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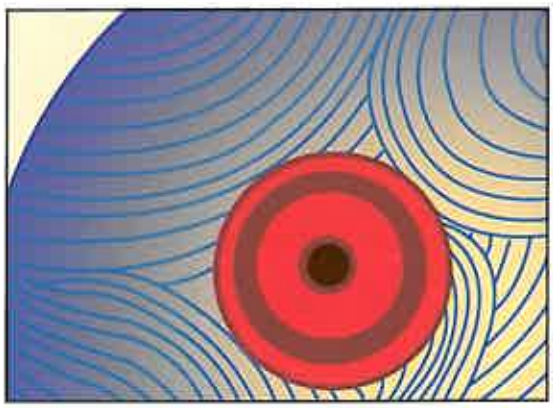

NEW SPECULATIONS ON REFRACTIVE ERROR

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Abstract

*This paper speculates upon a unifying theory of the ametropias. It is proposed that refractive errors are outcomes of the physiology of the general adaptation syndrome with its consequences on the organism—***stress** *adaptive responses. Normal visual coping mechanisms are challenged by nearwork, containment, nutritional changes, and anxiety, producing the homeostatic responses that alter scleral and crystalline lens dynamics, leading to posterior chamber distention and to hyperopization. We measure them as adaptive diseases: myopia, hyperopia and astigmia. The variables involved in the type of refractive changes that occur are several, but personality style is suggested as the most highly dependent variable. This testable question and other speculations are raised. New or renewed clinical skills may be required to appropriately manage the clinical course of refractive errors.*

Key Words

ametropia, collagen, cortisol, emmetropization, etiology, homeostasis, personality, refractive error, stress

The eye has been called the most important square inch of the body's surface.[1] Its role in the study of disease should not be underrated:

> *The eye might have been intended to furnish us a little model for studying the processes of disease and the processes of reparation as they go on in all parts of the body, so admirably does it answer this purpose.*[2]*(p.1)*

Understanding stress is very important in understanding disease: stress is a major hallmark of life. Its impact on the body is relentless and each body functions like a crucible where the reactions of genetics, nutrition, environment, and experience produce a blend that is unique to the individual. Human physiology operates within ranges, and responses will be relative to the internal environment of the individual, as life meets with one's genetic bent.[3] Selye, the stress pioneer, defined stress as *the specific syndrome of all the non-specifically induced changes within an organism in response to any demand.*[4]

Distress creates chronic activation of the body's stress response and will result in disease over time. Brown[5] reports that 75-90% of all disease counts stress as a direct or indirect cause, but Selye said that every disease has some element of stress adaptation to it.[6] And so, any questioner needs to ask not *if* stress is a factor in an abnormal condition, but *how much of a role* stress is playing.

For the vision care practitioner, this must include refractive errors. The etiology of the ametropias has been debated among two major camps for decades. The first consists of professionals who endorse genetic theories versus the second camp, who endorse the functional theories. The literature shows that neither position is ironclad.[7-9] Each side may have good arguments but rigidly adhering to one side and refusing to speculate is an unscientific attitude. Both sides have points which must be considered.

The clinician may not be certain whether to attempt to functionally intervene (if it is indeed at all possible), or whether he is battling and merely monitoring the inevitability of the patient's genetic formula. Is there a possibility of a unifying concept that can incorporate the known and supposed factors that influence ametropia? Can we guide the clinician in the decision to treat? This paper offers a probable answer: Stress, in the form of any imposed stimulation, appears to be the unifying element in acquired refractive error and personality style appears to be the dependent variable modifying the error. The model is complex and a working understanding of the physiology of the stress response is necessary to understand how and why the visual system changes in response to distress.

I. THE GENERAL ADAPTATION SYNDROME

Stress Response

Selye[4] proposed that there is a two-stage reaction to stimulation, either physical or psychogenic. First, there is a specific response that is directed at the targeted tissue: inflammation, allergic response and metabolic changes. These are "pro-body" changes, needed to limit damage and to start repair. The second re-

sponse is a generalized one and tends to be "anti-body" because anti-inflammatory agents are released, which affect not only the target tissue but virtually every tissue in the body. He named this process the general adaptation syndrome (GAS).

As described, the GAS causes a cluster of organic changes that occur—without exception—when the body is distressed:

1. The adrenal glands enlarge
2. The thymus gland shrinks
3. The lymph glands shrink
4. Ulcers are produced

The stress response occurs in three stages: the alarm phase, a preparation for action and repair; the resistance phase, for repair and vigilance; and the stage of exhaustion, when overt disease or death ensues. The GAS's response to stress can either sensitize or desensitize a tissue's further response to the hormones of stress. In tissues directly affected by stress, a local adaptation can occur. Called the local adaptation syndrome (LAS), it can trigger the GAS if the activity in the strained part does not stop. The "...selective exhaustion of muscles, eyes, or inflamed tissue all represent final stages **only** in local adaptation syndromes...."[4](p.81) These are responses to alarm signals sent out from the directly stressed tissues to the central nervous system (CNS), then on to the endocrine system. Thus, each of the many local stress reactions has a chemical voice that adds to the extent of the counterstress measures that are taken. These measures can be very appropriate when the stress is real, but may be very inappropriate when the stress is a psychic phenomenon, a merely expected threat and not one actually presented to the organism.

Uniqueness of Stress Responses

An individual's stress response can be profoundly influenced because of three variables:

1. Our unique genetic endowment: parentage cannot be chosen. (Nature)
2. Our unique experiences: especially the early ones, creating a fund of prior response patterns. (Nurture)
3. Our apperception of stimuli: conscious, emotionally-charged responses to an experience built from each one's prior experiences, nurture and conclusions. (Beliefs)

These factors alter the preferential release of specific hormones. An individual's personality thus becomes the determinant of the type, the strength, and the length of the reaction. Aggressive, competitive personalities have been reported to have more acute, larger vasomotor responses and produce more norepinephrine. Sustained epinephrine release is associated with anxiety and helplessness, and elevated cortisol (hydrocortisone) levels have been correlated with reduced negative performance and fear in humans.[10] These two styles also appear to correlate with specific refractive errors (as this paper will expand upon).

II. THE HYPOTHALAMIC-PITUITARY-ADRENAL (HPA) AXIS

Cortical and Hormonal Processing

A stimulus, arriving at the brain, undergoes a sorting procedure in the thalamus and cerebral cortex. When a decision (notably, a *learned* response) has been made, a portion of the signal is routed through the hypothalamus to reach the hypothalamic-pituitary-adrenal (HPA) axis. The response that follows varies in precise manner and strength because of the three factors listed above.

A portion of an alarm signal is passed directly to the adrenal gland, resulting in the release of epinephrine and norepinephrine for an immediate response reaction. A second portion of the signal is routed to the anterior lobe of the pituitary gland, which engages the body's "second messenger" system: hormone release. The primary hormone involved in the adaptation of the eye is cortisol, and 95% of the adrenal cortex's function is to produce that powerful gluco-corticoid. Cortisol has direct effects on scleral integrity and upkeep (which will be elaborated upon below).

After stimulation, the stress response system would ordinarily shut down the pituitary's production of ACTH through a negative feedback loop. However, under distress conditions, the feedback loop is short circuited at the cortical level (supported by Sapolsky's[11] experiments) and ACTH continues to be produced. Because there is no major metabolic process by which excess ACTH is otherwise reduced and/or excreted, the ACTH level rises in the bloodstream and remains elevated until it is utilized in cortisol production. (Sapolsky found that cortisol levels stayed at elevated levels in male olive baboon subordinates for longer periods of time only because more had been produced in them. The rate of clearance was exactly the same in both dominant and subordinate members of the social family.)[11] Cortisol excess in combination with reduced serum testosterone levels has been suggested as one of the mechanisms of myopia by at least one other author.[12]

And so, an elevated cortisol bath is produced and begins to influence the tissues of the body, the eye included. The individual's affective style appears to be a major modifier of this chain of reactions.

The Stress-Modified Response

The normal stress response is upset by emotional stimuli. These can be real, imagined, or merely perceived symbols of prior threats and demands. Once set into motion, there is little that can be done to significantly modify an individual's HPA response. Indeed, if it were possible, it would almost certainly require a resetting of the customary attitudes leading to the individual's choice of response. It may be possible to influence the response behaviorally, but this lies outside the domain of physical sciences.[13]

Sapolsky discovered that the number of events that occurred to the animals he studied was less important than their reaction style and how they perceived and coped with the stressors.[11] As Hans Selye said,

> *Both on the cellular and the interpersonal level, we do not always recognize what is and what is not worth fighting.*[6](p.41)

III. COPING

The GAS and Coping

When an individual has decided to press beyond the alarm phase of the stress response, or finds himself trapped into persisting under the stressor(s), he passes into the resistance stage of stress. At this point the hormonal balance shifts from a more epinephrine- and norepinephrine-dominant bath to a more cortisol-dominant one. Cortisol is also known as hydrocortisone, and it helps to reset a target tissue system's "thermostat" through chemical or structural changes. These permit the tissue system to function more adequately. This stage, the stage of resistance, is the phase of the GAS that lasts the longest. It is also the phase where adaptation most frequently originates.[4,5]

The shifts in chemistry, tissue function or tissue structure are the organism's attempts to cope with the stressor agent or

environment. There are three coping strategies that the body can adopt:

1. Escape. This removes the organism from the stressor environment. More frequently, this does not involve chemical or structural change. Death may be an extreme but inadvertent result of adaptive exhaustion and is the ultimate escape, intended or not.
2. Tolerance. Either denied or having ruled out escape, the individual "digs in" and tries to withstand the stress it has encountered. Performance becomes compromised and, therefore, less efficient, prolonging the stress. The homeostatic mechanisms are overtaxed, and gradual exhaustion ensues. Disease and auto-immune problems develop (due in part to thymus and lymph gland changes). However, under optimal circumstances, adaptive changes are initiated, becoming the third category of coping responses.
3. Adaptation. Structural or chemical changes permit the tissue system to function with reduced levels of distress. It is as if its "thermostat" had been reset for the more demanding environment. *If escape has not been an option, this is the most satisfactory coping strategy.*

In its end result, coping is the organism's well-intentioned attempt to escape from the stressor stimulus. Unfortunately, a successful adaptive change ("structure following function") can merely result in the individual's ignoring the warning that the process of adaptation has offered: the reduction in the signs of distress may encourage the individual to press on in the same behavior, making further change necessary.

Adaptation in the Eye

Adaptation functions to counteract and minimize the effects of stress, enabling the organism to perform as efficiently as possible.[3] In the same vein, the ametropias serve the organism's need for survival and conservation of energy in the visual system. Myopia is a very logical adaptation to the stress, in that it permits the system to function longer with reduced distress. Astigmatism may be thought of as myopia gone awry. It is a mechanism that permits the organism to partially focus at far and at near simultaneously, as long as the target is not too fine or the activity maintained for too long a period. In this way, it reduces the demand upon the accommodative mechanism. Hyperopia, more than the other ametropias, tends to reflect and reinforce an "escape" choice and it is not surprising that a higher percentage of children with learning problems are hyperopic.[14,15] Hyperopia, if over 1.50 D, may reflect the physiological style of action-oriented individuals and their need to act with their eyes.

IV. GENETIC vs. FUNCTION

Genetic Predisposition

The literature has historically reflected genetic explanations for ametropia.[16,17] Genetic predisposition is a factor, no doubt, but its role is far from exclusive. Rosner pointed out that there was enough discrepancy in the uniovular twin studies on ametropia to dampen any enthusiastic researcher's position that genetics was the sole explanation for the errors.[18] Other authors have noted a low predictive value of genetics.[19,20]

Functionalists generally agree that vision is a learned, dynamic process and that much visual distress is caused by a biologically unacceptable task provoking an avoidance response.[21] We see function's effects on the eye in the phenomenon of pre-presbyopic myopia and certain astigmias that are associated with head position and eye scanning.[22,23] Indeed, current research in chicks, tree shrews, and monkeys, in which myopia and hyperopia have been created, all do so by manipulation of the animal's environment.[24,25] However, the implications of that research have been confusing and even conflicting for reasons that aren't obvious. Generalizations using the results of experiments with chickens may be of questionable value since their scleras and ciliary muscles are atypical compared to most mammals,[26] as is their choroidal response.[27]

But it would be naive to deny that certain individuals are predisposed toward specific errors. Young[28] and Leary[29] have argued that if those certain genotypes were never exposed to the environment or stimuli that reveal the genetic weakness, the errors might never be displayed. They contend that it is a matter of genetic *potential* to myopia. Leary felt that the organism movement *was unidirectional toward myopia*. Nevertheless, he questioned why the same environment can be shared by hyperopes and yet they do not succumb. (This will be addressed later.)

With the exception of some relatively rare conditions, the vast majority of children who wear spectacle corrections were not born ametropic.[18,30,31] Almost all refractive error is acquired at a later date, well after the globe has achieved adult size. Refractive "family trees" do not closely support genetic causation, but do show certain relationships. In a study of optometry students, parent-child association of refractive error was poor, but a much stronger relationship existed between the students and their siblings.[32] This would give evidence to a mechanism where the triggers stimulating ametropia were more at play in the household constellations in which each set of siblings was being reared.

Stress, Visual Function and the CNS

The LAS, responding in the eye to retinal, vascular, muscular, and CNS signaling of distress, is largely—though not entirely—dependent on the balance between pro- and anti-inflammatory chemical messengers discharged by the endocrine glands.[4] The chemistry of the GAS is closely interactive with the LAS, and their dual responses create an internal milieu where the ametropic changes in the elements of the eye can result in reduced distress of the eye. This is true even when it may mean that the individual has been prompted to flee the visually stress-producing environment.

Neurologically, the effect of the near-centered task on an immature visual system is distressful since it pits the somatic nervous system against the autonomic nervous system as well as the parasympathetic and sympathetic branches against each other. Both of these sets of controls are reciprocal. They function reciprocally everywhere *but* in the visual process, since the control of the associated processes of accommodation and convergence is *simultaneous*. While this is possible, it is intrinsically untenable, especially over time. And so behavioral and mechanical coping mechanisms become viable strategies for relief.

V. ANXIETY

Accommodation, Time and Anxiety

Gawron[33] and Miller and LeBeau[34] looked to the CNS and its response to stress under anxiety, and across time as part of the mechanism for the production

of myopia. Ebenholz[35] found that anxiety greatly affected the dark focus values after accommodation. The work of these researchers bears independent review by the reader. However, because of their findings, it is sufficient to say, with near certainty, that accommodation of significant duration, under anxiety, affects the function of the accommodative mechanism.

The Child, Containment and Anxiety

Jemmot, et al[36] and Van Alphen[37] demonstrated and discussed the roles of performance anxiety and situation anxiety upon the child in the classroom as modified by each child's unique expectations. Levine believed that a change in the individual's expectancies or a lack of previously established expectancies were the basis for the best model to explain psychogenic stress. Both will cause a rise in gluco-corticoids.[38]

A child who is desk-bound for hours each school day is in an artificial environment highly unlike the natural environment for which the human body was designed. The student also finds him- or herself subject to the anxiety of social pressures as well. Children's actual responses to school desk containment will vary, of course, because of the three uniqueness factors listed previously. The school desk and its reduction of the opportunities for movement is a similar environment to that of the laboratory animal.

Containment of a laboratory animal clinically raises the production of ACTH, one of eight factors to do so.[39] The restraint also causes anxiety in the lab animals which results in the increase of norepinephrine, another of the eight factors which raise ACTH levels. As related earlier, ACTH is not metabolized in any major way other than in the production of cortisol.

So containment and anxieties in the classroom environment appear to set the potential for change to a high level. The student's physiology in those settings may be likened to a stage set for the development of ametropias in certain psychophysiotypes.[40,41]

VI. THE ETIOLOGY OF AMETROPIAS

Historical Models of Ametropia

Trachtman,[42] reviewing the literature, found many articles on ametropia in general, but relatively few that speculate about the causes. He found that when there is speculation, myopia is much more frequently considered than the other ametropias. He was able to list 16 different proposals for the cause of myopia. Trachtman's list did not include three other proposals: reduced hours of sunshine, lens index changes,[43] and a theory that myopia is a disease in its own right.[44]

The likelihood is that no one factor in myopia production is operating in isolation. And with all the possibilities created by 19 variables, how can one sort it all out? To make things simpler, it is possible to reduce the factors to seven categories, each representing a broad category of stressors:

1. Pathological sequellae
2. Malnutriture
3. Stress and apperception
4. Environmental factors
5. Information processing
6. Experimental escapades
7. Genetics

Of the seven categories above, only genetics is not a direct stressor. But genetics is itself the basis of our stress response mechanism. The unique hardware of each person's body and its capacities to respond to life's stresses are dictated by our genetics. Therefore, stress can be viewed as a common denominator to all the existing theories of myopia production.

As noted earlier, genetics and refractive error relationships do not have iron-clad support in the literature. There is more to refractive error than genetics alone can explain.

VII. MECHANISMS OF OCULAR ADAPTATION

Stress and the Sclera

Four areas of the globe of the eye have been suggested as possible anatomical sites for the development of myopia: the cornea, the anterior chamber, an optically discoordinated crystalline lens, and the axial length.[28,30,45] The most consistent correlation is with the axial length which has not been contradicted by recent technology.[24]

In considering the role of stress in myopia and astigmia, we need to study the anatomy of the globe. The pre-adult globe is not well fibrosed. It is made up of collagen fibers which constitute at least 70% of the dry weight of the sclera. The fibrils are tightly woven in the anterior portion and are in regular patterns in the areas of insertion of the extraocular muscles. This makes the anterior portion of the globe less susceptible to distention. However, the posterior sclera is loosely woven in less regular patterns and is developmentally the last portion to be laid down, being quite thin at birth and is still being formed at puberty.[46]

The sclera is known to distend and creep, the collagen's fibers sliding past each other. Collagen has poor elasticity, so reversal of the distention is not likely to occur. Young[47] found a functional relationship between accommodation and increased intraocular pressure; and research continues to show that myopes tend to have higher IOP than non-myopes.[48-50] Kelly, et al,[51] have contended that myopia is, in reality, "expansile juvenile glaucoma" and that the so-called "growth" of the eye in progressive myopia is merely irreversible ballooning of the globe due to increased intraocular pressure during reading. Experiments in controlling myopia with Timolol have not been successful, but at least one trial with Metipranolol, a Beta blocker, had remarkable results, arresting myopic progression in 18 of 20 subjects.[52]

Stress is known to reduce fibroblastic activity and to leech protein from the entire body through the action of proteolysis. Stress results in the almost instantaneous decrease of ascorbic acid levels and also greatly increases the excretion of calcium.[53] However, the upkeep and formation of collagen is dependent on calcium and ascorbic acid levels, among other processes, and Robertson[54] and Lane[55] have pointed to scleral changes in the reduced presence of these elements. It was noted by Robertson that it takes a relative lack of ascorbic acid to produce the changes and, also, the same relative lack increases intraocular pressure (Lane).

The lack of ascorbic acid reduces the enhancement of intracellular cement in collagenous tissues and this, added to the reduced fibrous production, increased IOP, plus the scavenging of the collagen's protein, creates a climate for the adverse creeping and sliding of the fibrils of the posterior sclera. Scleras in the treatment eye of monocularly deprived tree shrews showed just this sort of creeping process.[26] Adding to this, the posterior sclera is nested in a pocket of fatty tissue and is the warmest portion of the eye. Heat denatures collagen and has been suspected of

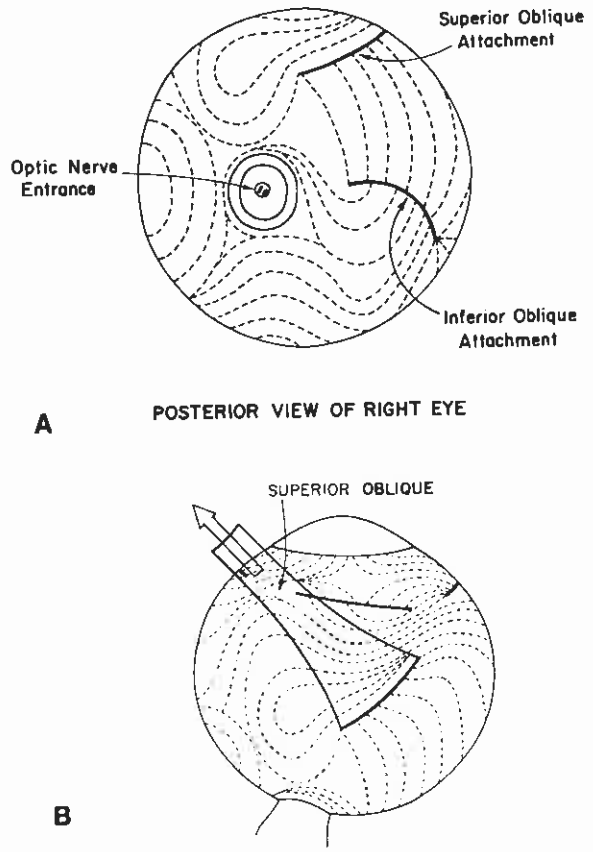

Figure 1. The primary fibril bundles of the posterior sclera show a pattern suggesting linear distention forces are at work. Anterior scleral fibril bundles are characteristically random and are thus less subject to distention. Greene,[57] an engineer, specuated that the myopic staphloma resulted from the weakening of the posterior pole of the globe because of the optic nerve foramen and the efforts of convergence at the points of insertion of the muscles. His illustration graphically shows a vertical stress plane that would create a horizontal toroidal retinal deformation along with elongation of the axis of the globe. Myopia and against-the-rule astigmatism would thus be interrelated. (Reprinted with permission of publisher.)

TABLE I
REFRACTIVE ERROR AND MINERAL CONCENTRATIONS IN HAIR TISSUE

	Initial Medians (PPM)		
MINERAL	MYOPIA	EMMETROPIA	HYPEROPIA
Calcium	665	173	468
Sodium	62	69	120
Potassium	06	24	140

Calcium concentrations in hair tissue from hyperopes and myopes are significantly higher than that mineral level in emmetropes. Sodium concentrations are unusually high in hyperopes, as are potassium levels, suggesting the activation of the sodium/potassium pump in hyperopes to maintain their reported higher levels of action readiness. Myopes' levels of potassium are noted to be unusually low. (Adapted from Lane[55])

contributing to the myopic process. Experiments with rabbits have confirmed this.[56]

Extraocular Dynamics and Astigmatism

The effects of the extraocular muscles on a weakened sclera would be detrimental. Greene proposed a mechanical model of myopia progression that, along with increased IOP, would produce the classic bulging of the posterior sclera in myopia known as a posterior staphyloma.[57] His illustration of the insertion of the superior and inferior oblique muscles, near the optic nerve foramen (see Figure 1), was intended to demonstrate how the posterior pole of the globe is structurally at risk. The illustration also shows how the usually random pattern of fibrosing becomes quite linear between the muscle insertions. So increased convergence—as in reading—along with reduced testosterone, increased cortisol and deficient ascorbic acid would set the stage for an eye to be at risk for not only myopia, but also against-the-rule astigmatism at the retinal plane. (The stretched fibers in the illustration would allow the posterior globe to distend in a toroidal manner to create the morphic plane of against-the-rule astigmatism.) The relationship of myopia and against-the-rule astigmatism has been found in other studies.[58,59]

Forrest,[22,23] Horner,[60] and Getman[61] have all noted the apparent effects of the extraocular muscles in the development of astigmatism. The latter two authors noted the apparent connection between accommodation and corneal astigmatism. Since the cornea's collagen content is even higher than the sclera's, it should be at least as vulnerable as the sclera is to the processes thus far described. More frequently, progressive myopia is associated with against-the-rule astigmatism.[50,58,59]

The selective exhaustion of a part of the body represents the final stage in the local adaptation syndrome (LAS) and calls for activity in the strained part to stop to prevent adverse changes.[4] But the personality and analytical cognitive styles of myopes would tend to encourage them to work on beyond exhaustion, into adaptation. Extended nearpoint work would therefore have the means to affect the globe with myopic and astigmatic changes and the cornea with astigmatic ones, for these reasons, especially in an at-risk eye, one softened by these stress processes. Myopia and against-the-rule astigmatism are natural adaptive outcomes to nearpoint stress.

VIII. EMMETROPIZATION? OR HYPEROPIZATION?

Homeostasis

Statistical study has shown that refractive error in adults assumes a highly leptokurtic (peaked) curve that is slightly hyperopic. However, the curve at birth is nearly Gaussian (bell-shaped).[30] Sorsby felt that it was a coordination of axial length, corneal power, and crystalline lens power that created this "emmetropization" factor. Of the three, he speculated that it was the lens that was most responsible.[30] Johnson et al, contended that the failure of the emmetropization process was the cause of low degrees of ametropia.[62]

It is suggested that there may not be a separate emmetropization process per se, but only a hyperopizing reaction process. As mentioned earlier, life may always tend to create myopic effects on the visual system. Retinal defocus and other stimuli then act to stimulate the hyperopization process. The recent primate research by Hung, Crawford and Smith[63] demonstrated that, within fairly broad parameters, overcorrecting with plus and minus will force compensating refractive shifts in the eye, tending to support the presence and function of homeostatic processes in the eye.

Electrolytes and Hyperopia

If, as suspected, emmetropization is merely the balance of life's myopizing effect and the body's hyperopizing counterresponse, then what might be fueling

the hyperopia engine? Electrolyte imbalances and sympathetic stimulation are the most likely answers.

Lane[55] demonstrated that both hyperopes and myopes spill excessive amounts of calcium when compared to emmetropes. But unlike either myopes or emmetropes, hyperopes spill huge amounts of potassium and sodium (see Table 1). Lane was measuring the minerals in hair tissue, a controversial analytical technique. Growth of hair provides a record of serum levels of minerals and this method has proven to be of value in criminology and drug-abuse study.[64] Lane's methodology was highly persuasive in that his data is inter-test reliable, at least with his batches.[65]

The spillage of calcium in both myopes and hyperopes gives strong evidence of the action of distress with its cortisol-induced hypocalcemia and the body's attempts to correct the deficit by drawing on tissue stores of calcium. The lenses of myopic eyes are known to be dioptrically weaker—more hyperopic—than the lenses of emmetropic eyes,[66-68] evidence that a hyperopization process was actively attempting to restore focus as part of a homeostatic mechanism. Low serum calcium levels affect the crystalline lens, increasing the lens capsule sodium permeability, resulting in geometric changes as the lens imbibes water and decreases the lens power.[69] Hyperopization occurs. It is conjectured that the hyperopia and loss of myopia associated with the progression of presbyopia is further confirmation of this latter process, since calcium loss in that age group is well-known.[39,46,53,69]

Lane's data[65] shows that the hyperope differs from the myope and emmetrope in that he systemically spills fairly large amounts of sodium and potassium. This may be evidence of either a sodium/potassium pump problem or of chronic central nervous system activation. (Potassium, released by the liver under stress conditions, augments the action of epinephrine in muscle tissue, enhancing muscular responses.)[70]

Lane also has implicated magnesium depletion in the production of myopia,[55] but since magnesium regulates calcium levels (and vice versa), this would add to the problem of hypocalcemia, since calcium balancing is initiated by as little as a 1% change either way. Rapidly decreasing tissue and serum calcium levels would result in acute progressive hyperopia, a relatively rare but observable clinical phenomenon.

Sympathetic stimulation also inhibits accommodation, flattening the lens,[71] thus promoting a hyperopic shift—perhaps at times an inappropriate, exaggerated movement of the optical system—but entirely useful in an axially distending eye. Gawron found sympathetic dominance in myopes, a further suggestion of just this process.[72]

Under visual distress, the hyperopization process continues an attempt to decrease the myopic tendency, until distress is relieved by retinal clarity. Once the coping mechanisms are unstressed, adaptation should cease.

Personality, the CNS and the HPA Axis

But if stress affects the calcium levels of both myopically-prone and hyperopically-prone individuals, what tips the refractive scale one way or the other? Among other potential differences, we have clinically observed that it is most probably the large difference in personality styles of each.

As a group, hyperopes have been described as being action-oriented, impulsive and extroverted.[7,73] Desiring to act rather than to withdraw, retreat or reflect, the hyperope under a stressor situation more frequently and more consistently stimulates his sympathetic branch to swing into action. Epinephrine, norepinephrine, cortisol, and potassium are released. In a stressor situation, the myope's personality—shy, anxious, suffering[33,74]—leads him to withdraw, to think, to worry, to absorb, and adapt. The hyperope's response is to approach and subdue, or to flee. The clinical impression of the difference between the two is that the myope frequently may feel out of control with his world, and the hyperope seems to need to impose inordinate control upon his world. Each style of response will have its own chemical effect on the structures of the eyes over the long run. The affective differences modulate the CNS signals to the hormonal response system. The apperception of a stimulus—perception colored by emotions—is the modifier of the route and the degree of response.

The potential myope and the potential hyperope can share the same environment and yet undergo quite opposite refractive responses.

IX. THE STRESS OF NEARPOINT WORK

Animal and Human Studies

Many of the studies on myopia contend that there is a causal effect in nearpoint activities.[48,75-77] Young created myopia in monkeys by confining them in visually restricting hoods.[78] He later demonstrated that he could prevent this adaptation with cycloplegics.[79] The source of myopia was felt to be the triggering of the lengthening of the globe by accommodative spasm.[33,80] A non-accommodative mechanism has been asserted for the action of atropine—and the role of the effect on scleral metabolism considered[81]—but this experiment was conducted with chicks, and mammalian eyes are not clearly subject to the same mechanism, as noted earlier. Others have noted a relationship between myopia and astigmatism in conjunction with accommodation.[82]

Human studies with submariners and officers in a Minuteman launch facility showed a relationship between those enclosed environments and myopic refractive shifts.[83,84] However, in the second study cited, the amount of time spent on alert status was the dependent variable. Luria, one of the primary submarine myopia researchers, has indicated that in all the studies done to that point, stress, anxiety and fear had not been studied nor controlled for.[85]

Young[61] correctly points out that if a genetic etiology were the dominant cause of myopia, then cycloplegia should not arrest its progression.[80] However, myopia has been produced in monkeys strapped on their backs or fronts, or suspended upside down, with no control hoods at all. One element, at least, was common to all those animal experiments: restraint, or containment.

Nearpoint work alone is not sufficient to explain the production of all ametropias. The myopic population is not a homogeneous one and a single mechanism will not suffice.[86,87] But the combination of factors: genetics, nearpoint stress, personality style, anxiety, nutrition, increased IOP—all appear to have contributing roles in the development of refractive error through the action of the GAS and its effects.

It will be interesting to see whether focused light can be shown to modulate homeostatic mechanisms in the human eye. Wallman, et al,[88] blocked local regions of the retina in chick eyes and showed that local growth into myopia occurred in those areas. This is consistent with the LAS of Seyle's theory.[4] Wallman went on to speculate that large amounts of reading may simulate an impoverishment stimulus environment for non-foveal regions of the retina since neurons in those areas have large receptive fields.

X. SUMMARY

The physiological changes that occur in a physically or emotionally constrained, anxiety-producing environment, contribute to spiraling stress responses. This provokes further HPA axis hormonal shifts and, over time, structural and functional change, modified by personal response styles. As the body tries to cope and homeostatic balancing abilities become swamped, the body can defend and equip itself through adaptations in attempts to reduce the distress either physiologically or physically—even in the eye under environmental distress.[89]

When these processes involve the visual system, the functional and refractive changes that have been discussed in this postulation are natural outcomes of these defensive and adaptive coping processes.

All previous theories of the etiologies of ametropia subserve the unifying concept that stress and the HPA axis response appear to contain the generative processes that will result in myopia, astigmia, and hyperopia.

As Lesser said, the body attempts:

> *...to make (its) organismic decisions as comfortable and as gratifying as possible within the demands of (its) environment.*[90]

XI. IMPLICATIONS

Stress is produced in greater or lesser degree by imposed stimulation. Each individual responds in a unique, learned manner. The triggering variables involved in the individual's stress responses are multiple and include genetic predisposition, nutritional adequacy, immune responses, prior experiences, vocational and avocational activities, and personality style. These factors appear to induce physical ocular changes.

We, as clinicians, then measure the impact of these changes carefully, externally. We call the resulting stress adaptive diseases myopia, astigmatism, and hyperopia. Appropriate interventions would take the form of preventive lenses, visual therapy, bifocals, undercorrection, nutritional counsel, ergonomical and environmental consideration, and stress counseling.

The current clinical trend in general optometry and ophthalmology is to reduce the analytical role of the clinician, even delegating refraction and minimizing visual analysis and virtually ignoring visual therapy. This may be foolhardy, since ametropia is more appropriately considered a disease process, requiring appropriate diagnosis and intervention. Myopia is nearly epidemic, especially with the increasing flow of late-onset myopes being seen in every doctor's office.

This paper contains a number of testable questions and propositions. As research evolves, the central role of the clinician in actually preventing ametropia will increase in importance. Instruction in metabolic endocrinology, functional vision philosophies and psychological principles of stress will then become genuine priorities in optometric education and visual science in general.

The real question is not *if* stress is a factor in ametropia, but *to what extent* stress is a factor. It raises the clinical question, "What am I able to prescribe visually—or otherwise recommend—to modify this patient's distress?" Stress is inevitable, but distress is a unique perception of the individual— it originates in the intellectual processes and affects health when the rational mind confronts situations with which it cannot cope.[91] Ultimately, as Brown notes, "Stress is in the eye of the beholder."[5](p.139)

This paper has proposed a complex behavioral model. For that reason, support for it will be readily found, but absolute proof will be elusive.

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