

Abstracts from the 16th Annual International Symposium on Man and His Environment in Health and Disease - 1998

The 1998 Annual International Symposium focused on the environmental aspects of endocrinology with an emphasis on estrogen mimics. This conference explored some of the latest data and provided a forum for discussion as well as case studies to help the professional.

"Allergy Patients with Autoimmune Thyroiditis: Long Term Treatment Results"

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It is essential to evaluate allergy patients for the presence of concomitant hypothyroidism because allergy patients have been shown to present with a high incidence of Autoimmune Thyroiditis.

Patients who presented for the evaluation and treatment of allergic disorders had routine history and physical examinations and skin testing referable to an allergy workup. Additionally, these patients were evaluated for symptoms related to hypothyroidism. Blood was drawn for the laboratory assessment of the presence of antithyroid antibodies.

If indicated, natural desiccated thyroid hormone (Armour Thyroid) was used to treat patients. Each patient's dosage was adjusted based upon relief of symptoms, basal body temperature, and Free (unbound) T4 levels.

The results demonstrate that thyroid supplementation, when indicated in patients with allergic disorders, provides significant improvement in the patient's overall health, well-being, and energy level.

Additionally, male and female hormonal imbalances should be addressed in all allergy patients. Both male and female allergy patients realize substantial resolution of symptoms as discussed in this study upon receiving supplementation with natural male or female hormones when indicated.

Female patients were treated with natural progesterone or natural progesterone with testosterone when indicated. In addition to progesterone, post-menopausal women were treated with Bi-Est (60% Estriol, 40% Estradiol).

Male patients were treated with testosterone and Saw Palmetto when indicated. An overwhelming number of patients who were treated for their allergies in combination with thyroid supplementation and male or female hormone replacement therapy, when indicated, reported a marked improvement in their original symptoms.

"Molds & Mycotoxins Related to Hormonal Dysfunction"

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The effects of molds via their toxins was not appreciated until about 1960, when contaminated grain was recognized as the agent responsible for the catastrophic poisoning of an English turkey farm. Evidence has been accumulating about the antimicrobial, antineoplastic, and toxic effects of these compounds. A Medline search identifies virtually every organ effected by these compounds: toxic epidermal necrolysis, the gastrointestinal tract, liver and kidney failure, myocardial infarction, pulmonary failure, inflammation, immunosuppression, and bone marrow destruction, neuropathy, and leukoencephalomalacia. The biochemical effects of these toxins has been reported to involve lipid peroxidation of membranes as well as decreased function of the respiratory function of mitochondria via interaction with cytochrome P-450. Other mechanisms involve complement lysis, binding of S-H group proteins, cross-linking of proteins, and inhibition of protein and DNA synthesis. The effect of the fungal metabolite dicumarol from substrates in sweet clover is well known. Up- and down-regulation of critical function of macrophages has been described. Blocking of receptor sites and stimulation of receptor sites (as with estrogen receptors) have both been described. The immunologic effects of molds are well known, affecting all mechanisms: IGE mediated, membrane lysis, deposition of complexes in tissue, and CMI in infection. The endocrine organs can be effected by these mechanisms. Thyroiditis is a well-recognized disease. Ovarian hormone-related effects continue to be identified. Adrenal and testicular effects are less well known.

"Ovarian & Menstrual Dysfunction"

Randolph, Rea, and all others -- environmental -- bringing it all together

1940 --Finch-- Desensitized n&v of pregnancy using progesterone

1943 -- Hansen-Pruss and Raymond-- Allergic women have highest titer of serum allergen on the last day of menstruation

1945 -- Zondek and Bromberg -- Allergic response to endogenous hormones
Intracutaneous and subcutaneous testing best Employed serial dilution Relieved allergic disease with desensitization to hormone

1949 --Phillips-- Specific dose hormone determined by skin testing

1951 -- Heckel-- Found sesame oil best; did skin test controls

1953 --Heckel-- Skin whealing positive using metabolic product of hormone
Suggested gonads are target organ for hormonal "allergy"

1974 -- Miller -- Serial end point titration technique defined improved safety and effectiveness

1980-- Crook-- The Yeast Connection

1984 --Mabray-- It works in a busy Gyn office safe and effective

1983-- Mabray -- Endometriosis & other common problems respond to "mini-hormone" Abnormal immune markers in common Gyn diseases

1989 -- Saifer & Becker -- APICH syndrome

1997-- Eaves -- Protein power

"Peripartum and Perinatal Endocrine Dysfunction"

Maternal/Fetal immunologic relationship

Clustering of obstetrical problems compatible with pollen and mold exposure -- abortion, third trimester bleeding, PIH, hyperemesis ectopic

Focus on toxemia of pregnancy familia, sex ratio of babies, Ig renal deposits, HL-A histoincompatibility, exposure to multiple semen decreases diet, stress, socioeconomic, association of eclampsia and cardiovascular risk

Hormone mimics-- reproduction, fetal consequences, major offenders, practical advice

"Estrogen Mimics"

Abnormal sexual development in reptiles, birds, and fish has been reported (2-6). It has been suggested that this feminization has been due to the presence of toxic chlorinated and nonchlorinated hydrocarbons that act as estrogen mimics. Arnold, et al. Have shown that a combination of weak environmental estrogens but strong environmental toxics such as dieldrin, endosulfan or toxaphene were 1000 times more potent in hER receptor activation as any chemical alone. Similar hypotheses have been advanced in relation to an increased risk for breast cancer in women (7, 8) and decreased human semen quality in men (9,10). Most estrogenic environmental compounds have potencies 1/50 to 1/10,000 those of DES or the natural estrogen 17 α -estradiol. The following Tables 1 & 2 show the markedly increased affinity for the binding of a combination of toxic to estrogen

receptors. Fifty patients seen in the 1980s who had two or more estrogen mimics in their blood were reviewed. In addition to their marked chemical sensitivity, many also had endocrine dysfunction.

Table 1

Chemical	β -Gal EC50(microM)
17 β -Estradiol	0.0001
Endosulfan	>33
Dieldrin	>33
Toxaphene	>33
Chlordane	ND*
Endosulfan + dieldrin	0.092
Endosulfan + toxaphene	0.121
Endosulfan + chlordane	0.189
Dieldrin + toxaphene	0.210
Dieldrin + chlordane	0.286
Toxaphene + chlordane	0.306

*The EC50 for chlordane was not measured because it did not exhibit β -gal activity at any concentration tested.

Table 2

Chemical	hER binding IC ₅₀ (microM)
Endosulfan	>50
Dieldrin	>50
Toxaphene	>50
Chlordane	ND*
17 β -Estradiol	0.001
Endosulfan + dieldrin	0.324
Endosulfan + toxaphene	0.339
Endosulfan + chlordane	0.363
Dieldrin + toxaphene	0.498
Dieldrin + chlordane	0.514
Toxaphene + chlordane	0.533

* The IC₅₀ value was not determined because chlordane did not appear to demonstrate competitive binding activity at any concentration tested. It has been reported that the IC₅₀ values for endosulfan and toxaphene are 631 and 470 microM, respectively (15).

"Chemical Sensitivity, Endometriosis, and the Immune System"

George C. Miller, II, M.D., FACOG, FAAEM

Endometriosis is a unique and intriguing process. From early descriptions by the pathologist Rokitansky in 1860 to Sampson's classical surgical description and initiation of the term "endometriosis" in 1925, we now see an increasing number of new cases. Early menarche, short cycle intervals, heavy bleeding . . . all suggest high levels of estradiol and, in fact, studies show increased levels of estradiol correlate with endometriosis. Nearly all of these patients have a personal or family history for allergy/immune problems. Many have chemical sensitivity.

The mechanism of Ground Substance Regulation vis-a-vis chemical sensitivity is also closely linked to endometriosis. Both humoral and cellular immune parameters have been described. T-cell changes, macrophage, natural killer cell and autoimmune similarities are all seen here. This affects development of ova, causes antibody disruption of fertilization, implantation failure, and early spontaneous abortion in the absence of physical scarring or damage to the pelvic framework.

Estrogen mimics, our conference topic, depicted as part of the chemical changes in our environment since World War II are illustrated by dioxin in the Rier study of the Rhesus monkey. Dioxin and PCBs are ubiquitous in "industrialized" nations.

The use of immunotherapy as championed by Arnold Kresch, M.D., using estrogen, progesterone, testosterone, LH, and Candida as part of the treatment in reducing the total load, is relatively new and may lead to new treatment advances in the future.

Obstetrician/Gynecologists or other physicians caring for the health of women will need to add knowledge of the immune system, adverse effects of chemicals in the environment, and concepts of Environmental Medicine to their armamentarium to best care for the health needs of their patients.

"Human Growth Hormone"

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Cruetzfeldt Jakob disease was originally described in the cannibals of Papua, New Guinea. They had the practice of ancestor worship, and it devolved on the women of the tribes to eat dead relatives. It was the women who developed CJD (not their male children, only those who had been cannibals). They used to eat the brain tissue raw. This has been well documented.

Other cases of CJD have been noted following the use of human growth hormone. This was extracted from the pituitary glands of cadavers at post-mortem and used again unaltered. CJD has occurred in a number of cases since then. People who have dura mater transplants have also been reported to contract CJD. Patients having corneal grafts have also developed CJD. In all of these cases it was raw brain tissue from the central nervous system that was transferred from the donor to the recipient; the cornea, for example, being adjacent to aqueous and vitreous humor and the brain through the optic nerve. Finally, CJD has appeared in patients who have had stereo-tactic surgery. It was originally thought that this could be from contamination of instruments, but it seems to be extremely unlikely that this was so because if it were then instruments used in any other brain surgery would be equally unsterilisable, and it has not been recorded that there has been an increased frequency of occurrence of CJD in other operative interventions. It could be that the type of degradation of brain material that occurs in stereo-tactic surgery is partial degradation of some cells transited by the instruments, and hence the reaction to the partially degraded material may be similar to the response from other transplanted or consumed material.

All this indicates that the most likely cause of CJD is not infected material but brain material, per se, and the histological pathological response that is seen is a rejection or inflammatory response by cells present in the central nervous system, glial cells, but not necessarily in the peripheral nervous system. There has been no similar recorded transmission of CJD from the use of muscle tissue or transplant of heart or kidneys, for example, nor, indeed, from the consumption of muscle tissue.

The reason why it is unlikely that CJD has been transmitted by pathological tissue in these cases is because the incidence of CJD in the general population is one in a million; hence, the likelihood that the donors of dura mater, pituitary gland, and corneal grafts had CJD is infinitesimal. CJD is, therefore, unlikely to be due to a virus and far more likely to be due to a brain component from which anyone can be at risk, if there is raw or contaminated brain linked to material being transferred to the recipient, or their consumption of the raw brain or spinal neurological tissue.

Bovine Spongiform Encephalopathy (BSE) shows very similar histological features to those of CJD, but there is one further factor, which is that in the direct cases of CJD there is human to human transmission. With BSE, it is likely that there was sheep to bovine transmission, and perhaps with the new variant of CJD consumption of brain tissue by humans and cross-species, sensitization of some brain components is the most likely scenario. If the conclusion drawn from these observations is true, then the consumption of brain tissue/spinal cord or contamination by transplant of CNS related tissue is the only risk of new variant CJD being contracted from BSE cattle. CJD, new variant, and BSE can both be eradicated by measures to avoid such exposure.

It becomes totally unnecessary to cull cattle because the condition is neither a viral disease nor a contagious agent, except that it can be contracted with live central nervous system tissue exposure.

Association between consumption of squirrel brains and CJD has been reported in the Lancet. These creatures are obviously not going to have been fed artificially as they are wild, and this association corroborates the other findings reported in this paper.

"Light and Melatonin: What's new?"

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Melatonin, the chief secretory product of the human pineal gland, is regulated by the prevailing light/dark cycle; melatonin levels in the blood are 5-15 times higher at night than during the day. Exposure to light at night causes a rapid drop in blood melatonin levels. Thus, light is a "drug" by virtue of its ability to suppress melatonin production. The consequences of the use of light at unusual times, i.e., at night, may be substantial because it suppresses melatonin. In particular, the regular suppression of nocturnal melatonin may (1) alter sleep processes, (2) induce fatigue and disrupt circadian rhythms, and (3) enhance free radical damage. In reference to the latter effect, in recent years melatonin has been shown to be an effective antioxidant; thus, its reduction by light allows free radicals to go unimpeded and damage macromolecules. The resultant damage is related to a variety of diseases, in particular, a number of neurodegenerative conditions of the aged. In experimental models, melatonin has been found to combat neuronal damage associated with Alzheimer's and Parkinson's disease. The loss of neurons in these conditions is generally accepted to be related to free radicals. Additional conditions where melatonin has proven effective include the destruction of brain tissue in models of porphyria, hyperexcitability, and stress. Finally, a primary cause of aging is believed to be accumulated free radical damage; this is known as the free radical theory of aging. Thus, the reduction in melatonin production with age may be significant in determining the rate at which an individual ages and the likelihood that an individual may develop a free-radical related disease. Since light suppresses melatonin, excessive use of light may accelerate the accumulation of free radical damage in cells.

References:

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"Environmental Incitants of Endocrine Dysfunction"

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It has been shown that many toxic chemicals influence the endocrine system. At the Environmental Health Center-Dallas a large percentage of patients who have proven chemical sensitivity have these toxics in their blood. A series of patients was reviewed and found to have a diverse response. Thyroid, adrenal, ovarian, and testicular abnormalities were found. These will be discussed in detail.

"Overcoming the Carcinogenic Effects of Xenoestrogens and Even Reversing End-Stage Cancers"

Sherry A. Rogers, M.D., FABFP, FABEM, FACA

Since government studies confirm that at least 50-90% of human cancers are caused by diet and environmental chemicals, attempts to reverse and heal damaged pathways has produced optimistic results when applied to prevention of cancers, as in the example of the inhibition of xenoestrogen-induced breast cancers. More importantly, when all that medicine has to offer has failed, collation of scientific evidence from such pillars as Harvard and N.I.H. has been used to reverse and heal metastatic end-stage cancers in humans in some cases.

This includes reinstating processes of cellular redifferentiation, genetic reprogramming of mutant p53 cancer-promoting genes, dumping of bioaccumulated xenobiotics, re-establishing gap junctional (connexin) proteins, utilizing enzymes to dissolve the sialoglycoprotein protection about cancer antigen-antibody complexes (which now makes them vulnerable to the host's immune system attack), inhibiting enterohepatic recirculation of carcinogenic hormones, and special nutrients (including minerals, vitamins, amino acids, essential fatty acids, orphan nutrients, lipotropes, and phytochemicals that heal xenobiotic transformation), and using a nontoxic mineral that provides relief from morphine-resistant cancer pain. Case examples will demonstrate.

References:

1. Falck, F., Jr, A. Ricci, Jr., et al. "Pesticides and Polychlorinated Biphenyl Residues in Human Breast Lipids and Their Relation to Breast Cancer." *Archives Environmental Health* 47 (1992): 143-46.

2. Heerdt, A.S., W.J. Young, et al. "Calcium gluconate as a Chemopreventive Agent in Breast Cancer." *Israel J Med Sci* 32:2-3 (1995): 101-105.

Over 1,000 references on various aspects of the program can be found by contacting Prestige Publishing, Box 3161, Syracuse NY 13220 (1-800-846-6687) and obtaining the following two books:

Rogers, S.A. *Wellness against All Odds*. Syracuse, NY: Prestige Publishers.

Rogers, S.A. *Depression Cured at Last*. Syracuse, NY: Prestige Publishers.

"Melatonin: Functional Significance in Sleep, Jet Lag, and as an Antioxidant"

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Melatonin has been widely investigated in terms of its effects on sleep, in the treatment of circadian rhythm disorders, e.g., jet lag, and as an antioxidant. Melatonin's precise role as a sleep aid continues to be debated with some researchers claiming it is an essential component of physiological sleep mechanisms in humans while others state that the sleep inducing properties of melatonin are only pharmacologically relevant. When melatonin does promote sleep, the mechanisms by which this is achieved may involve any of several interactions of melatonin. Thus, melatonin may be a direct soporific, i.e., merely cause sleep onset when it is administered. Secondly, rather than being a soporific agent, it may alter other underlying sleep mechanisms and thereby "open the sleep gate." Finally, melatonin may only influence sleep by changing the underlying circadian phase of sleep propensity. While melatonin may have utility in treating sleep problems in young and middle-aged individuals, there is also considerable interest in its use in the elderly as well as where sleep inefficiency is often observed. The loss of sleep efficiency in the aged may relate to the loss of the melatonin rhythm, which occurs naturally in the aged. Since melatonin has the capability of adjusting the biological clock, its use in the treatment of jet lag has also been considered. The mechanisms to accomplish this may be very similar to those that show melatonin is beneficial for sleep. Since melatonin has the capability of changing circadian rhythms and endogenous melatonin is normally elevated at night, when melatonin is administered to humans, it is typically given just before bedtime. The use of melatonin not only has potential utility for sleep and jet lag but also for use in shift workers and as an antioxidant. In this latter context, there is currently considerable interest in the use of melatonin in forestalling some of the signs of aging, since a primary theory of aging involves the accumulation of essential molecules damaged by free radicals, which are now known to be scavenged by melatonin.

"Environmental Effects of El Niño"

Douglas Seba

As noted in the speaker's previous paper, the earth is a water planet and changes there will have strong terrestrial effects. El Niño, the name given to the natural periodic warming of seawater off the west coast of South America, is part of a larger phenomenon called the Southern Oscillation which has dramatic, worldwide weather effects. The world's populations are becoming increasingly vulnerable to the natural disaster cycle of extreme weather events, which have profound effects on health.

Immediate health effects of death, starvation, and infectious disease capture headlines. However, extreme weather events present evolutionary challenges and opportunities to the global ecology and all the flora and fauna dependent on it.

The human race is not exempt from this ecology crisis, and by examining changes in wildlife distribution, we can learn things about our strengths and weaknesses that would not be apparent in times of normal weather patterns. Whether it is the appearance of a new disease in Caribbean soft corals or an excess of rattlesnakes in southern California, we are all tied to the same weather event.

"Oceanic Estrogen Mimics"

Douglas B. Seba

"Estrogen mimics" is a currently popular press term for a subset of adverse health effects from the broader category of hormone dysfunction or, more properly, the emerging science of endocrine disruptors. The term is given to any artificial substance that assumes or inhibits the normal functioning of natural hormones. Many of these xenobiotics are pesticides, plastics, detergents, and other everyday chemicals. Often, these pollutants disrupt the steroid hormones, which commonly determine sexual characteristics and behaviors. Since the mother directly passes the contamination that affects the fetus's growth with lifetime impacts that may become visible only in adulthood, the phrase estrogen mimic has been coined to express this linkage.

The earth is a water planet with far more biomass in the ocean than terrestrial. The fluid nature of the sea and the air above it ensures rapid distribution of these chemicals and makes it likely that the first effects of endocrine disruptors might be noted in an aquatic environment.

The current alarm over estrogen mimics is really an old story, first popularized in 1962 by Rachel Carson's book *Silent Spring*. The fate and transport of these chemicals has been a focus of the speaker's research for several decades and contemporary findings will be reviewed.

"Carbohydrate Science"

Robert Siegal, M.D.

Most illnesses early in the Twentieth Century were acute. Penicillin quickly cured a Strep throat. Today illness is often chronic and resistant: rheumatism, diabetes, lupus, cancer even heart attacks are end states of chronic disease.

Modern medicine offers no quick cure "penicillin" for the immune dysfunction which underlies chronic illness. Fifty percent of Texas internists, usually limited to treating symptoms, are frustrated. Half our population seeks alternative health care.

But a century ago, an immune stimulant was discovered. Doses of E. Coli endotoxin quickly cured animal sarcoma. They also killed the host.

Recently, Carrington Laboratory simulated that immune response. Instead of bacterial liposaccharide, they used Aloe polysaccharides to modulate immunity, gaining USDA approval for animal tumors.

The activator switch was decoded. KDO, 3 deoxy octulosonic, 2 keto D mannose activated giant Mono-Macrophages to orchestrate up regulated/down regulated cellular/humeral immune cascades of T and B cells, cytokines, and chemokines.

The docking mechanisms of Mannan trigger-receptor, key-lock bonding is now defined using crystal graphics, etc. A C-type, mannose oligosaccharide, trimeric recognition domain proves a primordial sensor structure to discriminate Non Self from Self molecules.

The Mannose tri cone geometric binding model traces throughout life species. Mannan/mannose binding domains offer acute and chronic inflammatory pathways and critical metabolic pathways. In the extracellular matrix, they serve Macrophages patrolling vital organ sites (liver, kidney, spleen, brain, and more) to defend tissue and serve Fibroblasts to repair tissue.

Their docking mechanisms specialize as species evolve. In mammals, long chain mannans, resistant to pepsin digestion, are ingested intact by Endosomes, customized by lysozymes and synthesized in the Reticulum and Golgi organelles. They also build Glyco Protein membrane receptors, which identify pathogens: virus, bacteria, tumor, mycobacteria, damaged molecules, toxins.

Mannose phosphate receptors also serve molecular salvage, clearance, and tissue repair and even remodel envelopes to prevent viral docking.

Hence, natural safe Aloe mannans offer potentials for a wide spectrum approach to support immune wellness health care.

"Functional Imaging in Clinical Diagnosis Management"

Theodore R. Simon, M.D.

Functional information has long been sought as aiding in diagnosis and clinical management. The development of fast data processing capabilities has permitted an expanded opportunity to extend this information into two, three and sometimes four dimensions. This information may be electrical, magnetic, electromagnetic, biochemical, thermal, and even mechanical. These data have traditionally been divided into various specialties with the onus placed on the clinician for integration into specific clinical applications.

Recent developments are speeding and objectifying the integrative process making the diverse imaging and correlative information into a metaimage that succinctly displays functional information over multiple modalities. Diagnosis and management thus become increasingly orderly, which facilitates communication with patients. Such orderliness may also be useful in communicating diagnostic and therapeutic strategies to interested third parties with regard to reimbursement or legal issues. Various innovative imaging and metaimaging strategies are discussed and their clinical applications are considered especially with regard to endocrinology, neurotoxic responses, and psychiatry.

"Thyroid Dysfunction and the Environment"

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At present, no less than 200 million of the world's population have goiters and associated diseases, resulting in a public health and socio-economic problem of major proportions. A large number of agents in the environment, both naturally-occurring and manmade, are known to affect the thyroid gland. Agents that cause thyroid enlargement or goiter are known as environmental goitrogens. Antithyroid compounds may enter into the food, water, and air exposure pathways, becoming an important environmental goitrogenic factor in man. We demonstrated that Vitexin, one of the three major flavonoids in Pearl millet, exerts clear in vivo antithyroid effects, providing direct evidence that flavonoids are the goitrogens in this staple food of people with goiter living in the semiarid tropics, an ecological zone that almost encircles the earth. Flavonoids, which are present in a large number of food plants, are an obligatory step and integral part of the biogeochemical cycle of organic goitrogens in nature. Coal is also a source of a large variety of antithyroid and goitrogenic compounds contaminating supplies of drinking water. The most abundant of these pathogenic organic compounds are phenol and dihydroxyphenols, thiocyanate, disulfides, hydroxypyridines, substituted dihydroxybenzenes, phthalate esters, phthalic acids, and halogenated and polycyclic aromatic hydrocarbons. Many of these organic pollutants, which are present in drinking water from iodine-sufficient goitrous areas, form dissociable complexes with large

organic molecules called humic substances (HS). Decaying organic matter plants and animals become the substrate of lignin and flavonoid types of HS during fossilization or coalification. Thus, flavonoid structures are the link between phenolic goitrogens in foodstuffs and those present in coals, shales, soils, and water. Finally, microorganisms in soils and water, as well as in the gastrointestinal tract, play an important role in the process of biomagnification or activation of many food and coal-derived organic goitrogens. Results of this investigation emphasize the importance of our environment in the etiology of disease and provide basic information to develop cost-effective medical and/or public health measures to prevent and/or treat goiter and its associated disorders.

"Androgen Deficiency in Adult Women"

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The ovaries and the adrenals of women secrete androgens. The total amount of androgenic hormones produced by a young healthy adult woman approaches 60 to 70% of what a healthy young man secretes. A young woman produces daily an average of 19 mg of dehydroepiandrosterone (DHEA), 2 mg of testosterone, 1.5 mg of androstenedione, and 0.3 mg of dihydrotestosterone and many other androgens that influence her health. In comparison, a young adult man produces moderately more androgens: approximately 30 mg of DHEA, 7 mg of testosterone, 0.8 mg of androstenedione, and 1.5 mg of dihydrotestosterone.

Similar to the age-related decrease in female hormones, the production of "male" hormones, androgens, progressively declines with age in women, bringing women slowly into a certain degree of androgen deficiency. This age-related androgen deficiency expresses itself in physical signs (muscle hypotrophy and hypotonicity, decreased muscular strength, increased abdominal fat and cellulite, etc.) and mental complaints (excessive emotionality, fatigue, lack of sexual drive, etc.), which decrease or even disappear with adequate androgen replacement therapy. Results of laboratory tests for androgen levels appear in female androgen deficiency either completely under the lower reference values or as borderline low values (as most aging women have rather moderate forms of deficiency). A carefully monitored androgen replacement therapy may be indicated and able to improve the quality of life and the global health of the treated women.

An overview of the scientific literature on the subject is given, accompanied by information on how to manage androgen deficiency in women (diagnosis, therapeutics, follow-up, and safety).

"The Andropause and the More Moderate Degrees of Androgen Deficiency in Men"

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Similar to the female perimenopause and menopause, an androgen deficiency appears in aging men generally in a slower, more progressive manner, which may ultimately lead to a real male climacteric, or "andropause." The most common cause of this androgen deficiency is a progressive aging of the whole hypothalamo pituitary gonadal axis, which occurs at practically all tissue levels, bringing slowly the target cells into a clinical androgen deficiency.

This age-related decay of the gonadal axis is reflected in abnormal laboratory test results (low testosterone and dihydrotestosterone blood levels, high estradiol, estrone and SHBG blood levels, low testosterone and androsterone urine levels) and in physical symptoms (small wrinkles, muscular hypotrophy and weakness, dryness of mucosal membranes, hot flushes, etc.) and mental complaints of androgen deficiency (excessive emotionality, lack of mental strength and resistance to stress, depression, etc.). Consequences of persistent androgen deficiency are important and can be debilitating: cardiovascular diseases, obesity, osteoporosis, diabetes, and overall aging.

An overview of the scientific literature on the subject is given in this lecture. Focus is on how to manage androgen deficiency in men (diagnosis, therapeutics, follow-up, safety).

"The Menopause and Perimenopause in Women: Symptoms, Consequences, and Treatment"

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Deficiencies of female hormones appear in women not only at menopause, but already in the perimenopause, the period of eight to ten years that precedes the menopause. The different levels of the hypothalamo pituitary ovarian axis age with time in the adult woman. The ovaries end up secreting insufficient progesterone and oestradiol. The target

cells get progressively in a female hormone disbalanced state, which finally results in a severe female hormone deficiency at menopause.

Progesterone deficiency symptoms (excessive breast tenderness, menorrhagia, increased occurrence of anxiety, irritability, aggressiveness, especially premenstrually, etc.) appear rather early and progressively in the aging adult woman, often years before estrogen deficiency symptoms occur. Physical signs of estrogen deficiency (dropping breasts, vaginal dryness, upper skull hair loss, small wrinkles, etc.) and psychic complaints (permanent fatigue, depression, lack of sex drive, etc.) appear also progressively in the aging woman. These symptoms regress mainly through adequate female hormone replacement therapy.

Female hormone replacement therapy in the perimenopause and menopause can counter adequately the effect of these hormone deficiencies. The consequences of not treating these hormone disbalances or deficiencies in female patients are not to be underestimated: increased risk of cardiovascular diseases; osteoporosis; (possibly) diabetes; breast, ovarian, and uterine cancer; and, last but not least, acceleration of overall aging.

An overview of the scientific literature is given on the subject and special focus is on how to manage estrogen and progesterone deficiency in women (diagnosis, therapeutics, follow-up, safety).