CHEMICALS AND DISEASE CONDITIONS - Beldeu Singh

For the environmentally aware, there is no need to describe the environmental problems we face today. Literally thousands of books, articles and films have been produced showing that the biosphere has been dramatically disturbed and chemically changed by human activities (Ecology 30). But the average individual may not know that in 1989 alone, more than 1,000,000,000 pounds of chemicals were released into the ground, contaminating our farmlands and drinking waters. Over 188,000,000 pounds of chemicals were also discharged into surface waters such as lakes and rivers. More than 2,400,000,000 pounds of chemicals were pumped into the air we breathe. A grand total of 5,705,670,380 pounds of chemical pollutants were released into the environment that we eat, breathe, and live in—all in just one year (cf: Nicole MR 2002, ISP, College of Lifelong Learning; Wayne State University). Since WWII, over 80,000 chemicals have been developed and used. Many are pesticides that degrade soils and contaminate water.

All of these chemicals are toxic to some degree and generate free radicals that can induce free radical damage in the body. Some of these chemicals are similar to biomolecules in the body and they are utilized in metabolic reactions resulting in disease conditions because their metabolism in the body produces toxic metabolites or simply because the body cannot differentiate between them. Their metabolism in the human cells can lead to excess hydrogen peroxide that must be converted into water and oxygen by the SOD-catalase-glutathione antioxidant system. When this process is slow, the excess hydrogen peroxide reacts with the oxygen free radicals (OFR) to yield the highly toxic secondary radical called the hydroxyl radical. The hydroxyl radical is highly reactive and can oxidatively damage cell membranes as well as the genetic molecules. Such damage to the genetic molecules impairs health and can cause developmental defects. A large percentage of pesticides sprayed in gardens, plantations and golf courses end up in the ecology and in ponds and lakes. This explains the significantly large number of frogs with deformities and developmental defects compared to forty-fifty years ago.

Free radicals are highly reactive species that can be damaging to the body at the cellular and molecular level, causing oxidative stress to cell membranes, damaging molecules including lipids, hormones, proteins and mitochondrialose reactive chemicals can damage the cell components and disrupt biochemical pathways by inactivating

enzymes involved in the Kreb,s cycle and receptors for cellular molecules. Since 1985, there is overwhelming scientific work to show that free radicals actually contribute to or hasten heart disease, cancer, diabetes, arthritis and other age-related diseases.
Evidence was accumulating over the past three decades that most of the degenerative diseases that afflict humanity have their origin in deleterious free radical reactions. These diseases include atherosclerosis, cancer, inflammatory joint disease, asthma, diabetes, senile dementia and degenerative eye disease (Florence TM, Centre for Environmental and Health Science Pty Ltd, Sydney, NSW, Aust N Z J Ophthalmol 1995; 23(1) Feb: 3–7).

Since free radicals are involved in carcinogenesis and since some epidemiological studies have suggested that certain antioxidants may reduce cancer risk, some survivors and clinicians might conclude that antioxidants are effective in preventing cancer recurrence (Jean et al, Nutrition During and After Cancer Treatment: A Guide* for Informed Choices by Cancer Survivors, CA Cancer J Clin 2001; 51:153-181© 2001 American Cancer Society) while many oncologists believe that antioxidants interfere with chemo-drugs and radiotherapy. The interference is primarily on account of the fact that chemo-drugs and radiation generate large amounts of hydroxyl free radicals that kill cancer cells (as well as normal and healthy cells) and antioxidants scavenge these free radicals. So, while research has shown that free radicals and involved in carcinogenesis, oncologists attempt to treat cancer patients with free radical generating agents as in chemotherapy and radiotherapy.

In fact a study of the relevant literature on cancer risks, whether associated with alcohol, smoking, pollutants, chemicals, toxins or sun exposure (ultraviolet radiation) all point to free radicals produced by these agents and/or a poor diet that is low in antioxidants. Put together, it means poor free radical scavenging activity in the body as the primary initiating factor for the risk and the cause of the disease condition and its progress. One way to appreciate the harmful effects of chemicals when introduced into the human body indirectly through the ecology is to understand their effects when they are introduced directly into the human body.

Would medical science prescribe a cancer causing drug to cancer patients? Last March, the U.S. federal government issued an unusually detailed alert to the nation’s 5.5 million health care workers: The powerful drugs used in chemotherapy can themselves cause cancer and pose a risk to nurses, pharmacists and others who handle them

(The Washington Post, Tuesday, February 15, 2005; Page HE01, Jim Morris). Chemotherapy drugs in human and animal studies have shown they have the potential to cause cancer or reproductive problems, said Thomas Connor, a research biologist with the National Institute for Occupational Safety and Health (NIOSH).

Chemo-drugs, like radiation, generate huge amounts of the highly reactive hydroxyl radical that damages cell membranes and disrupts the electron transport system in cells as well as protein synthesis. Natural enzyme and micronutrient levels drop rapidly and that accelerates cell death. Such a new surge of free radicals is generated by chemo-drugs which are cytotoxic to cancer cells as well as normal cells. Thus many young normal cells die due to the treatment. Most of the known carcinogens, including benzene and at least 40 other toxic chemicals in cigarette smoke and pesticides generate free radicals that create oxidative stress in cells, impairing their aerobic respiration or damaging DNA and mitochondrial DNA, turning them into cancer cells. It is this very same toxicity that is common to carcinogens and chemotherapy-drugs. Hence the NOISH alert really comes as no surprise (see: Dangerous Philosophy of treatment in Medical Science). Fortunately some of the regulatory bodies are recognizing the dangers of chemicals. The European Chemicals Agency (ECHA) has issued its first recommendation for harmful chemicals that should undergo Europe's new strict 'authorisation' process. The EU countries in the ECHA Member States Committee have adopted an opinion supporting the recommendation. ECHA recommend that seven substances of very high concern (SVHC) should be subject to use and market access only with explicit authorisation under the EU's REACH law (ref: Chemicals Health Monitor, 5th June, 2009).

Over the last 100 years, sperm count in males is declining while breast cancers in females have been rising. This phenomenon coincides with the increasing use of chemicals in industry and in medical science. Interestingly, three of the seven chemicals proposed by ECHA are officially classified in Europe as toxic to reproduction. One is officially classified as carcinogenic and three are recognized as being persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB). The flame retardant HBCCD has also been identified as a persistent, bioaccumulative and toxic substance by an EU working group, with potential effects on the liver, brain, nervous and hormone system.

Three chemicals DEHP, DBP and BBP, phthalates or plastic softeners, are already banned in toys and childcare articles in the EU. Medical

devices containing DEHP must also be labeled according to the revised European Medical Devices Directive. These phthalates (which become more powerful when present simultaneously), are examined in a recent report on male reproductive health disorders. The existing knowledge about the contribution of phthalates to human testicular disorders points to the need to reduce people's exposure to phthalates, especially pregnant women (ref: Chemicals Health Monitor, 5th June, 2009) .

Polls show that the public is concerned that the environment may be playing a role, and many respondents consider that the EU is not doing enough to address this aspect in prevention, education and policy. The real concern is rooted in the fact that "over the last 50 years, the incidence of cancer has increased rapidly. The officially recognized risk factors for cancer, including age, genetics, smoking, lack of exercise and so on, are unable to account for the rise in incidence for other cancers" (see: Chemicals Health Monitor, 22nd June, 2009). This concern is well founded and can be better understood in the way chemicals create problems in the mammalian biological systems. Wherever there are cells that are rapidly dividing as in the testicles for production of sperm and where there is fatty tissue the relative risk increases sufficiently to result in health concerns and higher risk to the development of disease states. Toxic chemicals tend to interfere with cell division while on the other hand they tend to bioaccumulate in fatty tissue. They can also generate free radicals that rob electrons from hormones leading to problems like diabetes in people with excess visceral fat and breast cancers in women as female breasts have fatty tissue.

Another reason is attributable to the fact that metabolism of chemicals leads to depletion of minerals in the body, especially iron, managanese, zinc and copper. The metabolism of these D-form substances yields a lot of hydrogen peroxide that must be converted into water and oxygen failing which its reaction with the oxygen free radicals (OFR), the secondary radical called the hydroxyl is formed that is highly reactive and very deleterious to health. These minerals, in the organic and bioavailable form, work in the body's natural antioxidant system to catalytically enhance the role of the natural antioxidant system to convert hydrogen peroxide into water and oxygen.

It is therefore not surprising at all that a report, commissioned by Health and Environment Alliance's (HEAL) partner organization CHEM Trust titled Male Reproductive Health Disorders and the Potential Role of Exposure to Environmental Chemicals. written by one of the world's

leading experts in reproductive biology, Professor Richard Sharpe of the Medical Research Council (MRC) in Edinburgh, UK, reveals that many everyday chemicals in the environment or in consumer products have the potential to block the action of testosterone, and a baby's exposure to this mixture of chemicals may undermine this process and harm future male reproductive health. Birth defects in male genitals, low sperm counts and testicular cancer, collectively called Testicular Dysgenesis Syndrome (TDS), may all have their origins during development in the womb. The link is convincingly proven in the report as it highlights animal studies that have clearly established that certain hormone disrupting chemicals, in particular testosterone disrupting chemicals, can cause TDS-like disorders (see: Chemicals Health Monitor, 13th May, 2009).

Bisphenol A (BPA) is employed in the manufacture of a wide range of consumer products. It is an endocrine disruptor at amounts to which we are exposed, alters the reproductive organs of developing rodents has caused concern. At present, no information exists concerning the exposure of human pregnant women and their fetuses to BPA. The suggestion that BPA, at amounts to which we are exposed, alters the reproductive organs of developing rodents has caused concern, if not an alarm. At present, no information exists concerning the exposure of human pregnant women and their fetuses to BPA. There is broad human exposure to this chemical.

In a study, blood samples were obtained from healthy premenopausal women, women with early and full-term pregnancy, and umbilical cord at full-term delivery. Ovarian follicular fluids obtained during IVF procedures and amniotic fluids obtained at mid-term and full-term pregnancy were also subject to BPA measurements. The results showed that BPA was present in serum and follicular fluid at 1–2 ng/ml, as well as in fetal serum and full-term amniotic fluid, confirming passage through the placenta. These results suggest accumulation of BPA in early fetuses and significant exposure during the prenatal period, which must be considered in evaluating the potential for human exposure to endocrine-disrupting chemicals (Yumiko et al, Human Reproduction, Determination of bisphenol A concentrations in human biological fluids reveals significant early prenatal, Vol. 17, No. 11, 2839-2841, November 2002).

Regulation is now moving in the direction to ensure that chemicals which act in combination to disrupt hormones are regulated according to their total combined effects (cumulative risk assessment). European Council is likely to adopt the next critical step to establish a definition

of ‘endocrine disrupting’ pesticides which will determine which pesticides will be banned.

This is important to properly move towards setting targets to reduce pesticides use and eliminating or restricting pesticides use in public places. Member State targets therefore can and should include significant reductions in the use of hormone disrupting pesticides; and eliminate their use in public places as soon as possible. However, the problem remains with regard to facilitating their biodegradation upon entering the eco-systems as they can still enter the human body through water and food chains and will come back to create health problems.

Many of the toxic chemicals are used in combination or as a mixture. In mixtures, toxic chemicals will produce cumulative and dose-additive effects.

Scientists have already conducted studies with mixtures to provide a framework for assessing the cumulative effects of "antiandrogenic" chemicals. Rats were dosed during pregnancy with antiandrogens singly or in pairs at dosage levels equivalent to about one half of the ED50 for hypospadias or epididymal agenesis. The pairs include: AR antagonists (vinclozolin plus procymidone), phthalate esters (DBP plus BBP and DEHP plus DBP), a phthalate ester plus an AR antagonist (DBP plus procymidone), and linuron plus BBP. This study proved the expected effects. All binary combinations produced cumulative, dose-additive effects on the androgen-dependent tissues. We also conducted a mixture study combining seven "antiandrogens" together. These chemicals elicit antiandrogenic effects at two different sites in the androgen signaling pathway (i.e., AR antagonist or inhibition of androgen synthesis). In this study, the complex mixture behaved in a dose-additive manner. The results indicate that compounds that act by disparate mechanisms of toxicity display cumulative, dose-additive effects when present in combination (Rider et al, Cumulative effects of in utero administration of mixtures of "antiandrogens" on male rat reproductive development, Toxicol Path, 2009;37(1):100-13. Epub 2009 Jan 15).

Chemicals used in pesticides also have antiandrogenic properties and endocrine toxicity. Antiandrogenic chemicals alter sexual differentiation by a variety of mechanisms, and as a consequence, they induce different profiles of effects. For example, in utero treatment with the androgen receptor (AR) antagonist, flutamide, produces ventral prostate agenesis and testicular nondescent, while in

contrast, finasteride, an inhibitor of 5 alpha-dihydrotestosterone (DHT) synthesis, rarely, if ever, induces such malformations. In this regard, it was recently proposed that dibutyl phthalate (DBP) alters reproductive development by a different mechanism of action than flutamide or vinclozolin (V), which are AR antagonists, because the male offsprings display an unusually high incidence of testicular and epididymal alterations--effects rarely seen after in utero flutamide or V treatment. In one recent study, we present original data describing the reproductive effects of 10 known or suspected anti-androgens, including a Leydig cell toxicant ethane dimethane sulphonate (EDS, 50 mg kg-1 day-1), linuron (L, 100 mg kg-1 day-1), p,p'-DDE (100 mg kg-1 day-1), ketoconazole (12-50 mg kg-1 day-1), procymidone (P, 100 mg kg-1 day-1), chlozolinate (100 mg kg-1 day-1), iprodione (100 mg kg-1 day-1), DBP (500 mg kg-1 day-1), diethylhexyl phthalate (DEHP, 750 mg kg-1 day-1), and polychlorinated biphenyl (PCB) congener no. 169 (single dose of 1.8 mg kg-1). Male offsprings display a higher incidence of epididymal and testicular lesions than generally seen with flutamide, P, or V even at high dosage levels. Overall these toxic chemicals display several mechanisms of endocrine toxicity. Ketoconazole did not demasculinize or feminize males but rather displayed anti-hormonal activities, apparently by inhibiting ovarian hormone synthesis, which resulted in delayed delivery and whole litter loss. This study shows the effects of chemicals in pesticides in developmental toxicity (Gray et al, Administration of potentially antiandrogenic pesticides (procymidone, linuron, iprodione, chlozolinate, p,p'-DDE, and ketoconazole) and toxic substances (dibutyl- and diethylhexyl phthalate, PCB 169, and ethane dimethane sulphonate) during sexual differentiation produces diverse profiles of reproductive malformations in the male rat, Toxicol Ind Health, 1999 Jan-Mar;15(1-2):94-118).

Bioaccumulation and severe or prolonged exposure to chemicals leads to health problems whose symptoms mimic disease conditions from other causes. When such exposure to chemicals is not understood and taken into account, its treatment is impossible and the patient keeps coming back for more drugs. Unfortunately, conventional allopathic treatments are not geared towards the break-up of chemicals in the body and to remove them with non-toxic approaches. Hence, headaches, backpains and symptoms related to or caused by chronic inflammations initiated by free radicals generated by chemicals in the body tend to persist. These health problems can be compounded when there are also populations of protozoa in the body as their allergens also cause chronic inflammation. These protozoa feed on vitamin 12 at night. Symptoms may therefore become more severe at night. In

psoriasis patients, the itch increases at night. Such persons may also become deficient in B vitamins especially vitamin B12. Protozoal infections are more common that currently thought and that explains the relatively high incidence of 25% in the US for vitamin B deficiency. Such deficiency in people with protozoal infections can also lead to numbness in hands and neuropathies, chronic hypertension as well as borderline elevations in glucose and LDL levels. Vitamin B12 supplementation only results in a short-lived improvement and the problems can become more aggravated over time as the protozoa feed on the increased supply of vitamin B12 and multiply.

The exposure of people with protozoal infections to chemicals and toxic dust clouds is a problem that needs serious attention and funding for research. The dangers of exposing people and especially pregnant women to hormone disrupting chemicals in consumer products are now well documented and more members of the public know about it. The focus is on the risks these pose to baby boys and to healthy reproductive biology but compounding factors such as protozoal infections must be also considered. Chemicals can also cause problems in other tissues and organs such as in the dermis and the respiratory tract.

In recent years, cleaning has been identified as an occupational risk because of an increased incidence of reported respiratory effects, such as asthma and asthma-like symptoms among cleaning workers. Due to the lack of systematic occupational hygiene analyses and workplace exposure data, it is not clear which cleaning-related exposures induce or aggravate asthma and other respiratory effects. Currently, there is a need for systematic evaluation of cleaning products ingredients and their exposures in the workplace. Ingredients of concern in cleaning agents include quaternary ammonium compounds, 2-butoxyethanol, and ethanolamines. Cleaning workers are at risk of acute and chronic inhalation exposures to volatile organic compounds (VOC) vapors and aerosols generated from product spraying, and dermal exposures mostly through hands (Bello et al, Characterization of occupational exposures to cleaning products used for common cleaning tasks--a pilot study of hospital cleaners, Environ Health, 2009 Mar 27;8:11.). An often overlooked problem with regard to chemicals that affect respiratory health is their impact on the endothelium in the major arteries over time that can lead to disruption in the production of nitric oxide (NO) and the formation of the peroxynitrite oxidant that is also highly reactive specie that very often oxidatively damages cell membranes causing joint-pains. Such disruption in the NO yields also leads to hypertension and erectile dysfunction.

Other chemicals found in the environment and in our homes such as formaldehyde can also lead to health problems depending on exposure and period of exposure. Formaldehyde is an economically important chemical, to which more than 2 million U.S. workers are occupationally exposed. Substantially more people are exposed to formaldehyde environmentally, as it is generated by automobile engines, is a component of tobacco smoke and is released from household products, including furniture, particleboard, plywood, and carpeting. The International Agency for Research on Cancer (IARC) recently classified formaldehyde as a human carcinogen that causes nasopharyngeal cancer and also concluded that there is "strong but not sufficient evidence for a causal association between leukemia and occupational exposure to formaldehyde." In a new meta-analysis of these studies, focusing on occupations known to have high formaldehyde exposure, we show that summary relative risks (RRs) were elevated in 15 studies of leukemia (RR=1.54; confidence interval (CI), 1.18-2.00) with the highest relative risks seen in the six studies of myeloid leukemia (RR=1.90; 95% CI, 1.31-2.76). The biological plausibility of this observed association lead the researchers to hypothesize that formaldehyde may act on bone marrow directly or, alternatively, may cause leukemia by damaging the hematopoietic stem or early progenitor cells that are located in the circulating blood or nasal passages, which then travel to the bone marrow and become leukemic stem cells (Zhang et al, Formaldehyde exposure and leukemia: a new meta-analysis and potential mechanisms, Mutat Res, 2009 Mar-Jun;681(2-3):150-68, Epub 2008 Jul 15). Unfortunately traces of formaldehyde are also found in haze from burning vegetative matter and forest fires.

Although risk assessments are typically conducted on a chemical-by-chemical basis, the 1996 Food Quality Protection Act (FQPA) required the Environmental Protection Agency (EPA) to consider cumulative risk of chemicals that act via a common mechanism of toxicity. The common underlying toxicity of chemicals lies in their ability to generate excess hydrogen peroxide in the body leading to the formation of secondary radicals such as the hydroxyl and the oxidant called the peroxynitrite.

The key issues being the role of chemicals in inducing and accelerating free radical damage and their bioaccumulation in human tissue, it is only proper that we note the interest in exposure assessment that has shifted from pollutant monitoring in air, soil, and water toward personal exposure measurements and biomonitoring. That process is important to assess the level of contamination together with the levels

of natural antioxidants in the blood and to monitor both levels as against symptoms and health problems. Biochelation procedures and interventions will therefore become the more important and the more critical part of a modern healthcare system as a large variety of chemicals are already in our environment and more are entering the human body directly through “medications” and indirectly through the ecosystems and through wars that use chemicals to defoliate and weapons that use depleted uranium 235. The lingering health problems of chemical warfare will therefore be astounding if they are surmountable.

The cancer rate in the USA in 1900 was three out of one hundred. Today, one in three people will get cancer and one in four will die from it. This amounts to over one million people yearly, killing some 520,000 of us annually. That is one grave problem related to becoming industrialized wherein society is led to use more and more chemicals in industry and at home. One recent report commissioned by the California EPA done by University of Calif. researchers estimate that in 2004, 200,000 California workers suffered from chronic diseases linked to workplace exposure to industrial chemicals and 4,400 people died of these diseases including cancer, emphysema and Parkinson's disease. New research is beginning to show that low-level synthetic chemical exposure over time can disrupt the natural development of infants and children.

The Collaborative on Health and the Environment (CHE) database report shows links between chemical contaminants and 180 diseases or conditions in humans ranging from skin conditions to fertility to cancers. Chemicals that bioaccumulate in the brain can lead to Alzheimers and Parkinson’s disease as they cause chronic inflammations in brain cells. The World Health Organization (WHO) has released a report stating that one-quarter of the world's disease burden -- and one-third of the disease burden among children -- is due to environmental factors that could be modified. Today the human biological system among urban populations is contaminated and so is human breast milk. The chemical origin of diseases must be recognized and included in the medical school program. The problem is paradoxically aggravated by trying to treat symptoms caused by chemicals by other toxic chemicals called drugs that are prescribed as “medications.” There is now the need to go for non-toxic treatments and to apply non-toxic pesticides to modify the environment and our ecosystems in order to modify the world’s disease burden that is a drag on every economy. In many developed nations it has become a burden on the household.

Business interest sometimes seems to override health concerns. One of the criteria used to lobby in favor of businesses is that the sole basis of hazards based on the toxic properties of a chemical should not prompt its inclusion in Europe's new strict 'authorization' process. But the paradox in medical science still stands which is the use of toxic chemicals to treat health problems. For instance the chemical called AZT which is "toxic by inhalation" and can cause the same symptoms as AIDS is used to treat AIDS patients. Quite naturally, six national representatives raised concerns about the inclusion of the flame retardant HBCDD, arguing inclusion on the list could harm small businesses. This goes against REACH which mandates that harmful chemicals be lined up for the authorization procedure solely on the basis of the hazards posed by their toxic properties.

Before toxic chemicals are banned, substance producers or users will have to show that the risks of a particular use can be adequately controlled, or for certain chemicals, that there are overwhelming socioeconomic benefits to the substance's use (that outweigh the health and environment risks) and that no alternatives exist. The real problem is that most of the controls exist only at the production stage and there is little or no control once they are released into the markets and into the ecology.

Health science is beginning to recognize the significance of bioaccumulation of chemicals and chemicals used in pesticides as a cause of persistent pain and chronic disease conditions. Drugs are not a solution to this chemically induced problem that may be associated with heavy metal bioaccumulation in tissues. The most effective and fast way is to use alpha-lipoic acid and pectins obtained from edible substances in the nano-form to biochelate for safe removal from the human biological system through the urine.