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REVIEW ARTICLE

STRESS, STEROIDS, AND "OJAS" : NEUROENDOCRINE MECHANISMS AND CURRENT PROMISE OF ANCIENT APPROACHES TO DISEASE PREVENTION

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Abstract: Recent research on causes of disease and aging has increasingly supported the importance of stress. One theory of the relationship between stress and disease is based on the concept of homeostasis, a term coined by Cannon over 50 years ago to signify those states and mechanisms responsible for the "staying power of the body". Bernard, Cannon, Selye and other leading researchers held that full, normal function of the self-regulating or homeostatic power of the body maintains the balanced, integrated condition we recognize as health. Failures in this capacity, such as those produced by frequent stressful experiences, can result in disease or death. Theories of health and disease surprisingly similar to this have existed since ancient times, and in widely different cultures. This review discusses both the fundamental elements of these theories and the current neuroendocrine research supporting their validity and immediate relevance. The connections between ancient and modern knowledge described herein were made possible largely by the work of Maharishi Mahesh Yogi, a scholar and teacher of the ancient vedic tradition of India. A key part of Ayurveda that has been obscure to modern science is the substance "ojas", which the classical texts say maintains balance of the physiology. In this article, specific steroids or steroid classes are proposed as likely candidates for both the "ordinary" and the "superior" types of ojas described in Ayurveda. Current evidence for the functions of these steroids, as well as their role in stress, disease and the maintenance of health, is reviewed. The knowledge of Ayurveda, as recently brought to light by Maharishi, includes methods for recovering and maintaining optimal function of steroidal systems. Such effects may help mediate the improvements in health and increased longevity attributed to Ayurveda and other ancient methods.

Key words: homeostasis cholesterol hypothalamus resistance aging steroids prevention

INTRODUCTION

In recent decades, the proportion of the economy going to medical care has risen steadily in most advantaged countries. For example, in the United States it has increased from 9.4% in 1980 to 14% in 1990, and is projected to reach 18% by the year 2000 (29). Although little discussed, disease prevention may be

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one of the more promising approaches to halting or reversing this trend (71). Because of reductions in communicable diseases and mortality rates achieved mainly through improvements in sanitary conditions and per capita food supply, the diseases most prevalent today in modern countries are disorders related to life style or stress (129, 162). Thus, further gains in health will likely come through substantial reduction of individual stress and improvements in life style (71, 127). These areas have proven particularly resistant to the approaches of modern medicine due in part to the incomplete understanding of the role of stress in disease and how to prevent or deal with the deleterious effects of stress (36, 49, 50, 59, 60, 71, 91, 93, 129, 191, 230).

Stress has long been considered a major factor in ill health and disease (59, 60, 93, 185, 190). However, only recently has clinical research begun to rigorously demonstrate some of the mechanisms involved (36, 70, 88, 91, 126, 150, 168, 171, 180). An important part of the advance in understanding concerns "chronic stress", that is, prolonged stressful experiences or frequent intermittent stressful experiences. Chronic stress appears to distort, for varying lengths of time, the neuroendocrine mechanisms responsible for maintaining physiological stability in the face of environmental change (126, 168, 170-172). Additionally, chronic or frequent stress places a constant load on these homeostatic or adaptive mechanisms. Both the chronic load and the distortions in regulatory mechanisms appear to weaken resistence to subsequent environmental challenges, resulting in ill health and disease (126).

Cannon and Selye were among the first in modern times to investigate the mechanisms responsibile for maintaining stability of the organism in the face of environmental change. Cannon focused mainly on the role of the autonomic nervous system in maintaining the relatively stable conditions of the bodily fluids under acute challenge (30). Selye, however, focused largely on the role of steroids (185, 187, 190). In extensive animal studies, he found that different steroids can either maintain, increase or decrease the resistance of the body to environmental chemicals and other types of stressors (187). In further animal studies, he identified "pluricausal" diseases, that is, diseases which arise from specific combinations of prior learning experiences (conditioning) and acute stressors (188). Here also, a particular steroid or steroid class was found to protect the organism while another was found to exacerbate the disease. More recent research has extended his findings by showing that stress-related changes in the level or regulation of various steroids can alter the organism's ability to adapt to, or cope with, environmental challenge (7, 88, 91, 93, 126, 166, 168, 171, 228). This same research also describes the ways in which these changes contribute to disease and aging.

Steroids are, of course, important to many other aspects of normal function besides protecting against environmental change. They play key permissive, mediative and regulatory roles in sex and reproduction, growth, the differentiation and maintenance of tissues, regulation of food intake and metabolism, and, as recent evidence suggests, also in emotional and mental function. Thus, any technique or procedure for reducing stress and strengthening the well-being and resistance of the body might be expected to have a major influence on adaptive mechanisms, and in particular, on those mechanisms involving steroids.

The legacy of prevention in the West is usually traced to ancient Greece (52). The Hippocratic writings contain knowledge attributed by the Greeks to the goddess Hygeia and summarized as follows : "...both health and disease are under the control of natural laws and reflect the influence exerted by the environment and the way of life. Accordingly, health depends upon a state of equilibrium among the various internal factors which govern the operations of the body and the mind; this equilibrium in turn is reached only when man lives in harmony with his external environment" (52). The Hygeian school also held that health is the natural order of things, a positive attribute to which men are entitled if they but govern their lives properly. This view further concluded that "...the life of the patient as a whole is implicated in the disease process," and that "...the cause [of the disease] is to be found in a concatenation of circumstances rather than in the simple direct effect of

some external agency" (52). These views are quite similar to the conclusions of modern science mentioned above, namely, that ill health and disease often result from a combination (or concatenation) of circumstances. In particular, when linked with the long-term effects of stress on adaptive mechanisms, a new environmental challenge can overcome the natural internal balance and resistance of the organism (88, 91, 93, 126, 168, 171, 230).

The understanding from early Greece of the causes ad prevention of disease thus bears a striking resemblance to a modern understanding that continues to gather support. Since the Hygeians believed health to be a man's birthright, and felt it to be attainable by wise living, it seems likely that early Greek culture also had concrete physical and mental ways of aiding the process of achieving or maintaining health. The main purpose of this integrative review is to suggest that this is not only likely but highly probable. Some of the procedures described in the available accounts of ancient Greek medicine appear in fact to have been intended as preventive measures. Moreover, other ancient cultures, including those of Egypt, China, and India, had both an understanding of disease and what appear to be preventive technologies similar to those of the Greeks. However, rather than to focus solely on written reports of the preventive medical knowledge of Greece, or of any other country where written reports are all that remain of the ancient knowledge, this review will center on the Ayurvedic medical system of India, which is still in use today in India and other parts of the world (10).

OJAS AND EQUILIBRIUM OF THE DHATUS

A. Properties and functions of ojas : Ayurveda (from the Sanskrit "ayus", meaning life or life span, and "veda", meaning knowledge or science, hence the "science of life or of life span") is thought to be one of the best preserved systems of traditional medicine currently in practice. Some say it has been in use continuously for over 8000 years (43). Ayurveda contains descriptions of the causes and preventation of disease that agree well with those in the Greco-Roman tradition. Furthermore, with the aid of modern science, some of the more obscure meanings of Ayurvedic texts and practices are beginning to be understood in familiar terms.

The classical ancient treatises of Ayurveda have been broadly classified into two groups: the Brihat trayee (greater triad) and the Laghu trayee (lesser triad) (176). Caraka Samhita, Sushruta Samhita and Ashtanga Sangraha (or, as some scholars claim, Ashtanga Hridaya) make up the former, while the latter group consists of Madhava Nidana, Sharngadhara Samhita and Bhavaprakasha. The dates of these six texts are not certain, but they are said to have been written by different scholars of the tradition which originated with the direct cognition of this knowledge by Bharadvaja (31). Caraka, who is considered in Northern India to be the most famous of these scholars, appears to have flourished in the eighth century B.C. (31). The classical texts of Ayurveda not only describe the symptoms, causes and treatments of over a thousand diseases, along with hundreds of detailed surgical practices, but contain extensive discussions of preventive methods on the levels of mind, body, behaviour and environment (31, 32, 176, 208, 214).

The Ayurvedic texts state that: "The very object of this science [Ayurveda] is the maintenance of the equilibrium of the tissue elements [dhatus]" (Caraka, Sutrasthana, I. 53). Accordingly, Ayurveda defines disease as "any disturbance in the equilibrium of dhatus" and defines health as "the state of their equilibrium" (Caraka, Sutrasthana, IX. 4). This ancient system of medicine also has a "theory of natural homeostasis" which states that "the dhatus come to normalcy automatically irrespective of any external causative factor" (Caraka, Sutrasthana, XVI. 27). This is similar to the belief attributed to Hippocrates that the sick body calls into play natural forces that tend to restore the disturbed equilibrium and re-establish health, the concept communicated in the famous expression, "*vis medicae naturae.*"

The prime purpose of Ayurveda, therefore, appears to be to maintain "equilibrium of the dhatus", or what might today be called homeostatic balance or a balanced state of functioning of the homeostatic

mechanisms. Disturbance in the equilibrium of the dhatus, which is responsible for pathologic states, is believed to arise from factors which in modern terminology would be called "stressors." These include "wrong utilisation, non-utilisation and excessive utilisation of time, mental faculties and objects of sense organs" (Caraka, Sutrasthana, I. 54). These give rise to "...three types of diseases: endogenous, exogenous and psychic" (Caraka, Sutrasthana, XI. 45).

Translators of the original Ayurvedic texts have defined dhatus in a number of ways, e.g., as "tissue elements", "root or fundamental principles", and "supports." Dhatus are reported to be transformed and transported in the physiology via "shrotas" (Caraka, Vimanasthana, V. 3), which can be translated as channels for the flow of information, but may specifically refer to the secretory cells and organs, including what appear to be descriptions of neurons and nerve tracts (Vagbhata, Sarirasthana, III. 41-48).

Within the context of modern knowledge, the dhatus would appear to be regulatory substances or hormones. Likewise, the shrotas may be surmised to mediate and include neuroendocrine pathways for regulating these hormones, including various feedback and feedforward mechanisms. If this interpretation is correct, then it would not be surprising to find that improper function of the shrotas could also be a source of disease. In fact, shrotas whose functions are obstructed or "vitiated" (having impaired value or quality) are also identified in Ayurveda as important contributors to the etiology of disease (Vagbhata, Sarirasthana, III. 41-42).

The classical texts of Ayurveda (31, 176, 208, 214) define the following eight dhatus: 1) rasa dhatu (principle upholding the first products of ingested food), 2) rakta dhatu (principle upholding blood), 3) mamsa dhatu (principle upholding muscle), 4) medas dhatu (principle upholding adipose tissue), 5) asthi dhatu (principle upholding bone), 6) majja dhatu (principle upholding bone marrow), 7) shukra dhatu (principle upholding semen or sperm in males and ovum in females), and 8) sattva dhatu (principle upholding mind or mental faculties). Sometimes only the first seven of these are mentioned. The eighth, sattva dhatu, was probably overlooked in some cases because it is not as clearly linked to a visible, material tissue or substance as the other seven. Here we include sattva dhatu because it is mentioned in several of the verses (e.g., Caraka, Vimanasthana, VIII. 102, 110-114). The dhatus are said to arise from or find their essence in a material called "ojas". Some commentaries divide ojas into two types, the "ordinary type", which exists in large quantity (1/2 anjali, which is translated and 1/2 double cupped handful, in the whole human body; Caraka, Sarirasthana, VII. 15; Vagbhata, Sarirasthana, III. 80-82), and the "superior type", found in much smaller quantities (eight drops; Caraka, Sutrasthana, XVII. 73-75, and commentary).

Ojas is described as a precious material substance which acts as the "vital power" or "quintessence of all fundamental principles" responsible for sustaining life and regulating balance throughout the physiology (Sushruta, Sutrasthana, XV. 23). In addition to being the "essence of the dhatus", ojas is said to be a material which "pervades all over (the body)" (Vagbhata, Sutrasthana, XI. 37-38). It is said to be a solid substance and is described by adjectives such as "white" (Sushruta, Sutrasthana, XV. 25), "unctuous", and "greasy" (Vagbhata, Sutrasthana, XI. 37-38). Diminution of ojas is said to result from fear, weakness, grief, anger, fatigue, starvation and cheerlessness (Caraka, Sutrasthana, XVII. 73-75; Astanga, Sutrasthana, XI. 39-40). The texts also state that "Loss of ojas amounts to the loss of life itself." (Caraka, Sutrasthana, XXX. 9-11). Optimal levels of ojas are responsible for strength, power of resistance, contentment, and improved digestion (Sharngadhara, Prathama Khanda, V. 18; Vagbhata, Sutrasthana, XI. 41; Sushruta, Sutrasthana, XV. 31). Milk and ghee (clarified butter) are often mentioned as being particularly conducive to production of ojas (e.g., Caraka, Sutrasthana, XIII. 14; XXVII 217-224).

The "seat" of ojas (superior type) and of the dhatus is called the "hridaya", which is translated as, "the heart" (Caraka, Sutrasthana, XXX. 6-7). In this context, heart clearly does not refer to the central organ of the circulatory system. The portions of the texts associating ojas with hridaya refer to hridaya as that

organ "...indespensible for all the normal mental and physical activities...", and as "...the controller of the mind" (Caraka, Sutrasthana, XXX. 6-7) as well as "...the primary seat of consciousness" (Sushruta, Sarira Sthanam, IV. 35). This hridaya is said to be "the breadth of two fingers" (Caraka, Vimanasthana, VIII. 117), implying certainly not the whole of the brain, but perhaps a part. Hridaya is also said to be the source of sensory reflexes and perception (Caraka, Sutrasthana, XXX. 6-7). A number of "vessels" which aid in the manifestation and regulation of ojas are reported to be attached to the hridaya. These "great vessels" are said to represent entities such as the mind, intellect and consciousness [Caraka (2nd translation), Siddhisthana, IX. 4] (32). In other parts of the texts, the term hridaya clearly sometimes refers to the heart of the circulatory system, since it is associated with veins, arteries, capillaries and the flow of the blood (Vagbhata, Sarirasthana, III 18-38).

B. Proposed chemical identity of ojas: If these descriptions from Ayurveda of the source of pathological states and the maintenance of health are to be accorded validity, there should be identifyable equivalents in modern medicine of both the ordinary and superior types of ojas. Here we propose what appear to be the most likely candidates, based on the current knowledge of physiology and health. First, if indeed ojas does exist as a material substance, then it is highly unlikely that western physiology would not have detected a substance present in such a large quantity (1/2 a cupped double handful, estimated at between 100 and 160 grams). Of the various substances which might appear to be reasonable candidates (e.g., a specific hormone, neurotransmitter or other signaling substance) only cholesterol, precursor of all steroid hormones, is found in the body in the appropriate amount. The total cholesterol of the human body is estimated at between 140 and 150 grams (116), in the same range as the quantity indicated for ojas in Ayurvedic texts. At room temperature cholesterol is a white crystalline solid, having a melting point of 148.5°C, consistent with the description of ojas as a "white solid." Further, ojas is also referred to as "unctuous" and "greasy." Cholesterol is a non-polar molecule having lipid-like characteristics. The food items milk and ghee, which are said in the Ayurvedic texts to be conducive to ojas, are known to be high in cholesterol (115). The main question, then, is whether cholesterol and its derivatives could fit the descriptions applied in the Ayurvedic tradition to the two types of ojas. In fact, evidence supporting the affirmative answer is extensive, and is presented here in abbreviated form. (See also summary in Table I.)

TABLE I : Summary of Parallels Supporting the Equivalence of Ojas and Steroids

Ayurveda	*Modern Science*
Principal Ojas :	
Ojas is responsible for sustaining life and regulating physiological balance.	Cholesterol is a vital membrane component necessary for life and is crucial for balance.
1/2 anjali (100-160 g) of ojas pervades the body.	Approximately 150 g of cholesterol are distributed throughout the human body.
Ojas is a white, untcuous, greasy solid.	Purified cholesterol is a white, lipid-like solid.
Milk and clarified butter increase ojas.	Milk and butter are high in cholesterol.
"Loss of ojas is loss of life." Diminished ojas is associated with anger, grief, fear, cheerlessness, etc.	Low levels of plasma cholesterol are associated with violence and suicide, with depression in the elderly, and with antisocial personality and aggressive behavior.
Derivatives or "Superior Types" of Ojas :	
Ojas is the "essence of the dhatus." "Superior types" of ojas may be synonymous with the eight dhatus.	Cholesterol is the precursor of steroid hormones, which can be logically organized into five or more action groups.
The eight dhatus are the fundamental principles or essential	Five or six principal-action or synthetic-pathway groups of

elements upholding the seven tissues and one 'activity' type.	cholesterol derivatives match well with the description of specific dhatus; two are less certain, based on currently known steroids.
Disease is defined as "any disturbance in the equilibrium of the dhatus" and health as "the state of their equilibrium."	The presence and appropriate regulation of most steroids are vital to health; their absence or poor regulation usually results in disease or death.
Excessive, wrong or non-utilization of body and/or mind causes disturbances in the equilibrium of the dhatus.	The modern concept of "stressful experience" is any experience that leads to a change in function that is principally detrimental to the organism.
Dhatus are transformed or transported through "shrotas", or channels for the flow of information; impairments in the value or quality of shrotas causes or contributes to disease.	Most specific steroids are regulated through complex "axes" involving neural and endocrine regulatory molecules and extensive modulatory and feedback mechanisms; dysfunction of any of these can contribute to or cause disease.
The hridaya or "seat" of ojas is said to aid in functions of ojas and to be the breadth of two fingers—also said to be the seat of mind, soul or mental operations.	The hypothalamus (about two fingers wide) plays the major role in regulating the conversion of cholesterol to its derivatives—also vital for emotions and mental operations.
Increase or decrease of the structure or function of the shrotas leads to disease.	Disturbances in endocrine axes which cause a chronic increase or decrease of hormones or alters their regulation results in disease.
"Ojas marks the beginning of the formation of the embryo. It is the nourishing fluid from the embryo." Ojas formed in the body of the fetus moves to the body of the mother, and *vice versa*.	Estrogen from the embryo helps trigger implantation. Steroid hormones are critical in all phases of pregnancy, with either hormones or precursors passing from the fetus to the mother and *vice versa*.

In humans, cholesterol is a vital structural component of biological membranes and thus of every bodily tissue, being especially high in the brain and spinal cord. Therefore, cholesterol "pervades all over (the body)." In addition to the effects of cholesterol on the fluidity and viscosity of plasma membranes and on maintenance of the osmotic and electric gradients across the membrane, and of electrical stability of the membrane (116), cholesterol is known to prevent lipid peroxidation in cell membranes (156), and to be required for cell growth, DNA synthesis, cell differentiation, and phosopholipid synthesis (239). Moreover, cholesterol and/or other steroids have been found in virtually all biological organisms so far examined (i.e., invertebrates, vertebrates, bacteria, fungi and plants) (136, 235). Although some primitive organisms apparently lack steroids *per se*, they do have related chemicals originating from the isopentenoid pathway that seem to mimic the role of steroids (136). Thus the existence and vital importance of steroids throughout evolution provides another circumstantial link between cholesterol and ojas, consistent with the Ayurvedic description of ojas as the "vital power" responsible for sustaining life (Sushruta, Sutrasthana, XV. 23).

Interestingly, lower levels of the evolutionary chain are characterized by a number of "dominant" steroid precursors, as well as the greatest diversity of different precursor types (13). In contrast, at higher levels of the evolutionary chain, cholesterol assumes an increasingly dominant position, so that in vertebrate organisms it becomes the principal steroid and precursor to all other active steroids. Such a convergence from the diversity of steroids and steroid precursors in lower forms of life to less diversity and the sole dominance of cholesterol as precursor in higher forms may suggest a kind of evolution or selection process (13).

Excessively high blood levels of cholesterol are a well known risk factor for atherosclerosis and coronary heart disease. Hence, like virtually all physiological substances, cholesterol levels must be maintained within a specific range to avoid deleterious effects on the body. In Ayurveda a number of unpleasant psychological states (e.g., fear, weakness, grief, anger, fatigue, and cheerlessness) are said to

diminish ojas and also are ascribed to diminished levels of ojas (Caraka, Sutrasthana, XVII. 73-75; Vagbhata, Sutrasthana, XI. 39-40). Similarly, in recent research, abnormally low levels of plasma cholesterol have been associated with increased depression in the elderly (133), increased death from suicide and other violent acts (61), increased antisocial personality (218), increased homicides (219), and increased aggressive behaviour in monkeys (106). Some have reported that the increase in non-cardiac mortality due to excessively lowered cholesterol offsets any benefits that the lowered cholesterol might have in reducing coronary heart disease (138). Aside from its vital role in the cell membrane, cholesterol is required for physiological resistance, since it is the precursor of the steroid hormones and bile acids, with their essential regulatory and digestive roles. Such roles are entirely consistent with the functions attributed to ojas in Ayurveda. Thus, the proposed equivalence of ojas and cholesterol appears to uphold the unified view in Ayurveda that health arises from the "homeostatic" or "equilibrium" conditions maintained by ojas.

C. Proposed identity of the dhatus: Another set of correspondences which may support the identification of ojas as cholesterol arises from the relationship between ojas and the dhatus. Some of the commentaries on the Ayurvedic texts speak of the "superior types of ojas" or higher expressions of ojas (e.g., Caraka, Sutrasthana, XXX. 6-7). Thus, because ojas is said to be the "essence of the dhatus", and there are eight dhatus (see comment above), the possibility arises that the ordinary or general form of ojas is transformed into each of these dhatus. It is well known that cholesterol is the common precursor of all steroid hormones. Furthermore, two centuries of research on cholesterol and its derivatives, resulting in 21 Nobel prizes as of 1993, have clearly demonstrated the biological importance of these steroids for growth, reproduction and health. Thus, the following paragraphs (summarized in Table II) propose matches of each dhatu described in Ayurveda with a specific steroid or steroid class.

Since it is beyond the scope of this article to discuss in detail the diversity of steroid endocrinology, this review emphasizes only the proposed relationships of steroid functions to the dhatus described in Ayurveda. It is worth noting that although a given steroid or steroid class usually has one role which is considered its primary function, increasing evidence indicates that most steroids also can act in other capacities in many systems and in the overall development and maintenance of the organism; see for examples (132, 227). Following are the proposed matches of each dhatu with specific steroids or steroid classes known to exist in the human body.

TABLE II. The Dhatus or Principles Upholding the Tissues, and Proposed Matching Steroids

	Dhatus	*Tissue, Product or Function Upheld*	*Steriod Class (Examples)*
1.	Rasa	First product of injested food—plasma or chyle	Bile acids (cholic acid, chenodeoxycholic acid)
2.	Rakta	Blood (blood pressure)	Cardiac-active steroids (digoxin-, digitalis- and ouabain-like compounds)
3.	Mamsa	Muscle tissue	Anabolic steriods (testosterone derivatives)
4.	Medas	Adipose tissue, fat	Glucocorticoids (cortisol)
5.	Asthi	Bone	Vitamin D_3 (1, 25-Dihydroxyvitamin D_3)
6.	Majja	Bone marrow	Androgen derivatives (metabolites of 5β-androgen and 5β -progestin)
7.	Shukra	Semen or sperm (male)	Androgens (testosterone)
		Ovum (female)	Estrogens, progesterone (17 (β)-estradiol, estrone, estriol)
8.	Sattva	Mental faculties, spirit, mind, consciousness	Neurosteroids and anesthetic steroids (pregnenolone-S, DHEA-S)

(1) "Rasa dhatu", the first dhatu, is generally understood to be the principle upholding the first product of injested food. "Rasa" is sometimes translated as plasma or chyle, and the various descriptions of rasa dhatu fit with the functions ascribed in Western physiology to bile acids or bile salts. These steroidal derivatives of cholesterol are the major secretion products of hepatocytes, constituting 50% of the organic components of bile. They exert detergent-like properties essential in the absorption and digestion of fats. Proper synthesis and metabolism of bile acids are essential for cholesterol homeostasis and for effective liver function. Problems with the synthesis of bile are important in various liver diseases and can lead to gallstones (53, 57). Aside from fat absorption, bile salts are involved in other aspects of digestion. For example, unconjugated bile salts stimulate pancreatic secretion, whereas conjugated bile salts tend to inhibit pancreatic secretion and to decrease cholecystokinin levels (131).

Although bile salts appear to be the principal steroids involved in early digestion, other steroids are also of relevance. For example, vitamin D and its metabolites play a key role in calcium absorption as well as in stimulation of mucosal proliferation (19). Corticosteroids affect intestinal ion transport (165). In fact, expression of the gene for the mineralocorticoid receptor appears higher in gastrointestinal tract than in the kidney (72). In addition to exerting effects on digestion and absorption of food, steroids also appear to play a role in appetite, feeding behaviour, and selection of food. Mineralocorticoid (or type I) receptors may modulate fat intake, whereas glucocorticoid (or type II) receptors may control carbohydrate ingestion (209). Also, administration of testosterone propionate appears to decrease caloric intake in rats (107).

(2) The second dhatu is "rakta dhatu", which is generally translated as the principle sustaining blood. We interpret rakta to signify aspects of the blood such as its buffering ability against extremes of pH, the regulation of its pressure and total volume, and variations in activity of the cardiac muscle, rather than signifying the 45% of the blood which consists of the formed elements. (The formed elements are covered under another dhatu—see below.) The other 55% is the plasma, primarly composed of water and proteins. The Ayurvedic texts state that "Decrease of rakta produces... loss of tension of veins (and arteries) and dryness" (Vagbhata, Sutrasthana, XI. 17), which may support the above interpretation.

During the last decade, mounting research supports the existence of endogenous cardiac steroids in man, such as a ouabain-like compound indistinguishable from the plant-derived cardenolide (87), as well as digoxin-like (216), and digitalis-like (48) compounds from the steroid family known as cardiac glycosides. These chemicals are specific and potent inhibitors of Na^+-K^+-ATPase, the enzymatic component of the sodium-potassium pump responsible for maintaining the gradient of these ions across plasma membranes. Such mechanisms are important in blood volume and pressure regulation, pH homeostasis, ionic fluxes, cardiac muscle contraction, pregnancy, inhibition of renin secretion and promotion of vasoconstriction (84, 215). The existence of these compounds may have clinical implications for a range of cardiac disorders, particularly hypertension (84, 233, 234, 237). A number of other adrenal steroids also have important cardiovascular roles. For example, the principal mineralocorticoid, aldosterone, plays a crucial role in the renin-angiotensin system of electrolyte regulation, particularly sodium resorption and potassium excretion in the distal tubules of the kidneys (80). And stress-induced alterations in aldosterone metabolism may play a key role in hypertensive heart disease (91, 229).

(3) From the steroids currently known, the proposed identity of the third dhatu, "mamsa dhatu", which maintains muscle tissue, is the whole class of anabolic steroids. These include testosterone and its derivatives, which of course also exhibit androgenic effects in addition to anabolic effects. Although these steroids have numerous and potent effects on muscle, the possibility remains open for discovery of a steroid or steroid class whose primary function is maintenance of muscle. Among the roles of androgens in muscle, testosterone is known to increase muscle mass and muscle protein synthesis (81), as well as oxygen consumption and nitrogen-retention by muscle (132),

and mitotic activity in myoblasts (152). In skeletal muscle a number of direct biochemical changes, e.g., increased glycogen synthesis, enhanced RNA polymerase activity, and increased phosphorylation and uptake of 2-deoxyglucose (132), all occur in response to increased anabolic steroids. Specific receptors located in cardiac muscle respond to androgens, inducing biochemical and morphological changes as well as an enhanced growth-hormone-mediated cardiac growth. Castration of rodents appears to inhibit cardiac muscle growth in addition to decreasing the contractile force of cardiac muscle, which has been linked to a reduction of Ca^{2+}-myosin ATPase activity. In smooth muscle, testosterone appears to increase muscle size and weight (132).

Other steroids are also important in the maintenance or function of muscle tissue. For example, it is now clear that skeletal muscle is a target tissue for vitamin D or its metabolites. The influences of vitamin D include increasing phosphate uptake into muscle, increasing synthesis of contractile proteins and regulation of intracellular Ca^{2+}, such as in the sarcolemmal membranes which play a key role in the contraction-relaxation cycle (23). Chronic high levels of glucocorticoids can cause muscle atrophy, apparently in part through induction of glutamine synthetase (64) and elevation of myofibrillar protease activity (183). Such effects, however, are reversible with exercise (64).

(4) For the fourth dhatu, "medas dhatu", or principle upholding adipose tissue, there is ample evidence supporting the role of steroid hormones in, for example, distribution, accumulation and metabolism of fats. As in the case of muscle, however, a steroid or steroid class whose primary function is maintenance of fat tissue has not been discovered. Furthermore, a number of diseases (e.g., diabetes mellitus and cardiovascular diseases) have been associated with obesity (111). These involve apparent contributions from both elevated glucocorticoids and suppressed sex steroids. Glucocorticoids have direct effects on adipose tissue which are mediated through specific receptors (157), both in adipose precursor cells and in the fully differentiated adipose tissue cells, of which the largest number is located in the intra-abdominal region (158). In the presence of insulin these steroids stimulate lipoprotein lipase activity, the main enzyme regulator of lipid uptake, and enhance differentiation of adipose precursor cell systems (75).

Sex steroids appear central to the gender-related differences in regional fat distribution (e.g., larger adipocytes and deposits in the gluteo-femoral region for females, and specific fat localization in truncal-abdominal regions for males). However, no detectable receptors for female sex steroids have been located in fat, and their effects may be indirect (157). On the other hand, progesterone can compete with glucocorticoids for glucocorticoid receptor sites, and enhances lipoprotein lipase activity specifically in the gluteo-femoral region (20). Androgens, however, have specific receptor sites with regional specificity for increasing lipolysis (20). Administration of the adrenal androgen, dehydroepiandrosterone, results in antiobesity and antidiabetic effects, apparently through enhanced hepatic glucose oxidation and supression of gluconeogenesis (128, 236). As a whole, differential sensitivity to steroids may explain why adipose tissue is not regulated homogeneously, with different steroids exhibiting fat accumulating or mobilizing effects, depending on the anatomical region. Stressful experiences can cause chronic neuroendocrine dysregulation, altering glucocorticoids and sex steroids. Such effects of stress may underlie deleterious changes in the expression and regulation of adipose tissue (25, 159).

(5) The proposed identity of the fifth dhatu, "asthi dhatu", or principle upholding bone, is unambiguous. Vitamin D, especially its biologically active form 1,25-dihydroxyvitamin D (1,25 $(OH)_2D$), is essential for life in higher animals due in part to its well established, pivotal role in the homeostasis of bone calcium and phosphorus. Historically this seco-steroid and its metabolites have had clinical significance for the healing of rickets and other metabolic bone disorders. The presence of $1,25(OH)_2D$ is known to promote differentiation of bone cell precursors—both osteoblasts (regulating bone formation) and osteoblasts (regulating bone reabsorption)—most likely by its effects on a number of cytokines (18). Calcitonin,

parathyroid hormone and $1,25(OH)_2D$ comprise the core hormones involved in bone physiology. In addition to the classical effects on bone remodeling, Ca^{2+} resorption in the kidneys, and intestinal Ca^{2+} absorption, $1,25(OH)_2D$ has a vast array of physiological and pathological effects important for general health and development. These include effects on the muscular, gonadal, hepatic, immunological, hematopoietic, cardiovascular, lymphatic, integumental and neuronal systems (227).

(6) From the available literature and known steroids, the most probable identity of the sixth dhatu, "majja dhatu", or principle upholding function of the bone marrow, is the 5β-androgen and 5β-progestin metabolites. The bone marrow comprises the seedbed of our blood, from which pluripotential stem cells give rise to various committed progenitor cells, which in turn produce virtually all differentiated blood cells. The 5βmetabolites of the C-19 and C-21 steroids testosterone and progesterone have been shown to induce the rate-limiting enzyme required in heme and globin biosynthesis, δ-aminolevulinic acid synthase, thereby regulating porphyrinogenesis and heme synthesis (177). These steroids also have both direct and indirect (i.e., through erythropoietin) effects on bone marrow. They stimulate the population of pluripotential stem cells, regulate stem cells destined for heme-synthesizing erthyroid precursor cells, and regulate the early burst-forming units and the late progenitor spleen colony-forming units (14,200). Castration of male rats results in a four-fold decrease in platelet aggregration compared to normal values, which are ten times higher than in females (103). Replacement of testosterone restored the responsiveness level to that of uncastrated males.

Evidence from many species has indicated that pluripotential stem cells of bone marrow have a unique receptor response to these steroids, independent of virilizing or reproductive mechanisms (11). The effects of estrogens on erythropoiesis and stem cell production appear opposite to those of the androgens (148). Either hypophysectomy, adrenalectomy, thyroidectomy or orchidectomy results in depression of erythropoiesis, which is reversed by administration of the appropriate hormones (149). In the case of adrenalectomy, decreased cell fragility and development of reticulocytosis are also apparent (78). Administration of testosterone propionate promotes earlier and faster recovery when the hematopoietic system is damaged by agents such as x-irradation and chemotherapy (97).

(7) "Shukra dhatu", the seventh dhatu, refers to the principle upholding semen or sperm in males and the ovum in females. The proposed identity with the sex steroids is supported by the massive volume of literature available on the importance of these substances in reproduction, growth and secondary sex characteristics. Though not absolutely necessary for life, these steroids are required for propagation of the human species. All reproductive tissues are largely dependent on androgens, which exert numerous roles in prenatal and pubertal development. Testosterone is essential for spermatogenesis; it alone is able to restore sperm production in hypophysectomized rats. Growth of the prostate, structural and functional integrity of the seminal vesicles, penis morphology, gametogenesis and sperm maturation in the epididymis, vas deferens, etc. all depend on testosterone and/or 5α-dihydrotestosterone (132). Steroids, at least in part, are responsible for membrane destablization during capacitation, the conditioning period for sperm in the female reproductive tract which is necessary for fertilization (77). In general androgens are essential in sexual organogenesis and overall sexual behaviour/ mood, although their relevance to libido is still controversial.

Female sex steroids are well known to be responsible for development of secondary sex characteristics in young women as well as for the maintenance of proper function of reproductive organs and ovarian follicle maturation during the typical 28-day menstrual cycle. Estrogens and progesterone exhibit vital roles in the preparative stages for pregnancy, such as in ovum transport, decidualization, implantation, endometrial cell proliferation and differentiation, as well as in the embryogenesis, maintenance and delivery stages (3). During pregnancy such steroids, and others, are involved in the collaborative interaction between the mother and fetal-placental unit. For example, the

anti-inflammatory and immunosuppressive qualities of progesterone seem necessary to avoid rejection of the products of conception. Ayurveda also notes the importance of an interaction of ojas from the mother and fetus, especially in the eighth month of pregnancy (Caraka, Sarirasthana, IV. 24; Vagbhata, Sarirasthana, I. 62-63).

Male fertility persists into old age but is marked by a decrease in virility and in the levels of bioavailable androgens (217). In contrast, most female mammals lose fertility during midlife. The ovary has been proposed to act as a pacemaker in what is called "ovary-dependent neuroendocrine aging" (65). Evidence for a role of ovarian hormones in aging may support a more general theory that aging is "event-dependent" (e.g., a result of hormonal and neural events or cascades) rather than "time-dependent" (65). The effects of chronic stress on the female reproductive system may involve sex steroid changes. For example, elevated estrogens may mediate psychogenic blockage of pregnancy (120). Similarly, diminished testosterone and sex drive as a result of chronic stress in males may be caused by effects of elevated glucocorticoids on brain neurons involved in the regulation of testosterone (35).

(8) The eighth and final dhatu is "sattva dhatu", or that which upholds the "mental faculties, spirit, mind or consciousness" (Caraka, Vimanasthana, VIII. 102, 110-114). This implies regulation of information processing, states of "wakefulness" or "arousal", and the like, all of which are largely based on the actions of the central nervous system. About 50 years ago Hans Selye reported that several 3 α-hydroxy, A-ring-reduced pregnane steroids have anesthetic and sedative-hypnotic properties (184). More recently, strong evidence has supported the existence of "neurosteroids", steroids which are produced by, and influence events within, the central nervous system independent of peripheral aid (12). Glial cells, and possibly neurons, have the capacity to synthesize new steroids such as pregnenolone and dehydroepiandrosterone (DHEA) from cytochrome P_{450} catalyzed side-chain cleavage of cholesterol, and, upon further oxidation, progesterone (104). Such steroids remain high in the brain even after adrenalectomy and gonadectomy combined (161). The actions of some of these endogenous steroids mimic those of benzodiazapines and anesthetic barbiturates (125). Specifically, neuroactive steroids such as allopregnanolone and allotetrahydrodeoxycorticosterone are some of the most potent ligands of the type A receptors for γ-aminobutyric acid (GABA), the principal inhibitory neurotransmitter of the brain. These effects may be either agonistic or antagonistic, and, at low nanomolar concentrations, are capable of enhancing GABA-activated Cl^- currents to levels comparable with the most potent barbiturates (155). In rats under the influence of acute stress, neuroactive steroids are observed to rapidly increase to levels capable of modulating $GABA_A$ receptor activity (155). Oral administration of either DHEA or pregnenolone is known to enhance memory retention in rodents (66-68). If such mechanisms are present in humans, it is possible that these steroids could be useful in treating amnesia or other memory disturbances. New effects of steroids on one or another aspect of brain function are reported on a frequent basis, making it likely that the role of steroids in the brain includes those categories of function listed under "sattva dhatu." It also is highly likely that other neurosteroids remain to be discovered.

Thus, the derivatives of cholesterol appear to fit the required characteristics of the dhatus remarkably well, and, therefore, add support to the proposal of cholesterol as the ordinary or general ojas. Among the proposed matches of specific steroids or steroid classes with the eight dhatus, steroids satisfying the principle functions of that dhatu, and often even steroid classes deriving from separate metabolic pathways, exist for six—bile acids, cardiac-active steroids, "vitamin D", the 5β metabolites of the androgens and progestins, the sex steroids, and the neurosteroids. Although various steroids have been proposed to match the other two dhatus (the ones upholding muscle and fat), these steroids are better known for other functions. Thus, it is possible that individual steroids or steroid classes other than those named above may yet be found which will be better matches for these two dhatus.

D. Relevance of ojas to the "hridaya", the "shrotas", and disease: Based on this analysis of ojas

in terms of current knowledge of neuroendocrinology, re-examination of the interpretation of "hridaya", the "seat" of ojas, in relation to the shrotas and disease may be useful. As discussed earlier, due to the properties ascribed to the "hridaya" by Ayurveda, this part of the physiology probably corresponds to some region of the brain. Of the various brain regions or endocrine glands which might be reasonable candidates, the hypothalamus, which plays a central role in neuroendocrine information processing, including steroid regulation, appears the most likely. Neuronal activity within the hypothalamus also mediates or modulates emotional states and has numerous regulatory influences on the autonomic nervous system and on the entire internal environment, including regulation of blood pressure and heart rate, body temperature, water and electrolyte balance, and feeding behaviour (109, 110). Most of these functions are either mediated or modulated by steroids whose levels are regulated by activities in the hypothalamus. Therefore, to speak of the hypothalamus as the "seat" of ojas would be consistent with the chief proposal of this review. Further, the size of the hypothalamus matches relatively well the physical dimensions attributed to the hridaya by Ayurveda, i.e., the "breadth of two fingers" (Caraka, Vimanasthana, VIII. 117).

Not only does identifying hridaya as the hypothalamus appear consistent with the proposed steroidal identity of ojas, it also may add strength to the interpretation of the "shrotas" described above. "Shrotas" is usually translated as openings, channels or pathways of flow (e.g., Sushruta, Sarirasthana, V. 4). External shrotas are identified as the orifices of the body (Vagbhata, Sarirasthana, III. 40). However, for the internal shrotas, because Ayurveda has a general word for veins and arteries ("siras"), and separate words for arteries ("dhamanis"), capillaries ("rasavahinis"), and ducts ("nadis") (Caraka, Vimanasthana, V. 9), which are seldom used in the context of ojas and its functions, it is not likely that the term shrotas refers to any of these. Rather, the internal shrotas, which are also said to be the "seats of life" or "the seats of the activities essential for existence of life" (Vagbhata, Sarirasthana, III. 41-42) appear to represent, especially, the activities of secretory cells and glandular tissues, including what appears to be neurons, and specifically including those activities of the hridaya which aid in the transformation and function of the dhatus (Vagbhata, Sarirasthana, III. 41-48, and commentary; Caraka, Vimanasthana, V. 3). The most probable correlate that would include the idea of flow is the neuroendocrine communication channels, such as the different neuroendocrine axes, with their feedback and feedforward loops. For example, the hypothalamic-pituitary-adrenocortical (HPA) axis and the hypothalamic-pituitary-gonadal (HPG) axis regulate adrenal corticoids and sex steroids, respectively. Steroid hormones regulate (and are regulated by) other endocrine and neurotransmitter substances in numerous interactions, or "flows of information", vital to the integrity of the whole body. For example, the glucocorticoids, key among the hormones regulated through the HPA axis, exert powerful regulatory influences on the activity of the HPG axis (35), as well as on most other cells of the body.

The Ayurvedic texts list the signs of "vitiations" or abnormalities of the shrotas that can lead to disease. These include : "increase or decrease of structure or function, formation of lumps, tumors, thickenings, etc. and movement in unusual or wrong paths" (Vagbhata, Sarirasthana, III. 45). In parallel, modern research has identified situations in which abnormalities develop in a specific axis. Often these involve enlargement (or shrinking) of a gland such as the adrenal, and usually result in hypersecretion or hyposecretion of a given steroid or other hormone. Such abnormalities tend to result in a proliferation of imbalances, which in turn lead to disease.

A prime example may be found in the glucocorticoid cascade hypothesis of disease and aging (171); the feedback effect of elevated glucocorticoids (normally activated during stressful experiences) down-regulates the number of adrenocorticoid receptors in the hippocampus, leading to temporary deficits in glucocorticoid regulation. If glucocorticoids are increased on a frequent basis, a more permanent receptor loss is observed, and a more permanent impairment of negative feedback mechanisms results. In rodents this ends in chronic hypersecretion of cortisol. In man, evidence suggests that such deficits

of adrenocorticoid regulation can be partly responsible for a variety of common diseases and pathophysiological states, including hypertension, arteriosclerosis, osteoporosis, muscle atrophy and probably depression as well as other mental or behavioral disorders (89, 91, 93, 168, 171, 174). Cancer is another disease which appears to be made more probable by excessive glucocorticoid levels (169). Likewise, glucocorticoids and other steroids exert powerful influences on the immune system which may alter susceptibility to diseases (15, 41). Thus, the Ayurvedic identification of impaired value or quality of these shrotas as a cause of disease appears consistent with the modern understanding of the relevance of the multiple functions of the neuroendocrine axes to health.

In one last example supporting the likelihood that ancient Ayurvedic masters were referring to steroids when they used the term ojas, their understanding of the importance of ojas in implantation and pregnancy is discussed. Various passage concerning the role of ojas in these vital functions are rather uniquely interpretable in terms of steroids. For example, Caraka states : "Ojas marks the beginning of the formation of embryo. It is the nourishing fluid from the embryo." (Caraka, Sutrasthana, XXX. 9-11) Steroid hormones are critical in conception and in all phases of pregnancy (3). Particularly interesting is evidence that the preimplantation embryo synthesizes steroids and that its synthesis of estrogen may be part of the trigger for implantation (42). Changes in estrogens and progesterone (which later come from the placenta but even then are dependent on the fetus for precursors) provide signals initiating or maintaining most other stages of the process. Throughout much of pregnancy, especially the later stages, the dehydroepiandrosterone needed for synthesis of estrone and estradiol is provided largely by the embryo (205). This may be the "nourishing fluid" spoken of in the translation above as coming from the embryo. Another translator of the same passage of Caraka renders it, "The ojas, ...which is the initial essence of embryo and also the essence of its nourishing material..." (32).

Steroid hormones and hormone precursors such as pregnenolone and dehydroepiandrosterone, as well as cholesterol itself, pass easily through cell membranes. Due in part to this property, maintaining the proper levels of specific steroids in fetal, placental and maternal circulations is an elaborate, collaborative process which changes dramatically at several stages of pregnancy (205). For example, the fetus depends on the mother for essential precursors (cholesterol or pregnenolone), while the mother depends on the fetus and placenta (which gets most of its 19-carbon precursors from the fetus) for progesterone, estrone and estradiol. That Ayurveda had knowledge of such a relationship at the time the texts were written is illustrated in other passages as well; for example, "...the ojas formed in its [the fetus'] body moves to the body of the mother and *vice versa* through the channels carrying nourishment from the mother to the fetus because of the immaturity of the fetus" (Caraka, Sarirasthana, IV. 24).

Further verifying the importance and intricate nature of steroid regulation by fetus, placenta and mother are recent studies of how the fetus is protected from some of the maternal hormones. For example, the fetus would be harmed by the higher cortisol (as much as 75-fold) in the maternal bloodstream, but is protected by enzymatic inactivation of cortisol by the placenta. In fact, there is recent evidence that inability of the placenta to adequately inactivate cortisol may contribute to hypertension in later life, due to glucocorticoid-induced changes during intrauterine development (56). The fact that exposure to high glucocorticoids, even shortly after birth, can cause impairments lasting a lifetime has recently been demonstrated in the rat (130).

The classic Ayurvedic texts place emphasis on the eighth month and after the end of the ninth month as dangerous times for childbirth (Caraka, Sarirasthana, IV. 25). The truth of such claims has been well documented by modern science (205). Part of the reason for this seems to be that near the end of the eighth month the adrenal gland of the fetus undergoes its second (and final) major growth spurt. Ayurveda attributes the danger of this time to the "unsteadiness of the ojas" which gives rise to "...wavering feelings of joy and sorrow" in the mother and similarly in the

fetus (Caraka, Sarirasthana, IV. 24). Increased emotional lability involving marked and frequent mood swings have been noted, especially in the third trimester (113). Furthermore, the mothers questioned about these mood swings specifically noted that "...it was more difficult to relate them to a precipitating event than had been possible before pregnancy" (113). It is easy to envision the likelihood that this period would involve major oscillations in steriods as the fetal contribution is magnified. It is also easy to imagine that premature birth would expose the fetus to major adaptive needs at a time when the adrenal gland has not fully established its independent control mechanisms. Likewise, the wavering feelings of the mother during this time, and the prolonged depression which often occurs following parturition, may be due in part to altered control of her own adrenal secretions, especially glucocorticoids (121), which are well known to be related to depression.

If the proposed equivalence of ojas with the body's steroids is indeed correct, then there is another important aspect to understanding the links between ojas and disease. Steroid hormones show potent abilities to regulate expression of specific genes (2, 35, 82, 147, 210, 213, 238). This property of steroids is critical to developmental processes and to adaptation to the constantly changing envrionment. Steroid hormones induce (or occasionally inhibit) different genes depending on the steroid and the cell in which it is acting (2, 35, 238). The particular genes whose expression is activated or inhibited by a given steroid are intricately coordinated to form a "web" or "network" of appropriate changes throughout the body (2, 238). Thus, it is easy to see how chronic stress or other disturbances that lead to deficiencies or excesses of one or more steroid hormones could have wide-ranging detrimental effects.

The rapid, primary effects of cortisol in the rat liver, for example, are estimated to involve regulation of 50 genes by this steroid (2). It is not known, however, how many secondary changes in gene expression may be brought about by the products of these primary actions. In insects, where such studies are simpler to perform than in mammals due to the rapid growth rates and short life cycles, a single steroid hormone, ecdysone, coordinates the molting cycle. It induces six major new sites of RNA synthesis in the primary step. After some time, the products of these genes, in the secondary response, activate expression of another 100 genes (2). It can be anticipated that similar processes occur in humans, albeit probably more complex and over much longer periods of time.

This coverage of some of the key material on ojas has attempted to give a reasonable appreciation of its potential significance to health and disease, as seen through a modern interpretation related to stress, steroids and hypothalamic function. The review will now return to its central theme, namely, ancient approaches to disease prevention. Certainly, if ancient traditions of medicine had this deep an appreciation of the factors responsible for health and disease, they also must have had methods for preventing disease and optimizing health.

ANCIENT METHODS FOR OPTIMIZING HEALTH

As discussed above, stress is coming to be accepted as a major cause of disease (59, 60, 91, 93). On the other hand, progress in this field has been hampered due to confusion over the nature, origin, and even the definition of stress (96, 112, 190, 230). Understanding stress may be most meaningfully approached in terms of the homeostatic mechanisms responsible for the stability of the whole organism. Weiner (230) delineates evidence for defining stress in such organismic terms. In speaking of the effects of altering communication channels involved in homeostasis, he states: "Any perturbation of one component of the feedback loop may radically alter the quality of the signal. The concept of perturbation leading to a change in function is central to, and the basis of, stress theory." Weiner does not, in fact, attempt to define the term stress, but speaks only of "stressful experience", that he defines, more or less, as the entire, active process of an organism's perception of and reaction to a change, challenge or obstacle in the dynamic envrionment. While this approach may be unduly broad, it appropriately emphasizes the relationship to adaptive mechanisms, and allows different individuals to perceive the same envrionmental event as stressful or not stressful, with different

implications for health. Thus, as implied in the above quote, the most important characteristic of the stressful experience may be the physiological mark it leaves on the organism as a whole. Weiner seems to say that in situations where perturbing the organism results in a reduction of its adaptability to future environmental changes, then this perturbation, with all its biological effects, constitutes a stressful experience. Explicitly or implicitly, similar definitions have been given by others (91, 93, 96, 112).

Therefore, since stress appears to depend upon the whole organism, including past experiences or conditioning, present perception of the situation, and mental/physiological response, the possibility arises that stress can be reduced or eliminated by enhancing the organism's adaptive mechanisms, changing its perception of the situation, or both. This appears to have been the objective of many ancient procedures for prevention of disease and enhancement of health. Here these approaches have been divided into "mental" and "other", recognizing of course that the mind must play a role in many of the other approaches. The discussion will focus on mental techniques, both because research is most extensive in this area and because consciousness appears to have been understood in a far more profound way by many ancient traditions than in most current views.

A. ANCIENT MENTAL TECHNIQUES FOR ELIMINATING STRESS AND ATTAINING PERFECT HEALTH

1. Mental techniques and the field nature of consciousness:

Most ancient traditions appear to have had mental techniques for preventing disease and optimizing health. In general these techniques promote experiences of what some have referred to as "the deep structures of consciousness" (198). Others have described these experiences as progressive stages in adult growth, or "higher states of consciousness" (4). Systematic procedures for having these extraordinary experiences have existed in the major traditions of Asia, and in the philosophical and medical traditions of ancient Greece. Religious leaders worldwide also have emphasized the value of such experiences, and many of the greatest philosophers, artists, and scientists throughout history (e.g., Plato, Descartes, Wordsworth and Einstein) have reported not only having had such experiences, at least occasionally, but also that the experiences were partly or wholly responsible for their creative genius (27, 198). These experiences, and, in the ancient traditions, techniques promoting them, are consistently reported to produce beneficial effects on mental and physiological functioning (4, 100, 135, 139, 191, 198).

In the Vedic tradition, and to varying degrees in other ancient traditions, such experiences are related to a completely /different view of the nature of consciousness than the views currently prevalent. On one extreme, as described by Sperry (206), some modern scientists have held that consciousness is nothing more than an epiphenomenon of brain activity, or even worse, an error in terminology or mirage of semantics. On the other extreme, and this camp includes some of the most successful neuroscientists, such as Sherrington (199), Granit (79), Penfield (146), Eccles (151), and Sperry (206, 207), are those who endow consiousness with the ability to direct important aspects of brain function, whether they treat it as a separate entity interacting with and determining the brain's activity or as an "emergent property" of the brain. In between these extremes are those who propose consicous agency to be just another type of brain activity, a sort of supervisory level, with mutually exclusive sources of data regarding its function, namely, subjective experience or "what-that-brain-activity-'feels'-like", on the one hand, and objective data obtained from the (sensorily-mediated) instrumental observation of brain activity on the other (118).

The Vedic tradition, however, holds the view, said to be based primarily on direct experience, that consciousness is a field of pure intelligence, vastly greater than (and the ultimate source of) the individual nervous systems through which it is experienced. One of the most pointed statements of this from Rik Veda (I.164.39) has been translated as follows: "The verses of the Veda exist in the collapse of fullness (the kshara of 'A') [the arising of qualified states] in the transcendental field, self-referral [pure] consciousness,

the Self, in which reside all the devas, the impulses of creative intelligence, the laws of nature responsible for the whole manifest universe. He whose awareness is not open to this field, what can the verses [sounds of the Veda] accomplish for him? Those who know this level of reality are establised in evenness, wholeness of life" (124). The self-referral or pure consciousness state described above is the unqualified state of the field (before the 'collapse'), and the individual's experiences of thoughts, perceptions, etc. are excited or qualified states of the field, expressing through the material structures of the physiology [also explained by Hagelin (86)].

By analogy, the Vedic view of consciousness appears similar to the operation of a television set, where specific modifications of the electromagnetic field are transduced by the electronics of the television to produce a visual image on the screen. In this analogy, the unperturbed (unqualified) carrier frequency of the electromagnetic field parallels the "pure consciousness" state, and the modulations of the carrier frequency which are transduced into images on the screen parallel the excited or qualified states of the consciousness field, i.e. those that manifest as the thoughts, perceptions and emotions of individual consciousness.

This view of consciousness as a field, found in many Eastern philosophical traditions, draws considerable support from the areas of quantum field theory and superstring field theory (39, 40, 85, 99, 105, 143), rational empiricist philosophy (198), developmental psychology (4, 6) and direct experiments on a social scale (44-46, 140, 141).

A requisite characteristic or property of consciousness is "self-awareness." In field theory, an Abelian field such as electromagnetism shows no self-interacting behaviour, but non-Abelian gauge fields, such as the gluon field of quantum chromodynamics and the grand unified field, do possess this ability (85). Self-interaction appears to be a prerequisite for, or an attribute of, self-awareness. As field theorist Hagelin has analyzed in detail, the most consistent and well supported unified field theories in physics can be realistically described in terms identical to those used to describe the characteristics of "pure consciousness" in Eastern traditions (85, 86). Maharishi Mahesh Yogi and Hagelin have proposed that the unified field of natural law approximated by these theories is identical with the field of pure consciousness, as experienced through the Transcendental Meditation technique (85).

In philosophy, many angles of approach to consciousness as a field are supported by empirical data regarding subjective experience. Perhaps the most widely known is the experience of 'Self', the nonlocalized or unbounded source of the localized, individual 'self', and the ultimate source of all creativity, which, as reviewed by Shear (198), has been reported as a direct experience and discussed at length by philosophers and creative geniuses of the West, as well as its frequent mention in Eastern traditions.

Developmental psychologists have shown that the "pure consciousness" state, and the three other "higher states of consciousness" described in the Vedic tradition, fit stringent criteria for being called "higher", relative to the conceptual or representational level characteristic of the usual waking consciousness of adults (4). Further, Alexander and colleagues (4) have argued that due to the now extensive research showing growth of these experiences in "average" people who have learned Transcendental Meditation (in other words, not limited to a few remarkable people), the progression of each individual towards the highest of these states is in all probability the normal situation. Progress along this continuum of stages of consciousness appears to have been halted or "frozen" in most people by an excess of stressful experiences and/or the absence of exposure to the appropriate developmental technologies (4).

Planned experiments in which individuals are randomly assigned to procedures promoting the experience of pure consciousness or to control procedures with similar instructor attention and time investment provide compelling evidence for facilitation of adult development of the sort predicted to occur from repetion of such experiences (4, 6). Similar studies also provide evidence for benefits in the areas of reduction of stress and improvement of health (22, 191).

Furthermore, in a remarkable series of studies based on the apparent ability of groups of people simultaneously having the "pure consciousness" experience to enliven the qualities of the field in the surroundings, decreases in factors such as war deaths, suicides and crime rates have been reported (44-46, 141).

In sum, psychological research such as the above appears to demonstrate that no unusual personality characteristics are necessary to have the transcendental or pure consciousness experience or to derive distinct benefits from the practice of techniques which promote such experiences. However, growing evidence supports the conclusion that many techniques available today, especially those devised in a modern clinical setting as opposed to those based in an ancient tradition of knowledge, lack effectiveness at producing pure, self-referral consciousness and also may be relatively ineffective at producing any specific benefits whatsoever (7, 58).

"Transcendental Meditation", the technique that will be discussed in detail here, was made available in its present form on a widespread basis nearly four decades ago by Maharishi Mahesh Yogi (hereafter referred to as "Maharishi"), one of the foremost representatives of the Vedic tradition (34, 122, 123). After over 20 years of experience teaching Transcendental Meditation to thousands of people around the world, Maharishi began to explore other aspects of the knowledge of Ayurveda. Due to the long passage of time and to years of oppressive foreign rule, much of the traditional knowledge of Ayurveda has been lost in India. Thus, a few years ago, Maharishi began consulting with renowned "vaidyas" (ayurvedic physicians) in attempts to restore the current practices of Ayurveda to what he presumed to be their original level of effectiveness (182, 191, 197). One of his main contributions has been to bring to light once again the prime importance of consciousness, and of techniques for enlivening the highest states of consciousness, in the prevention programs of Ayurveda (191). He also has clarified, in terms of modern science, the origins of Ayurveda as described in the classical texts (e.g., Caraka, Sutrasthana, I. 1-40; XXX. 27; Sushruta, Sutrasthana, I. 1-16; Vagbhata, Sutrasthana, I. 1-3). Space limitations do not allow this review to deal adequately with this topic. However, chapters seven and eight in Sharma's recent monograph discuss it in some detail (191).

The Transcendental Meditation (TM) technique is the most widely researched technique of meditation (and probably the most widely studied approach deriving from any ancient tradition of medicine), with over 500 publised reports orginating from more than 200 institutions (4, 7, 100). Although the technique is considered by Maharishi to be part of Ayurveda, the basic knowledge from which it comes is contained in the ancient Rik Veda, the heart of the Vedic tradition, which he holds to be not merely a literary treatise but a direct cognition (by ancient seers) of the laws of nature governing human development, and indeed, governing all of objective and subjective existence (85, 124). The Transcendental Meditation technique is taught personally in a systematic manner by Maharishi or teachers specially trained by him. This technique of meditation is unique in that it involves neither concentration nor contemplation (122). Rather, it consists of an effortless manner of using a particular thought (a special sound called a "mantra", selected for the individual by the teacher) that promotes settling of the attention from the active, thinking level to progressively more subtle levels until all thoughts are transcended. Awareness is then experienced as a unified wholeness, termed in Sanskrit, "turiya", or "samadhi", and translated by Maharishi as "transcendental consciousness" or "pure consciousness" (122). Researchers in the West, beginning with Wallace (222), have supported the distinctiveness of this state from either sleep, dreaming, or the usual waking state of consciousness, and have called it a fourth major state (4, 100, 224). In this state, awareness is said to be fully awake to itself alone. This "self-referral" experience of awareness, like that experienced occasionally without a special technique and also through some other traditional techniques (198), is thought to be responsible for the many benefits attributed to TM (4, 7, 100, 122, 191).

With the exception of TM, techniques promoting the experience of transcendental consciousness are generally considered difficult (198). Even the correct practice of Transcendental Meditation, which is

reportedly both easy to learn and easy to practice, is a delicate matter and must be taught on an individual basis by specially trained teachers who can give information based on the unique experiences of each individual (22, 122, 123). Probably for these reasons, none of the traditional techniques, including those from ancient Greece, as discussed by Plato (198), is ever described in detail, if at all, in writing. Ayurveda is no exception to this rule. The benefits of meditation are mentioned in the ancient texts of Ayurveda, as in the following quote, "Diseases do not afflict an individual who is endowed with excellence of thoughts, speech and acts which are ultimately blissful, independent thinking, clear understanding, knowledge, observance of spiritual prescriptions and love for meditation" (Caraka, Sarirasthana, II. 47), but the authors of the texts do not attempt to describe how meditation is practiced. In fact, at various points in the texts (e.g., Caraka, Vimanasthana, VIII. 4, 5, and commentary), it is made clear that many aspects of the knowledge of Ayurveda must be passed from teacher to pupil, just as Maharishi Mahesh Yogi received the knowledge of TM from his teacher, Swami Brahmananda Saraswati, Shankaracharya of Jyotir Math in the Himalayas. (Jyotir Math is the northern seat of knowledge of the Shankaracharya branch of the Vedic tradition in India.) In the Vedic tradition it is said that, in this manner, key elements of the knowledge of the practices for having these Special conscious experiences have been handed down in an unbroken chain for thousands of years. Similar knowledge was apparently passed down within the tradition of medicine in Greece, going at least as far back as Asclepius, who is thought to have dated from 1300 BC or earlier and who was widely considered the father of medicine in the classical period (55). Shear (198) has recently dealt in detail with the phenomenology of such experiences and with the existence since ancient times of techniques promoting them. Thus, this aspect will not be discussed further here.

Since the occurrence of these experiences is apparently rare in the absence of a special technique promoting them, they have been largely ignored by our modern intellectual/scientific tradition. Only recently, due in large part to the wide availability of persons who have learned and continue to practice Transcendental Meditation (4.5 million people around the world who have learned since 1958), has there been a concerted effort to scientifically evaluate the significance of such experiences to mental and physical health. Evidence now strongly suggests that along with psychological growth comes increased physiological stability and better health, i.e. people actually may grow to be "...established in evenness, wholeness of life" as stated in the verse above from Rik Veda.

2. Eliminating stress through optimizing adaptive mechanisms:

As discussed earlier, stressful experiences appear to derive in part from the inability of the body's adaptive mechanisms to respond optimally to envrionmental changes (91, 93, 230). If this is correct, then optimization of these mechanisms would logically reduce or eliminate such stressful experiences. Of course, this outcome would depend upon accurate self-evaluation capabilities (112), to detect this optimization once it had occurred. Also, the overall benefit to health would depend upon also correcting any maladaptive psycological and physical responses (e.g., the tendency to become anxious or to use alcohol or drugs) which may have developed as defense mechanisms (228). Recent evidence suggests that optimization of adaptive mechanisms is one of the effects of regular practice of Transcendental Meditation and that this effect may explain some of the health benefits attributed to this technique (7, 119, 228, 229).

As mentioned before (see Introduction), chronic stress distorts adaptive mechanisms, especially the neuroendocrine mechanisms responsible for maintaining physiological stability in the changing environment (28, 167, 168, 170, 171, 173, 175, 240). Such distortions have been studied most with respect to glucocorticoid regulation by the HPA axis, but can occur in other axes as well (167). For example, evidence now supports chronic-stress-induced alterations in regulation of testoterone, growth hormone (GH), thyroid stimulating hormone (TSH), and DHEA, the precursor of most 19-carbon steroid hormones, and its sulfated form, DHEAS (9, 144, 167, 220). Chronically elevated glucocorticoids,

which can result from prolonged or frequent intermittent stress, may in fact be responsible for some of these changes in regulation of other hormones and precursors (9, 35, 144, 220). Thus, since the levels and regulation of cortisol, the principle glucocorticoid in humans, are among the most important factors affected in stress, the effects of Transcendental Meditation on this hormone have been examined in some detail, both during and outside the practice.

Jevning et al. (102) and Bevan et al. (16) found evidence that cortisol levels decline during the practice of TM. This effect was more pronounced in "long-term" TM practitioners, who had practiced TM 15-20 min twice a day for 3 to 5 years, than in subjects who had practiced for only 3 to 4 months (102). In addition, cross-sectional studies have shown average cortisol level in students who had practiced TM for 8·5 years to be about one-half the level found in age-matched students without systematic stress reduction (229). Moreover, a recent randomized, prospective, controlled study supports the conclusion that these cross-sectional differences were due to TM practice rather than to some uncontrolled variable (119). In fact, the latter study (119) showed that four months of TM had effects on cortisol opposite to those produced by chronic stress in non-human primates and rodents (166, 171). Specifically, baseline and average cortisol levels were lowered, while the cortisol response to an acute challenge, where a robust rise may be appropriate (134), was enhanced (119). In the same study, the effects of TM on responsiveness of testosterone, TSH, and GH to acute stress, as well as its effect on the ratio of DHEAS to cortisol, also appeared opposite to those produced by chronic stress. The ratio of DHEAS to cortisol may have special significance because DHEA can have antiglucocorticoid actions, including actions opposing some of the deleterious effects of cortisol on the immune system and fat deposition (21, 236). Thus, since DHEAS and DHEA are easily interconvertible, increasing DHEAS may be tantamount to lowering cortisol.

Other research, which employed cross-sectional instead of longitudinal designs, also has suggested that TM increases DHEAS levels (76) and the ratio of DHEAS to cortisol (229). In addition, an earlier longitudinal study, in which subjects served as their own controls, found that practice of the TM and TM-Sidhi program, a more advanced practice than TM alone, caused hormonal changes, especially in TSH, GH and prolactin, suggestive of increasing optimization (232). Similar improvements in TSH efficiency were found during a TM practice session (101).

The above evidence appears to support the conclusion that an ancient technique from Ayurveda can reverse deleterious effects of chronic stress on level and regulation of steroid hormones. An additional set of observations, this time involving cholesterol itself instead of the hormones derived from it, may add further support to the interpretation and significance of ojas presented earlier in this review. Elevated plasma cholesterol is considered by many to be a risk factor for coronary heart disease. Dietary intake is one way to elevate cholesterol, but stressful experiences, such as those resulting from preparation for medical examinations in humans or repeated mild tail shock in rodents, can also elevate cholesterol, even if dietary intake is low (17, 26). It was not surprising, then, that a controlled trial of effects of TM on plasma cholesterol in persons with elevated cholesterol would find a significant decrease (38). This effect was apparent after only 11 months of regular practice, compared to cholesterolemic controls who received no special treatment but also had volunteered to learn TM. Thus, aside from raising or lowering steroid hormones, depending on which direction seemed to approach optimal for that hormone, practice of this Ayurvedic technique appears to lower elevated cholesterol levels. Cross-sectional evidence also suggests that TM lowers the level of the mineralocorticoid, aldosterone, another steroid hormone important for health, when this hormone is higher than optimal (229).

3. Evidence for health benefits from metal procedures:

More than in most fields, medical research is frought with difficulties. Even randomized clinical trials suffer from self-selected attrition, differential rates of non-compliance, etc. which weaken the conclusions

that can be drawn. Studies on mental techniques are no exception to this rule, but there appear to be a number of outcomes sufficiently consistent and reliable to be taken seriously. The nature and magnitude of the results described below are illustrative of a much larger number of studies on Transcendental Meditation (7, 33, 142, 225). For TM, meta-analyses on psychological and physiological measures and risk factors for disease have shown positive effects usually two to three times larger than relaxation techniques, other meditation techniques and contrived placebo procedures (6, 47, 63). Similarly, primary studies on hypertension, morbidity and mortality have shown large effects in comparison to other procedures, even though these other procedures often produce larger effects than placebo controls [see for review (7)].

Reports supporting the health effects of mental techniques have accumulated rapidly in the last 20 years (135). A majority of these has involved the TM technique [see, for example, the five volumes of collected papers (33, 142, 225)], although many other techniques, including some from ancient traditions, have also been investigated (135). Of all the effects attributed to mental procedures, reduction of blood pressure may be the most prevalent, and possibly also one of the most important because hypertension can lead to serious cardiovascular disease and death. The 10- to 20-mm Hg reductions in blood pressure reported for such techniques (5, 93, 181, 226) are estimated to reduce cardiovascular morbidity and mortality by at least 30% (37, 211).

Henry and Stephens (93) reviewed early studies supporting the ability of meditation and relaxation techniques to reduce blood pressure, while Schneider et al. (181) reviewed similar research for the following 15 years. Although several techniques appear to significantly reduce blood pressure, when many types of techniques are pooled for purposes of statistical comparison, the outcome is not impressive (58). Thus, because the nature and origins of such techniques differ widely, it may not be appropriate to combine them in statistical meta-analyses, or to prejudge the effectiveness of any particular technique based on results with any other [see discussion in Alexander et al (7)]. Transcendental Meditation appears to be among those most effective at reducing blood pressure, both in hypertensives and in normotensives (5, 7, 181, 231). Furthermore, these effects may be produced, at least in part, by optimizing regulation of cortisol and aldosterone (119, 229). Due to its importance for the central theme of this review, this aspect is further elaborated in the next paragraph.

In their review, Henry and Stephens suggested, over 15 years ago, that elevations of glucocorticoids and aldosterone contribute to hypertension (93). These and other researchers have since explored this possibility, accumulating a variety of evidence for mechanisims involving these steroids (90-92, 94, 98, 108, 163, 178, 233, 234). For example, both glucocorticoids and mineralocorticoids increase contractility of vascular smooth muscle, an effect which could contribute directly to hypertension (108). Furthermore, both adrenergic receptors and angiotensin II receptors are induced by glucocorticoids (98, 163, 178). These effects could be directly involved in the hypertrophy, increased reactivity, and increased pressor response of vascular smooth muscle cells, which are all important in the development of hypertension (1, 69, 117). The lasting hypertensinogenic actions of these adrenal steroids require long-term or frequent elevations of these hormones, and are thus classed among the "slow pressor mechanisms" important in the etiology of essential hypertension (114).

Other health effects reportedly due to Transcendental Meditation may not be as directly related to alterations of steroids, although less direct roles are clearly possible (228). The effects appear to cover a broad spectrum of ailments, most of which have been investigated by researchers in different institutions, often in several countries (33, 142, 225). The range and magnitude of these effects may be most clearly indicated by a five-year, comprehensive, field study of medical insurance utilization in a group of 2000 TM practitioners compared to controls (139). Reductions were found for both inpatient and outpatient care in 17 of 18 major categories. For example, hospital admissions ranged from 87% lower for heart and nervous system disorders to 30% lower for infectious

diseases and mental disorders. Other categories included intestinal; nose, throat, and lung; genital and urinary; injuries; tumors; bone and muscle; metabolism; congenital; blood; and childbirth. The lower admissions for congenital diseases does not mean fewer such disorders, but appears to reflect enhanced ability of persons with these disorders to manage them successfully. The 18th category, childbirth, showed the same admissisons in the TM and control groups, as might be expected if the TM subjects were comparable to the controls in age, family size and occupation. The average reductions in total medical utilization were approximately 50% for children, 53% for young adults, and 72% for adults over 40 years of age.

The design of the above study precluded determination of medical care utilization prior to beginning TM practice. One possibility, therefore, is that the people who chose to learn and continue the technique were healthier at the outset. On the other hand, a similar study on medical expenses included a three-year baseline period prior to beginning the technique (95). This study showed that medical costs before beginning TM were not different from controls, but that costs dropped steadily over the next several years to a level approaching 50% lower than at the starting point. Both this and the above study were retrospective in design. Thus, at the time medical costs were incurred, TM subjects as well as controls were unaware that such a study would be done.

It is noteworthy that in both these studies the magnitude of effect apparently due to practice of TM was nearly 50% larger in persons over 40 than in those who were younger. Therefore, it is hardly surprisng that a longitudinal, random assignment study in the elderly (mean age 81 at pretest) found TM to not only reduce blood pressure and cause large improvements in measures of cognitive function and quality of life after only three months of practice, but also to significantly reduce mortality rate over the next three years, compared to other active treatment groups and untreated controls (5).

These results, although representing a small fraction of the studies on mental procedures of ancient origin, and even a small fraction of the studies on this technique from Ayurveda, appear strong enough to conclude that there are major benefits on the health of those who practice it. What may be most remarkable is that virtually all areas of health appear to be affected. This may be due in part to the ability of these techniques to reduce such factors as the use of alcohol and other substances damaging to health (8, 74). However, the reduction of stress through optimization of adaptive mechanisms may provide a deeper explanation which can independently contribute to reductions in substance dependence and overall health (228). Likewise, the effects of mental techniques on adaptive mechanisms may have a deeper explanation, one based on the techniques' ability to promote experience of the special state of transcendental or pure consciousness described above. While this latter point may be difficult to prove directly, it is probably not by chance that the Transcendental Meditation technique not only appears more effective at producing a variety of health benefits than many other mental techniques with generally similar characteristics (5, 6, 47, 63, 181) but also appears more effective at promoting the experience of transcendental consciousness (4, 6, 7).

It is important to note here that although the present discussion has focused on those physiological effects of TM that appear most directly related to the themes of steroids, stress, and adaptive mechanisms, other remarkable effects have been documented as well. Many of these, including changes in: oxygen consumption and respiration, circulation and tissue metabolism, function of the autonomic nervous system, function of the central nervous system (as indicated by electroencephalographic and evoked potential data), function of the peripheral nervous system and musculature, and the phenomena of aging, have been recently reviewed elsewhere (100, 223). Certainly these sorts of effects, whether or not they fit the adaptive-mechanisms framework elaborated here, could play a role in the health effects of Transcendental Meditation or of any other mental practice effective in improving health. Likewise, however, many of these effects conceivably are secondary to changes in steroids.

B. REVIVAL OF OTHER ANCIENT APPROACHES FROM AYURVEDA

In addition to mental practices, there are numerous other Ayurvedic approaches to improving health that are currently being used clinically, and also are being investigated with the techniques of modern science. Many of these have what appear to be parallels in the ancient medical traditions of Egypt, Greece, and most other parts of the world (55, 179, 212). These approaches include: oil massage, oleation, purgation, steam baths, special enemas and other procedures for purification; dietary prescriptions; specific postures and physical exercises; guidelines for behaviour; breathing exercises; special procedures for enlivening balance through the five senses, such as meditation techniques and music therapy (both of which use or derive from the sense of hearing), touching or stimulating specific vital points on the body, color therapy (sight), aroma therapy (smell); and herbal and mineral nutritional supplements, both for curing existing diseases and for disease prevention and prolonging life.

Because the proper usage of these techniques from Ayurveda, as well as the understanding of theories behind them and the mechanisms involved in their effectiveness, have eroded with the passage of time, there has been a recognized need to revive Ayurveda in its completeness. Stimulated by discussions with Dr. B.D.Triguna (191), past President of the All-India Ayurveda Congress, and Director of the National Academy for Ayurveda in India, Maharishi undertook to revive, in as pure a form as possible, all aspects of Ayurveda. To this end, he has periodically assembled renowned vaidyas and pandits or teachers of Ayurveda, along with pandits of other branches of the Vedic tradition, together with Western physicians, spending thousands of hours on reconstructing the original knowledge. From these efforts, a version of Ayurveda called "Maharishi Ayur-Veda" has been formulated, with the Vedic understanding of consciousness at its basis (191). There has been considerable research into the effectiveness and mechanisms of this revived form of Ayurveda, which has been reviewed in detail elsewhere (182, 191, 197). Thus, the present discussion will be limited to those examples having clear relationships to the central themes of this review.

All aspects of Mahrishi Ayur-Veda have as their ultimate goal the creation of perfect physical and mental balance, the result, or corollary, of which is held to be freedom from disease (191). The formidable task of understanding the mechanisms in terms of the knowledge of Western science has begun in several of these approaches. Here, in addition to the consciousness aspect discussed above, two other aspects of Maharishi Ayur-Veda will be briefly discussed: "panchakarma", a combination of treatments for purification of the physiology, and "herbal food supplements", used as preventive measures and for prolongation of life.

1. Panchakarm: treatments for purifying the physiology :

Panchakarma is a treatment recommended two or three times a year as a preventive measure. It includes oleation, purgation and elimination procedures, herbalized oil massage, herbalized steam baths and inhalation therapies, and special tratments producing deep relaxation. Although the precise effects in Western terms have not been fully verified, research to date suggests parts of this treatment, especially the oleation, purgation and elimination procedures, remove lipid-soluble toxins, such as polyaromatic hydrocarbons, as well as water-soluble toxins (202). Some of the changes observed following five days of panchakarma in apparently healthy individuals were: decreased blood pressure, lowered total cholesterol, elevated HDL ("good") cholesterol (which remained elevated three months later if original values were low), lowered lipid peroxides, a measure of free radical damage (three months later), and increased vasoactive intestinal peptide, a vasodilator (80% higher three months later) (196). In a similar study, which used only short-term (7-10 day) follow-up measures, the number of patients who had high risk profiles for heart disease or heart attack before treatment was decreased by 43% for males and 36% for females following panchakarma (221). Both total cholesterol and LDL-cholesterol decreased significantly. Taken together, these studies offer substantial support for rapid improvements in

cardiovascular risk factors as a result of panchakarma treatment. Furthermore, in another study, the self-reported mental/emotional state improved significantly with panchakarma, compared to a control group that received only a didactic class for the same length of time, even though both groups were apparently healthy beforehand (182). As a further suggestion of the wide range of effects that may be brought about by such treatments, the oils used in the message and eliminative procedures of panchakarma have been shown in cell cultures to differentially inhibit growth of human malignant melanocytes and human colon cancer cells (164, 203).

2. *Rasayanas: herbal preparations to prevent disease and prolong life:*

The use of herbal preparations to preserve and restore health is found in virtually every system of traditional medicine. Western science has barely begun to investigate the medically-related properties of the hundreds of preparations that exist in Ayurveda, but a number of significant effects have been found, mainly in animal studies or *in vitro* systems. In Ayurveda there are two types of herbal preparations. One type includes those targeted to a specific disease. The other type, however, is aimed at preventing disease and the degenerative effects of aging. The second type, called "rasayana", is proposed to increase resistance to disease and to activate tissue repair mechanisms. Any one of these herbal preparations typically contains 10 to 20 herbs. The general position of Ayurveda is that each herb contains several ingredients with beneficial effects, but that the carefully selected combinations of herbs (containing hundreds of potentially active compounds) produce additive or greater than additive ("synergistic") effects (191). It is also held that these combinations prevent the harmful side effects that can arise from administering one or a few potent substances (191).

Although Western-style research on ayurvedic herbs has gone on for some time, this has usually involved one or a few selected herbs from a complex preparation, and often is oriented towards identifying "active ingredients." In the research carried out so far on rasayanas prepared according to procedures revived in Maharishi Ayur-Veda, more attention has been placed on the overall effects, either on molecules (such as free radicals), or at the cellular, tissue or whole organism level, as well as the possible mechanims involved. In research using complex herbal preparations, one has to be concerned that the source of the herbs and the methods used to prepare the mixtures are precisely according to the instructions contained in the classical texts or handed down through an unbroken chain of well-trained vaidyas, and that there is as high a degree of uniformity as possible among batches of these preparations (191). Because these conditions can be verifyably met with these products, most of the research on the herbal formulations of Maharishi Ayur-Veda has employed the two rasayanas known collectively as Maharishi Amrit Kalash, and known individually as MAK-4, a mixture formulated as a paste, and MAK-5, a mixture in tablet form. The herbs in each have been listed elsewhere (192, 193).

A number of remarkable effects of MAK-4 and MAK-5 have been documented. These include antineoplastic (anticancer) (145, 153, 192, 193), immunomodulatory (43, 137), cardioprotective (194), and neurochemical effects (195), as well as reduction of Adriamycin- and toluene-induced toxicities (24, 62), antioxidant effects (54, 137, 160), and reductions of the cognitive declines associated with aging or head injury (73, 83).

Most of these effects have been determined in animals or *in vitro* preparations of human cells. However, the latter effects were in humans, and were obtained in rigorous, double-blind, randomized, placebo-controlled studies. One found that six weeks of MAK-5 significantly improved performance in an age-related, visual discrimination task in 48 healthy men over 35 years of age who were randomly assigned to placebo or the herbal mixture (73). The second found that six months of MAK-4 and MAK-5 reduced late neurological deficits following head injury, with significant improvements on visual-motor coordination tasks and a strong trend of improvement on memory scales (83).

3. *Possible roles of steroids in the effects of panchakarma and rasayanas:*

In the discussion on reducing stress through optimizig adaptive mechanisms (See above), reference was made to diseases that may arise from distortions of hormonal regulatory mechanisms. Examples of stress-induced alterations in regulation of the HPA axis, which result in chronic elevations of cortisol or aldosterone, were cited as likely contributors to cardiovascular and other diseases. The possibility appears worth considering that the purification procedures of panchakarma not only remove toxins of exogenous origin but also lower elevated steroid hormones, and thus help reset these regulatory mechanisms.

One aspect of panchakarma is the ingestion of large amounts of ghee (clarified butter) under conditions that result in high concentrations of ghee-derived chylomicrons in the blood (202). Smith and Salerno propose that lipid-soluble toxins drawn into this chylomicron fraction are more rapidly delivered to the liver, where they are detoxified through the cytochrome P_{450} system and/or processed into the gall bladder for rapid excretion through the gut during the subsequent purgation and elimination therapies (202). That such a treatment does, in fact, mobilize unwanted lipids or lipid soluble materials is supported by the rise in blood level of lipid peroxides (unwanted molecules produced by reaction of normal body lipids with free radicals) during the tretment, but a drop to levels lower than before by three months after treatment (196). The temporary rise of lipid peroxides in the blood during panchakarma may represent the mobilizing effect, while the lower levels afterwards may reflect a lower body content of these undesirable molecules as a result of panchakarma. The acute lowering of total cholesterol and LDL cholesterol by panchakarma (196, 221) also may support the conclusion that this treatment mobilizes and lowers some lipid soluble species, including steroids. Thus, in subjects whose average cortisol and /or aldosterone levels are chronically elevated, panchakarma might lower the levels for a sufficient period to permit resetting of the regulatory mechanisms. Although this possibility is speculative at present, it appears easily testable, for example, by a clinical trial of panchakarma in depressed patients, a substantial precentage of whom exhibit chronically elevated cortisol and a failure to suppress cortisol normally when given the synthetic glucocorticoid, dexamethasone (241).

Free radicals and reactive oxygen species are implicated in numerous diseases, including cancer, inflammatory diseases, degenerative diseases, atherosclerosis and aging (154, 160, 191, 201, 204). There appears little question that some of the documented effects of rasayanas and other herbal preparations are due to their content of highly potent antioxidants and free radical scavengers (54, 137, 160, 191). Another possibility that appears worthy of consideration, however, is that the effects of rasayanas or other herbal preparations are in part due to the steroids contained in these plants.

Possibly the most well known examples of potent steroid compounds in plants are the cardiac-active steroid, which were named "cardiac glycosides" before their steroid nature was discovered. Some of the unusual properties of a tea made from the roots, berries and leaves of the purple foxglove were known to the ancient Egyptians and Greeks, but the effects on the heart were not clearly demonstrated, at least not for recorded history, until the work of Dr. William Withering in the last part of the eighteenth century (235). Since then, many cultures have been found using plant preparations which contain either digitalis, digitoxin, ouabain or one of the more than 300 other cardiac-active steroids now known in plants (235). In traditions from many countries, plant preparations containing cardiac steroids have been used as poisons, such as the arrow poisons used by native Africans for felling elephants, or as emetics in humans. However, Withering found that the life-threatening and emetic effects are due to an overdose and that smaller doses produced beneficial effects on patients suffering from "dropsy", the term used at that time for congestive heart failure. Only in the last decade has evidence for the natural occurrence of cardiac steroids in humans and other mammals become compelling (see discussion above under "rakta dhatu"). As far as is known, the

cardiac steroids of plants are intended to protect the plants from predators, as are many other steroid poisons found in plants (235). Some of these poisons are antibiotics, acting on bacteria or other single celled organisms.

Today it is known that plants contain a vast variety of steroids, often in large quantities. For example, without the steroids cheaply available from plant sources, the steroid hormone industry, which today produces over three million pounds of hormones annually, might never have grown substantially from a few milligrams produces annually in the thirties (235). It appears that, aside from a the major steroids or, in a few cases, close relatives of steroids, that are required for the life of every cell, apparently due first to their role in the cell membrane (136), there are many steroids present in each plant in small qunatities that serve signaling or communicative functions. In plants, as in humans, steroids are important in sexuality and development (136, 235). Furthermore, plants are known to synthesize steroids that have protective effects in mammals, in some cases by activating (or blocking) the body's own adaptive mechanisms (136, 187, 235).

Selye, who collected information on the effects of over 2000 steroids, identified ten independent classes of actions of steroid hormones that may play a role in the body's normal adaptation to the changing environment (187). He suspected the existence of countless other classes which his experiments were not designed to detect. Since each of these classes generally involves different specific effects in different cells and tissues, the total number of genes whose expression is activated or inhibited by each class of steroid activity could easily be in the hundreds for the whole organism (see discussions above). Some exogenous steroids exhibit, for example, the glucocorticoid and mineralocorticoid classes of actions, and others the opposing, "antagonistic" actions, which in this case would be called "antiglucorticoid" and "antimineralocorticoid."

Two classes of activities perhaps less well known deserve special mention in the context of herbal preparations. One is the "syntoxic" type of action, in which a hormone or exogenous steroid permits *tolerence* of a "pathogen" (defined here as either an exogenous toxin, or an endogenous substance whose concentration has increased to a toxic level). The syntoxic class of actions seemed, in Selye's experiments, to be linked inseparable to other corticoid actions (e.g., glucocorticoid and mineralocorticoid). However, the second class of unusual actions is the "catatoxic" type. Catatoxic substances *eliminate* the aggressor (the pathogen) by activating adapative mechanisms of the organism to destroy it (186, 187, 189). Usually the mechanism involves accelerated biodegradation of the toxin, for example, by inducing or enhancing production of appropriate degradative enzymes in the liver (187).

Some of these steroid classes tend to be found together (e.g., anabolic and catatoxic), but others tend to occur alone (e.g., corticoid and folliculoid). Furthermore, sometimes a steroid will inhibit only selected aspects of one class of activity, allowing others within that class to go on undisturbed (187). Therefore, through selection of plants with the appropriate combination of steroids, an almost unlimited range of effects on the body's adaptive machinery could be achieved. This approach might, for example, counter any chemical imbalances involved in producing a specific disease.

Likewise, selected combinations of plant steroids might enhance the body's resistence to any future insult by stengthening or maintaining full readiness of its adaptive mechanisms, the sort of effect attributed to rasayanas. Finally, beneficial cognitive effects of plant preparations, such as those attributed to Maharishi Amrit Kalash (see above), might be due in part to the presence in the plant of either a neurosteroid, a vital precursor, or another steroid easily converted to one of these. In support of this possibility, direct injection of such steroids in appropriate brain areas of the aging mouse can return performance to its youthful level in certain memory tasks (66-68).

CONCLUSION

At the beginning of this review, preventive approaches used by ancient medical traditions were implied to hold promise for solving the health care problems of modern societies. Reference was made to the Hippocratic tradition to which modern Western medicine traces its roots. Contained within the Hippocratic writings are two distinct views, representing the opposite extremes of a pendulum that has moved back and forth through the 2500 years since this era of medicine began. On the one side is the "Hygeian" position that "...the most important function of medicine is to discover and teach the natural laws which will ensure to man a healthy mind in a healthy body", while on the other is the "Asclepian" view that "...the chief role of the physician is to treat disease, to restore health by correcting any imperfection caused by the accidents of birth or of life" (52). Dubos supported the position that these views in fact predated the Hippocratic era in Greece and are to be found in similar form in all traditions (51, 52). The Ayurvedic tradition chosen for the focus of this article is an apt example. Both views can be upheld from writings contained in the classical texts, depending upon the inclinations of the reader. It appears at present that the pendulum has swung away from the side of prevention, and that the reenlivenment of this side of medicine as it existed in many ancient traditions promises great practical benefits to modern society.

The match proposed here, between an understanding of health and disease contained in the classical texts of Ayurveda and an understanding rapidly gathering support within the confines of modern empirical science, appears to be only the beginning, the "tip of the iceberg." The large quantity of knowledge contained in these texts, and the unwritten knowledge passed from vaidya to student in the continuing practice of this system of medicine, should be tested empirically using the methods of modern science. In particular, the proposed interpretation in terms of the roles of steroids in health and disease, and modern evidence supporting the effectiveness of traditonal methods for optimizing steroidal function, offers a direction to future research. The implications of this component alone are vast, and unraveling them could fruitfully occupy dozens of laboratories for years to come. However, due to a long tradition of practice which has amply proven the effectiveness of Ayurveda, the direct application of these ancient approaches to the health problems of modern society is already underway (5, 181, 182, 191, 197).

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