Immunodeficiency, dioxins, stress, and the hormones

From the original article in 2006. Author: Ray Peat.

Critical points:

- There are many toxins which modify hormonal responses, activating cells and altering the immune system (including estrogens and dioxins.) When these act early in life, extremely small amounts can cause life-long changes.
- When respiratory energy production is blocked in stimulated cells, the cells are likely to die. (Cortisol, estrogen, polyunsaturated oils have this effect, especially on thymus cells.)
- Antibodies are involved in removing the debris of cells that have disintegrated. Intense cellular damage causes many "autoantibodies" to be produced. People with AIDS have a high incidence of "autoimmunity."
- Endogenous retroviruses are activated by toxins known to be associated with immunodeficiency. Everyone has endogenous retroviruses. The antibodies which are used to diagnose "HIV" infection can, in the demonstrated absence of that virus, be produced in connection with lupus, Sjogren's syndrome, and arthritis. These autoimmune conditions are promoted by estrogen.
- Estrogen activates the production of cortisol, and damages the normal feedback control, causing both cortisol and ACTH to be elevated.
- Estrogen causes chronically elevated free fatty acids, and synergizes with unsaturated fats.
- Estrogen inhibits thyroid function.
- Hypercortisolism is typically associated with hypothyroidism, and both tend to cause the loss of lean body mass.
- AIDS is often compared to Addison's disease, because of hyponatremia (loss of sodium) and fatigue. Hypothyroidism causes hyponatremia and many other features seen in AIDS.
- Increased levels of cortisol, estrogen, and polyunsaturated fatty acids, and decreased levels of the active thyroid hormone (T3) and (placental) progesterone have been found to occur in AIDS.
- Progesterone can contribute to the inhibition of HIV replication and transmission.
- Common environmental factors can produce hormonal changes leading to immunodeficiency.

One hospital in southern Vietnam admitted 437 septicemia patients between mid-1993 and 1994; 23% of the adults died.

In 8 months, 17,000 seals died of infections in Europe. In California, many seals die with an unusual form of metastatic cancer. Seals are highly contaminated with industrial dioxins.

In Africa, aflatoxin is strongly associated with immunodeficiency. In animals, both dioxin and aflatoxin activate the expression of viruses.

Endometriosis is stimulated by dioxins. Environmental estrogens affect the immune system.

It has been over ten years since I wrote about "AIDS" (e.g., "Repairing the Immune System," in *Cofactors in AIDS and HIV infection,* edited by R.R. Watson, l989) and the official doctrine that it is caused by the "HIV" virus still hasn't been supported by anything that resembles real science. Duesberg's arguments have never been answered (except by bureaucratic thuggery).

In 1989 I pointed out that septicemia, blood stream infection, in young adults, which used to be a rare thing, and which indicates defective immunity, has been increasing in a remarkably continuous way since the late 1940s, and I reviewed the many things in our environment that are known to suppress immunity, and which have become increasingly prevalent in our environment**--unsaturated vegetable oils, ferrous iron and carrageenan in our foods, lead in air, food, and water, exposure to medical, military, and industrial ionizing radiation, vaccinations, pesticides, chlorinated hydrocarbons, nitric oxide (smog and medications) and oral contraceptives and environmental estrogens, in particular.** Of these factors, only radiation and lead exposure have decreased in the last several years, after several decades of rapid increase. The widespread use of diuretics in pregnancy, which began in the 1950s and contributed to an epidemic of premature births, also declined after the late 1960s. Most of these environmental factors damage the thymus gland, which regulates the immune system, and by acting on the thymus their effects tend to be additive with other immunosuppressive factors, including cancer, traumatic injury, inflammation, toxins in spoiled food (e.g., aflatoxins) and malnutrition.

Cancer, AIDS, and extreme hypothyroidism have several features in common--they cause tissue loss and organ damage, with immunodeficiency and intense activation of the stress hormones, including cortisol. In cancer and AIDS, a good case has been made for the primacy of stress-induced wasting as the main cause of death. Whatever one might believe to be the cause of cancer and AIDS, it is always good for the patient to prevent tissue damage from the stress associated with the sickness. Since the stress hormones primarily destroy tissues by the activation of specific proteases, the use of protease inhibitors for treating AIDS could conceivably be affecting the stress response. However, the body's normal protection against the cortisol-activated proteases is centered on the protective hormones, progesterone, thyroid, and the androgens.

Environmental stress

One of the most broadly substantiated principles in biology is that a great variety of harmful causes all lead to a few forms of biological harm--the concept of the stress reaction shows the powerful implications of the principle. Stress, no matter what the specific cause, has a particularly destructive effect on three organ systems**:** The nervous system, the immune system, and the reproductive system. Inflammation, lipid peroxidation, tissue atrophy, the "calcium catastrophe" (when almost anything goes wrong, calcium can transmit and amplify and extend the problem, but isn't itself the source of the problem),

mitochondrial decay, and similar events help to define the stress reaction in greater detail.

Hans Selye showed that the thymus shrinks very early in the stress reaction. In his understanding of the process, when adaptation was followed by the "exhaustion phase," the adrenal glands had simply become exhausted from overuse. F. Z. Meerson's work showed that cortisol, and the free fatty acids mobilized by stress, have a toxic influence on the mitochondrial energy production system. Both cortisol and the free fatty acids block the efficient use of glucose for producing energy, creating a diabetes-like condition. The exhaustion problem caused by excessive stress is generalized, not just a matter of adrenal insufficiency.

Meerson's work created the basis for undersanding several degenerative processes, especially the phenomenon of "excitotoxicity," in which the combination of excessive stimulation and deficient energy supply damages or kills cells.

Selye believed that some hormones are antagonistic to each other. A few of the oppositions that he identified have been thoroughly researched, especially the catabolic/anabolic functions of glucocorticoids and androgens, and the shock/antishock functions of estrogen and progesterone, respectively.

Puberty, because of hormonal changes, especially increased estrogen, can be seen as the first stage of a chronic stress, resembling diabetes, since elevated free fatty acids cause "insulin resistance," with slightly impaired oxidation of glucose. The thymus shrinks considerably at puberty, under the influence of the hormonal changes and the increased free fatty acids (caused mainly by estrogen). The degenerative diseases can be seen as the cumulative result of stress, in which tissue damage results from the diabetes-like impairment of energy production.

The thymus, and the thymus-dependent areas of the spleen, are required for full and subtle control of immunity. In the absence of thymic control, the B cells are still able to produce antibodies, but they are more likely to produce autoantibodies.

Stress produces a variety of cellular changes, including the production of the "shock proteins." These proteins can make up 20% of the cell's total protein content. In themselves, the shock proteins are immunosuppressive. They can be recognized by the immune system as antigens, and so are a factor in the appearance of "autoimmune" antibodies. The autoantibodies themselves are often blamed for the diseases they are sometimes associated with, but since they can be present (for example, following removal of the spleen) in people who have no symptoms, their function is probably to facilitate the removal of tissues which are defective for some other reason. The shock proteins could be one of the signals that activate the immune system to remove damaged tissue, and they might be involved in the removal of senescent cells, though I don't think any experiments have been done to test this idea.

Besides activating the cells to produce massive amounts of the shock proteins, stress can also activate the so-called hormone receptors, such as estrogen receptors, even in the absence of the hormones. Stress also activates the endonucleases, which cut sections out of the DNA molecules, and activates mobile genetic elements, producing genetic instability. Like cortisol and estrogen, stress itself activates integrated retroviruses. The "endogenous retroviruses" make up nearly 10% of the human genome, and many of them locate themselves in regulatory sites in the chromosomes.

Since stress lowers the discriminatory ability of the immune system, and stimulates the expression of retroviruses, the antibodies sometimes seen in association with immunodeficiency may be similar to the various autoantibodies that are also produced by stress.

People who have autoimmune diseases such as lupus and Sjogrens syndrome (which are promoted by estrogen**:** Ahmed and Talal) have antibodies which sometimes react positively in the AIDS test, and searches for the HIV virus in such people have found no evidence of it. (Nelson, et al., 1994**;** Deas, et al., 1998.) Treatments for roundworms and other parasites cause antibodies to retroviruses to appear in animals that previously tested negative**;** this might account for the high rates of positive tests for HIV in areas such as Africa in which treatment for filiariasis is common (Kitchen and Cotter, 1988).

Organisms are most sensitive to environmental damage early in life, especially prenatally. This is the period in which normal hormone exposure masculinizes the brain, for example. The term "imprinting" refers to the extreme responsiveness of the organism at this time, and it has been extended to include long lasting influences which may result from abnormally high or low levels of natural substances, or from the presence of other, abnormal substances during the sensitive period. The effects of early "imprinting" can cause permanently altered sensitivities. In animal studies, L. C. Strong showed that prenatal influences determine the age at which puberty and reproductive senescence occur. In humans, premature birth, a powerful stressor, is associated with premature puberty. The thymus is damaged both by premature birth and by puberty. The effects of damage early in life will increase vulnerability in subsequent decades.

When babies are imprinted by the mother's disturbed hormones, or by diuretics, by milk substitutes, or by industrial effluents, the worst effects are likely to be seen decades later, or even generations later. A similar long-range effect can be produced by nutritional deficiencies.

Although more mature organisms are less sensitive to stress, both early imprinting, and the cumulative effects of exposure, will cause some individuals to be much more sensitive than others, and aging itself increases vulnerability.

If the present epidemic of immunodeficiency is produced by environmental stress, then we should expect to see a variety of other stress-related diseases increasing at roughly the same time. When a stressor is acting through imprinting, then the harmful effects may not be seen until 20 or 30 years later, but when the stressor has acute and immediate effects, the effects should rise and fall at roughly the same time as the environmental cause.

The rise of the Acquired Immunodeficiency Syndrome during the last 50 years hasn't been the only health problem that has grown rapidly during that time. The "flesh eating bacteria," causing necrotizing fasciitis and related conditions, should probably be classed along with septicemia/bacteremia as the consequence of a weakened immune system, but there are

many other diseases that have followed a similar pattern, which might be caused by the same factors which are causing immunodeficiency. ***Thyroid diseases (mostly in women), some autoimmune diseases including primary biliary cirrhosis (mostly in women) and inflammatory bowel disease, liver cancer, diabetes (doubling in children since 1949), prostate cancer, decreased sperm counts, premature births and birth defects, minimal brain dysfunction-attention deficit-hyperactivity, cerebral palsy, premature puberty (which is associated with premature birth), congestive heart failure, osteoporosis (independently of the changing age-structure of the population), depression (most common in women, more than doubling among children in recent decades), and multiple sclerosis have increased in prevalence during this period.*** *Some of these conditions are strongly associated with each other, for example, primary biliary cirrhosis, breast cancer, and osteoporosis.*

It is common knowledge, among people who study immunity, that radiation, polyunsaturated fatty acids, estrogens, and dioxins are toxic to the thymus gland, and can produce immuno-deficiency. They mimic or accelerate the thymic atrophy of aging, causing a deficient thymus-dependent immune response, usually without harming the ability of B cells to produce antibodies. There are probably many examples of damage to immune systems, besides immunodeficiency, caused by these agents. Slight damage to the immune system, such as can be produced by hypoglycemia or other energy deficit--creates an exaggerated inflammatory response, and the release of the mediators of inflammation, including histamine, serotonin, and prostaglandins, activates the stress hormone system, leading to further biological damage. Liver disease and several other "autoimmune" diseases involve abnormal immune responses, probably including thymic deficiency and an intensified inflammatory response. The fact that livers transplanted from female donors to male recipients are less successful than are livers from male donor transplanted into female recipients, is consistent with the idea that autoantibodies (which are far more common in women than in men) are a relatively harmless response to changes in the organs themselves.

Are antiviral therapies working? Ivan Ilich, in *Medical Nemesis,* showed that historically, many diseases have had characteristic incidence curves, rising to a maximum, and then falling away to relative insignificance, independently of what people were doing as treatment or prevention. As susceptible people are exposed to conditions that cause a disease, they will get sick, and then either die or develop resistance. The conditions which at first caused increasing disease incidence, will eventually tend to affect only children who haven't developed resistance.

If AIDS mortality rose rapidly to a peak a few years ago, and then began falling, we should ask whether this pattern fits that of other diseases discussed by Ilich. Looking for causes other than the virus, we might find a parallel in the rise and fall of some other factor.

In the 1950s, new diuretics came on the market, and millions of pregnant women took them. It was predicted that there would be an epidemic of brain damage as a result, and in fact the incidence of hyperactivity, attention-deficit, and other "minimal" brain damage disorders did rise during those years. After about 15-20 years, experiences such as the Thalidomide episode caused physicians to temper their enthusiasm for the use of drugs during pregnancy. **The incidence of low birth-weight babies in the U.S. peaked around 1965, and 28 years later AIDS mortality in the US peaked.** The rising curve had followed both the increase in radioactive fallout from atmospheric testing of large numbers of atomic bombs up to 1963, and the intense promotion of the new diuretics beginning in the early 1950s. The peak in AIDS mortality in 1993 came ten or twelve years after the long decline in SAT scores had stopped. (The most extreme declines in SAT scores had occurred among the brightest students, disproving the contention that the average score fell simply because more students were taking the tests.) The same prenatal damage which caused the extreme decline in SAT scores 18 years later (when the damaged babies reached that age) would have left many of the same individuals with weakened immune systems, which would fail prematurely, but at varying intervals, depending on the exposure to other factors.

The use of unleaded gasoline increased into the 1990s, and there was a corresponding decrease in tissue lead content, reflecting the smaller amount of lead being put into the environment. According to some reports, medical and dental x-ray exposures were declining during this period. Yet other factors, including dioxins and unsaturated dietary fats, were probably increasing.

Although the new protease inhibitors wouldn't be used until years after the AIDS mortality had begun falling, the government and drug companies are claiming that it is the drugs which are decreasing the mortality.

A Synthesis

Many things in our environment are increasing the incidence of certain kinds of liver disease. The liver processes things that are ingested or that enter the blood stream after being inhaled or absorbed through the skin, so in a toxic environment it is susceptible to injury. If deprived of good nutrition or adequate thyroid hormone it is especially sensitive to toxins. The body's own estrogen is a burden on the liver, causing women's livers to be on average slower than men's in processing enviornmental chemicals.

Almost any kind of toxin causes the liver to be less efficient at excreting other substances, including hormones. In malnutrition, sickness, and in aging, there is a tendency for higher levels of estrogen to remain circulating in the blood.

Natural estrogen, and environmental substances that act like estrogen, act as excitants in many types of cell, and at the same time, reduce the efficiency of energy production. Both of these properties relate to its known ability to activate the adrenal glands. A. L. Soderwall, who was my thesis adviser at the University of Oregon, found that estrogen caused hamsters' adrenal glands to enlarge, and that larger doses overstimulated the glands sufficiently to cause tissue damage. It is now known that estrogen acts directly on the adrenal cells to stimulate cortisol production, and that it also stimulates the pituitary to produce more adrenocorticotropin (ACTH), which also stimulates the adrenals**;** estrogen's effect is to impair the negative feedback, in which cortisol normally shuts down ACTH production. This impaired feedback is characteristic of aging.

Estrogen directly causes the thymus gland to atrophy, and several of its effects, such as increased adrenal activity and elevated free fatty acids, also contribute to the shrinkage of the thymus and the inhibition of its functions. While this is happening, the B cells, which normally are under the control of the thymus cells, are not killed by estrogen, and actually seem to be stimulated by estrogen to produce certain types of antibodies. This combination of effects, weakening the thymus and stimulating antibody production, is thought to contribute to the development of autoimmune diseases. Estrogen also stimulates mast cells and similar cells to release histamine and other promoters of inflammation, and these effects are probably closer to the actual problem in the autoimmune diseases. Several of the substances formed under the influence of estrogen interfere with energy production and contribute to cellular excitation, causing tissue injury.

Cortisol also stimulates antibody production while suppressing thymic immunity (Norbiato, et al., 1997).

Estrogen and stress cause increased levels of free fatty acids to circulate. The polyunsaturated fatty acids are immunosuppressive, antithyroid, diabetogenic, inhibit respiration, and promote the actions of estrogen and cortisol.

People suffering from AIDS have been found to have increased estrogen, with high cortisol and ACTH, and very low T3. (Unfortunately, some researchers and the editors who publish their ideas, conclude that the hormones don't cause the stress and wasting symtpoms, because they call thyroid a "catabolic hormone," and because they describe the fatigue and sodium deficiency as evidence of "deficiency of cortisol." Such is the state of the research establishment.)

In animal experiments, and a few human tests, the HIV and similar viruses have produced effects that could plausibly explain some of the conditions seen in AIDS, such as damage to brain cells (C. Pert, R. Sapolsky), and altered steroid secretion. But this is real science, that promises to link up with information about stress, aging, allergy, and biological adaptability.

For example, Sapolsky's group (Brooke, et al., 1998) found that the nerve toxicity caused by a viral protein (called gp120) synergizes with glucocorticoid toxicity, lowering the ATP level and inhibiting mitochondrial function, and that simply supplying the nerve with additional energy protects it from destruction. In other words, the viral peptide just increases excitotoxicity.

Another group (Amirhessami-Aghili and Spector, 1991) found that the presence of the virus can decrease the production of progesterone. Since progesterone blocks (Lee, et al., 1997) the expression (and transmission) of the virus, this suggests how the overgrowth of the virus might be triggered by stress--once progesterone synthesis falls, a vicious circle could get started.

Lee, et al., found that progesterone can help to prevent transmission of the virus from an infected mother to the fetus. But the most interesting study of the virus in pregnancy involved mice that were engineered to contain extremely large quantities of the HIV provirus (De, et al., 1997). At birth, they seemed normal, but within a few days their skin became diseased, and they quickly wasted away and died. The experimenters realized that something present in the mother's body had permitted normal development up to the point of birth, and then the wasting disease set in. The placental hormone, chorionic gonadotropin, is produced in large amounts during pregnancy. The experimenters gave newborn infected mice regular doses of human chorionic gonadotropin (hCG), and they developed normally.

Rodents don't respond to gonadotropins or other ovarian stimulation exactly the way pigs and primates and people do. For example, prolactin and melatonin usually inhibit progesterone synthesis in people, but in rodents, they increase it. So it's necessary to see exactly what happens to the ovarian hormones when a mouse is given hCG. In 1996, another group (H. Krzanowska and M. Szoltys) had done that, and found that hCG greatly **increases progesterone synthesis, but decreases estrogen.**

Considering the progesterone-HIV experiments together, I am reminded of a science fiction movie, in which a disease from another planet killed everyone in the lab that was studying it, except for one woman, who turned out to be pregnant.

The medical version of AIDS research, though, pushes aside all of the real science, in favor of a simplistic idea that the virus kills the cells of the immune system, and uses false diagnostic methods and deadly drugs to treat something which too often doesn't exist, while denying that there are other real causes of immune deficiency and wasting-sickness, etc.

Aging is characterized by loss of lean body mass, immunodeficiency, and a variety of autoimmune reactions. My perennial argument has been that decreased thyroid and progesterone, associated with increased estrogen and stress hormones, are largely responsible for those changes. The huge investment in AIDS research has found that these occur in AIDS, but, because of the medical pharmaceutical culture which has created myths about these hormones, no one is yet interpreting the hormone imbalances in ways that would reveal their responsibility for the symptoms. While the institutionalized theory claims that the HIV virus is responsible for the syndrome, the hormones are reduced to epiphenomena.

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Arkh Patol 1987;49(6):10-8 **[Combination of immunodepression and disorders in nucleic acid metabolism of lymphoid tissue as a manifestation of a paraneoplastic syndrome].** [Article in Russian] Potapova GI, Shapot VS Several physiological, biochemical, and molecular biological approaches to the study of factors determining immunodepression in tumor-bearing animals are considered. Cancer cells release substances of nucleic and peptide nature that suppress the functional activity of macrophages and lymphocytes and stimulate cell proliferation in organs and tissues of the host. Suppressor T cells capable of inhibiting the function of helper T cells and impairing the differentiation of killer T cells are activated. The suppression **of T- and B-cell-mediated immunity in the tumor host involves disturbances of nucleic acid metabolism in those cells as well as hypersecretion of glucocorticoids.** The impairments of lymphocyte proliferation and differentiation that result in reduced immune responsiveness are attributable to drastic alterations in the metabolism of purine and pyrimidine nucleotides and to the damage sustained by the lymphocyte's DNA.

Eksp Onkol 1987;9(6):62-7 **[Relation between disorders of glucose metabolism, secretion of somatotropic hormone, thyroxine, thyrotropin and hematocrit indices in rats with transplanted hepatomas].** Shelepov VP, Pasha-zade GR, Chekulaev VA, Shapot VS.

Am J Pathol 1987 Jan;126(1):103-13 **Dietary fatty acid effects on T-cell-mediated immunity in mice infected with mycoplasma pulmonis or given carcinogens by injection.** Bennett M, Uauy R, Grundy SM. To test whether or not diets enriched in w-6 polyunsaturated fatty acids are significantly immunosuppressive . . . mice were fed diets enriched for fatty acids: linoleic (POLY), oleic (MONO), palmitic (SAT), or eicosapentanoic (FISH). . . . only mice on the **POLY diet were significantly immunosuppressed, and only T-cell-mediated cutaneous sensitivity reactions were affected.** After instillation, mice on the POLY and MONO diets were suppressed for T-cell cutaneous responses. Deliberate infection with Mycoplasma pulmonis resulted in suppressed cutaneous T-cell responses in the POLY group of C3B6F1 mice, and aspirin partially reversed the immunosuppression. Mice on the FISH diet were resistant to immunosuppression. It is tentatively concluded that diets rich in w-6 polyunsaturated diets, while not **directly immunosuppressive, do predispose animals to suppression of certain T-cell-mediated immune responses. This immunosuppression can be "triggered" by infection and/or by exposure to carcinogens.**

Tumour Biol 1988;9(5):225-32 **Modulation of cell-mediated immune response by steroids and free fatty acids in AIDS patients: a critical survey.** Nunez EA. The overall data presented in this review show that cortisol and free fatty acids, in particular long-chain polyunsaturated fatty acids, each have immunoinhibitory properties on lymphoblastic transformation of **certain T lymphocytes. This effect is enhanced when the two factors are associated. These data could explain in part the immunosuppression observed in acquired immunodeficiency syndrome (AIDS) patients where enhanced concentrations of cortisol and polyunsaturated fatty acids have been observed.**

Basic Life Sci 1988;49:615-20 **Vitamin E and immune functions**. Bendich A. Supplementation of these diets with higher than nutritionally adequate **levels of vitamin E enhances immune responses. High levels of PUFA are immunosuppressive, and vitamin E can partially overcome this immunosuppression. High levels of vitamin C can protect tissue levels of** vitamin E and may indirectly contribute to the immunoenhancement by vitamin E. Severe selenium deficiency is immunosuppressive. Vitamin E can protect some aspects of immune responses from the adverse effects of selenium deficiency. These data clearly indicate that nutrients that affect the overall antioxidant status have important effects on immune functions. In addition, antioxidant nutrient interactions can synergize to overcome the adverse effects of polyunsaturated fatty acids on immune functions.

Transplantation 1989 Jul;48(1):98-102 **Enhancement of immunosuppression by substitution of fish oil for olive oil as a vehicle for cyclosporine.** Kelley VE, Kirkman RL, Bastos M, Barrett LV, Strom TB.

J Am Coll Nutr 1992 Oct;11(5):512-8 **Role of nutrition in the management of malnutrition and immune dysfunction of trauma.** Cerra FB Dept. of Clinical Nutrition, University of Minnesota, Minneapolis. Current nutrition support improves patient outcome in trauma patients. It appears to do so by limiting the adverse effects of specific nutrient or generalized nutrient deficiencies. Immunosuppression,

however, continues as a significant clinical problem. This **immunosuppression appears to be part of the inflammatory response that accompanies trauma, and in part, to represent the need for conditional** nutrients in this setting. Three nutrients that are being evaluated include arginine, uracil as ribonucleic acid and omega-3 polyunsaturated fatty acids. Animal studies report improved immune function. Early clinical trials are reporting improved immune function and patient outcomes.

J Nutr 1996 Mar;126(3):681-92 **Dietary butter protects against ultraviolet radiation-induced suppression of contact hypersensitivity in Skh:HR-1 hairless mice.** Cope RB, Bosnic M, Boehm-Wilcox C, Mohr D, Reeve VE. Dietary fats modulate a wide variety of T cell functions in mice and humans. This study examined the effects of four different dietary fats, predominantly polyunsaturated sunflower oil, margarine, and predominantly saturated butter, clarified butter, on the T cell-mediated, systemic suppression of contact hypersensitivity by ultraviolet radiation. There was a linear relationship ($r > 0.9$) between protection against **photoimmunosuppression and the proportion of clarified butter in mice fed a series of 200 g/kg mixed fat** diets that provided varying proportions of clarified butter and sunflower oil. The dietary fats did not modulate the contact hypersensitivity reaction in unirradiated animals. The observed phenomena were not primary due to the carotene, tocopherol, cholecalciferol, retinol, lipid hydroperoxide or the nonfat solid content of the dietary fats used and appeared to be a result of the different fatty acid composition of the fats.

Cancer Lett 1996 Nov 29;108(2):271-9 **Dependence of photocarcinogenesis and photoimmunosuppression in the hairless mouse on dietary polyunsaturated fat.** Reeve VE, Bosnic M, Boehm-Wilcox C. The photocarcinogenic response was of increasing severity as the polyunsaturated content of the mixed dietary fat was increased, whether measured as tumour incidence, tumour multiplicity, progression of benign tumours to squamous cell carcinoma, or reduced survival. When mice were exposed acutely to UV radiation (UVR), a **diet of 20% saturated fat provided almost complete protection from the suppression of CHS, whereas feeding 20% polyunsaturated fat resulted in 57% suppression**; the CHS of unirradiated mice was unaffected by the nature of the dietary fat. These results suggest that the enhancement of photocarcinogenesis by the dietary polyunsaturated fat component is mediated by an induced **predisposition to persistent immunosuppression** caused by the chronic UV irradiation, and supports the evidence for an immunological role in dietary fat modulation of photocarcinogenesis in mice.

Ann Acad Med Singapore 1991 Jan;20(1):84-90. **Clinical implications of food contaminated by aflatoxins.** Hendrickse RG.

Arch Toxicol 1996;70(10):661-71. **Host resistance to rat cytomegalovirus (RCMV) and immune function in adult PVG rats fed herring from the contaminated Baltic Sea.** Ross PS, Van Loveren H, de Swart RL, van der Vliet H, de Klerk A, Timmerman HH, van Binnendijk R, Brouwer A, Vos JG, Osterhaus AD. In a semi-field study, we previously showed that harbour seals (Phoca vitulina) **fed herring from the contaminated Baltic Sea had lower natural killer cell activity, T-lymphocyte functionality and delayed-type hypersensitivity responses** than seals fed herring from the relatively uncontaminated Atlantic Ocean. A novel model was established to assess the specific T-cell response to rat cytomegalovirus (RCMV). When applied to the feeding study, no differences between the Atlantic and Baltic groups in the RCMV-induced proliferative T-lymphocyte responses could be detected, but virus titres in salivary glands of infected rats of the Baltic Sea group were higher. These elevated RCMV **titres and changes in thymus cellularity** suggest that the dietary exposure to low levels of contaminants may have been immunotoxic at a level which our immune function test could not otherwise detect. While the herring diet per se appeared to have **an effect on several immune function parameters, lower plasma thyroid hormone levels in the Baltic Sea group of rats confirmed that exposure to the environmental mixture of contaminants led to adverse PHAH-related health effects.**

Environ Health Perspect 1995 Apr;103(4):366-71 **Dioxin activates HIV-1 gene expression by an oxidative stress pathway requiring a functional cytochrome P450 CYP1A1 enzyme.** Yao Y, Hoffer A, Chang CY, Puga A. **Aflatoxin B1, 2,3,7,8-tetrachlorodibenzo-p-dioxin** (TCDD; dioxin) and benzo[a]pyrene cause a significant increases in CAT expression in mouse hepatoma Hepa-1 cells. We conclude that induction of a functional CYP1A1 monooxygenase by TCDD stimulates a pathway that generates thiol-sensitive reactive oxygen intermediates which, in turn, are responsible for the TCDD-dependent activation of genes linked to the LTR. These data might provide an explanation for findings that TCDD increases infectious HIV-1 titers in experimental systems and for **epidemiologic reports suggesting that exposure to aromatic hydrocarbons, such as found in cigarette smoke, is associated with an acceleration in AIDS progression.**

Ann Trop Med Parasitol 1997 Oct;91(7):787-93 **Of sick turkeys, kwashiorkor, malaria, perinatal mortality, heroin addicts and food poisoning: research on the influence of aflatoxins on child health in the tropics.** Hendrickse RG. Aflatoxin exposure occurs in > or = 30% of pregnancies in tropical Africa and the toxins are often in cord blood, sometimes at extremely high concentrations. Aflatoxins are now incriminated in neonatal jaundice and there is circumstantial evidence that they cause perinatal death and reduced birthweight. Aflatoxin-induced immunosuppresion may explain the aggressive behaviour of HIV infection in Africa. There are similarities between observations on HIV cases in Africa and those on heroin addicts in Europe, where 'street' heroin is frequently contaminated with aflatoxin. Aflatoxins were found in 20% of random urine samples from heroin addicts in the U.K. and the Netherlands.

Ann N Y Acad Sci 1986;475:320-8. **Hormonal approaches to immunotherapy of autoimmune disease.** Talal N, Ahmed SA, Dauphinee M.

Cell Immunol 1998 Nov 1;189(2):125-34. **Estrogen increases the number of plasma cells and enhances their autoantibody production in nonautoimmune C57BL/6 mice.** Verthelyi DI, Ahmed SA.

J Rheumatol 1987 Jun;14 Suppl 13:21-5. **Interleukin 2, T cell receptor and sex hormone studies in autoimmune mice.** Talal N, Dang H, Ahmed SA, Kraig E, Fischbach M. The **administration of estrogen to pregnant mice late in gestation results in offspring with a permanently altered immune system. These mice develop features of autoimmunity similar to those that occur spontaneously in genetically susceptible autoimmune mice. T**his phenomenon may have etiopathological significance for familial SLE.

Endocrinology 1994 Dec;135(6):2615-22. **17 beta-estradiol, but not 5 alpha-dihydrotestosterone, augments antibodies to double-stranded deoxyribonucleic acid in nonautoimmune C57BL/6J mice.** Verthelyi D, Ahmed SA.

J Autoimmun 1993 Jun;6(3):265-79 **Antibodies to cardiolipin in normal C57BL/6J mice: induction by estrogen but not dihydrotestosterone.** Ahmed SA, Verthelyi D.

J Autoimmun 1989 Aug;2(4):543-52. **Estrogen induces the development of autoantibodies and promotes salivary gland lymphoid infiltrates in normal mice.** Ahmed SA, Aufdemorte TB, Chen JR, Montoya AI, Olive D, Talal N. . . . normal mice were **prenatally exposed to estrogens.** . . . mice prenatally exposed to estrogens had accelerated development of autoimmune salivary gland lesions indistinguishable from Sjogren's syndrome (SS) in humans. Further experiments are warranted to confirm these findings. The prenatal effects of estrogen may have relevance for familial and neonatal autoimmune syndromes.

Isr J Med Sci 1988 Dec;24(12):725-8. **Sex hormones, CD5+ (Lyl+) B-cells, and autoimmune diseases.** Talal N, Ahmed SA.

Ann N Y Acad Sci 1986;475:320-8 **Hormonal approaches to immunotherapy of autoimmune disease.** Talal N, Ahmed SA,

Dauphinee M.

Life Sci 1998;63(20):1815-22. **Exacerbated immune stress response during experimental magnesium deficiency results from abnormal cell calcium homeostasis.** Malpuech-Brugere C, Rock E, Astier C, Nowacki W, Mazur A, Rayssiguier Y. These studies first showed that an **abnormal calcium handling induced by extracellular magnesium depression in vivo may be at the origin of exacerbated inflammatory response.**

Magnes Res 1998 Sep;11(3):161-9. **Early morphological and immunological alterations in the spleen during magnesium deficiency in the rat.** Malpuech-Brugere C, Kuryszko J, Nowacki W, Rock E, Rayssiguier Y, Mazur A. Dietary magnesium deficiency in rodents, and especially in rats, causes inflammation and leads to alterations in the immune response.

Ann Rheum Dis 1994 Nov;53(11):749-54 **Polymerase chain reaction fails to incriminate exogenous retroviruses HTLV-I and HIV-1 in rheumatological diseases although a minority of sera cross react with retroviral antigens.** Nelson PN, Lever AM, Bruckner FE, Isenberg DA, Kessaris N, Hay FC.

Clin Diagn Lab Immunol 1998, Mar;5(2):181-5. **Reactivity of sera from systemic lupus erythematosus and Sjogren's syndrome patients with peptides derived from human immunodeficiency virus p24 capsid antigen.** Deas, JE, et al. We have previously demonstrated that **about one-third of patients with either Sjogren's syndrome (SS) or systemic lupus erythematosus (SLE) react to human immunodeficiency virus (HIV)** p24 core protein antigen without any evidence of exposure to, or infection with, HIV itself.

J Clin Lab Immunol 1988 Feb;25(2):101-3. **Effect of diethylcarbamazine on serum antibody to feline oncornavirus-associated cell membrane antigen in feline leukemia virus cats.** Kitchen LW, Cotter SM. Department of Cancer Biology, Harvard School of Public Health, Boston. Diethylcarbamazine (N,N-diethyl-4-methyl-1- piperazine carboxamide; DEC) is a drug frequently used for prevention and treatment of the filariases. An opsonic action of DEC may generate increased immune responses to microfilariae. We tested the hypothesis that DEC treatment could result in higher antibody levels to other infectious agents. A retroviral animal model was studied, **in light of the consideration that use of DEC as an antifilarial agent could conceivably alter seroepidemiologic surveys as well as serologic outcomes of vaccine trials in Africa regarding human immunodeficiency virus (HIV).** The effect of DEC treatment on serum antibody to feline oncornavirus-associated cell membrane antigen (FOCMA) in domestic cats exposed to feline leukemia virus (FeLV) was examined. Nine cats that **tested negative before treatment tested positive (greater than or equal to 1:10 serum dilution, geometric mean titer [GMT] = 278) for antibody to FOCMA after DEC treatment.** Among 19 cats initially testing positive for FOCMA antibody, higher titers were noted after treatment in 17 (pretreatment GMT = 264; posttreatment GMT = 6,158). We conclude that a history of DEC treatment should be considered in evaluating humoral responses to infectious agents. Whether use of ivermectin, a recently introduced antifilarial agent, in lieu of DEC will affect clinical expression of HIV infection in humans also warrants analysis.