavonoids, proanthocyanidins, alkaloids, etc. derived from these plants. Mottay and Neergheen-Bhujun reports on the potential anticholinesterase and antioxidant effects of traditional herbal medicines used in the management of neurodegenerative diseases. The high incidence of neurodegenerative disorders, primarily Alzheimer's disease and Parkinson's disease, has been linked to the devastating nature of the condition and the unsuccessful treatment options despite various advances in understanding the disease and treatment with conventional medicines. Given that oxidative stress and impaired cholinergic neurotransmission have played an important role in the pathogenesis of several neurodegenerative diseases, it would be implicative that restoring the balance of antioxidants and enhancing cholinergic neurotransmission might be possible mechanisms of action of herbal remedies.

The supplements tested included a supplement comprising *Ginkgo biloba* L. leaves, *Hypericum perforatum* L. stems, buds, leaves and *Salvia miltiorrhiza* Bunge roots and another comprising of dry ripe seed of *Ziziphus jujuba* Mill. var. spinosa Bunge, dried roots of *Angelica sinensis* (Oliv.) Diels, *Dioscorea opposita* Thunb., *Cistanche deserticola* Y. C. Ma, *Lycium barbarum* L., *Schisandra chinensis* (Turcz.) Baill., ripe fruit of *Alpinia oxyphylla* Miq., *Succinum*, *Bambusa arundinacea* Retz., *Dens Draconis*, *Anemone altaica* Fisch. Ex C.A. Mey., dried rhizome of *Gastrodia elata* Bl., *Radix Salvia Miltiorrhizae* Bunge, dried root of *Panax ginseng* C.A. Meyer and *Semen Biota orientalis* L. The former supplement modulated the levels of hypochlorous acid and hydroxyl radical and also exhibited strong iron chelating property. Given that the extracts tested by the authors inhibited acetylcholinesterase enzyme in a dose-dependent manner (the property of which was correlated strongly with total phenolics and total proanthocyanidins), it was suggested that the effects of herbal drugs used to slow the progression of neurodegenerative disorders might be partly ascribed to their antioxidant and anticholinesterase activity. There remains the context of demonstrating efficacy through extended clinical trials.

Mutagubya *et al* report on the regularity of laboratory supplies and delivery of histopathology services in the department of pathology in a hospital setting in Uganda, a context that has global health implications given the potential impact on patient care. The authors conducted a retrospective study in the department of pathology, Makerere University College of Health Sciences and Mulago Hospital, Uganda, between January 2002 and April 2003 to determine the regularity of laboratory supplies and delivery of histopathology services and found that there are weak procurement and supply systems of laboratory supplies in the health facility. Procurement at the hospital took long to issue most of the supplies after the requisitions were made, which greatly affected the turnaround time of the service due to over-accumulating of specimens which could have led to losses and/or misplacement of some specimens, thus affecting patient management. Mutagubya et al argued that, *g*iven the high turnaround time in the histopathology service, a computerized laboratory logistics and inventory management system should be established at the health settings in the country in order to ensure continuous availability of laboratory supplies and improve the turnaround time in laboratory services.

Tartrazine E102 (a water soluble trisodium salt of 3-carboxy-5-hydroxy-1-(p-sulphophenyl)-4-(p-sulphophenylazo) pyrazole) is a synthetic orange-yellow coloured azo-dye and one of the most commonly used food colourant. Imafidon *et al* report on a study focused on the haematological indices, blood glucose levels and lipid profile of rats administered Tartrazine E102. This work was done as a part of safety assessment to determine the effects of Tartrazine E102 on some haematological indices, glucose levels and blood lipid profile in rats. Imafidon *et al* showed a significant reduction in body weight gain and blood glucose levels in the study group compared with the control, as well as a non-dose dependent effect was observed on total cholesterol, LDL cholesterol, total white blood cells and monocytes. A slight but significant increase was observed in haematocrit at the highest dose levels. While Trtrazine E102 exhibited a hypoglycemic effect in rats , no negative effect was reported on lipid profile. So intake of Tartrazine at the doses administered may not produce adverse effects on glucose, blood lipids and haematological indices. This work was done

using an animal model; lower animals are used in some biomedical research work as a basis for interpreting the situation in humans, as discussed in the paper by Honess in this issue of AMBR. Any implication of potential lack of effects in humans will require human studies in which biomarkers like glucose, cholesterol, etc. are monitored on administration of Tartrazine.

Gbaja-Biamila *et al* report on the long term adverse drug reaction to Efavirenz (EFV) in a Human Immunodeficiency Virus (HIV) infected adolescent. CNS toxicity in children after long-term (>3 years) use of EFV has not been reported and this study reports a case of CNS adverse event occurring after more than 6 years on Efavirenz based antiretroviral therapy. Efavirenz is one of the medications used in combined antiretroviral therapy (ART) for the management of HIV infection in adolescents. Various central nervous system adverse reactions have been reported in patients commencing antiretroviral therapy with a regimen containing Efavirenz. These reactions tend to be acute, commonly occurring in the first six months of therapy. Adverse reactions following long term use of Efavirenz for ART is rare among adults and rarer still among children and adolescents. This report presents the case of a male HIV positive Nigerian patient aged 13 years. He presented with a five-day history of difficulty sleeping, abnormal dreams, inability to concentrate, restlessness, irrational behavior and long-term memory loss. There was no previous history of psychiatric illness and no suggestive social or family history. The patient was on Efavirenz containing regimen for about 6.5 years till presentation with adverse reaction mainly affecting behavior, thought processes and memory. After discontinuing Efavirenz and replacing it with Nevirapine in his combined ART regimen, all neuropsychiatric manifestations ceased, the patient regained his memory, no longer had bad dreams or demonstrated any irrational behavior or attitude. ART drugs are the mainstay of treatment for adults and children infected with HIV. Currently there has been an increase in access to highly active antiretroviral therapy and this has made the management of drug toxicities an increasingly vital part of HIV care in developing countries. The treatment is for life, and children will continue to take the medications for the rest of their lives unless a cure is found for HIV. The intake of these drugs can sometimes lead to unwanted effects to the body, which could be harmful, or life threatening. Physicians who are involved in the care of HIV infected patients need to be aware of the possibility of adverse drug reactions occurring in patients who have been on antiretroviral drugs for years.

Honess presents a salient history of primate research and addressed the global health improvements and ethical challenges. Although man's interest in, and recording of, the internal biology of other living animals dates back thousands of years to Classical times and includes those who laid the foundations for modern medicine, such as Galen and Aristophanes, the incorporation of non-human primates into systematic studies aiming to alleviate human suffering started much later, in the 1900s. Primates became the focus of a whole range of investigations covering everything from anatomy to physiology and behaviour. Further, while the quality of life of millions of people has rested on progress from primate research, the broader society has become more concerned with how we treat animals, and their use in research has come under particular scrutiny. Humans have benefitted from close relationships with animals for hundreds of thousands of years. However, it has only been in relatively recent times that they have made

use of the scientific investigation of animals: their anatomy, physiology and response to disease, in attempts to alleviate human suffering. Scientists rapidly realized the value of primates as research models since their evolutionary proximity to humans makes them better predictors or model of human biology. Systematic studies using primates began in the last century and massive demand for research subjects almost caused the extinction of some important wild populations. This resulted in initially *ex situ* and then latterly *in situ* breeding centers, purpose-breeding animals for biomedical research. Primate research typically follows that using less sentient animals (generally rodents) in which mechanism and proof of principle are established before examining effect and safety in primates. Honess points out that "despite the regulatory burden and scrutiny to which primate research is subjected, it still draws strong attention from the Animal Rights movement. This movement has a central tenet, which opposes human ownership of, and dominion over, any animal and this results in opposition to animal research". There is need for constant attention and (re-) education in animal welfare science and best practice in the care and management of the primate subjects and the employment of the most refined, high welfare research techniques. Honess concluded by pointing out that there is a further need for the engagement of dedicated animal welfare groups and animal welfare scientists with the research community to protect animal welfare rather than extremist action which threatens individual security, corporate or institutional viability and, not least, the potentially life-saving, or quality-of-life-enhancing, benefits that are derived from well-justified, well-regulated, and animal welfare-protecting primate research.

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