Glaucoma

Approximately 2 million people in the United States have had the disconcerting experience of being diagnosed with glaucoma. The loss of any of the special senses, especially eyesight, can be a traumatic event. Statistics justify the concern because glaucoma is the leading cause of blindness, affecting 89,000-120,000 people.

WHAT WENT WRONG?

Generally speaking, glaucoma alludes to elevated pressure within the eye due to either hindered or obstructed outflow of aqueous humor, a clear fluid found in the anterior or front of the eye. The aqueous humor flows into the eye at the usual rate but drains too slowly. Aqueous humor, though villainized in the progression of glaucoma, performs tasks that are absolutely essential to the health of the eye. It assists in maintaining normal pressure within the eye, refracting light (the bending of light rays as they pass from air into some other, more dense substance), and providing nutrients to the inner surface of the eye.

The inability to efficiently extricate the fluid from the eye causes an increase in intraocular pressure (IOP). The tiny, delicate nerve fibers that make up the optic nerve at the back of the eye are slowly destroyed. Because the optic nerve relays visual messages from the eye to the brain, where seeing actually takes place, the health of this nerve is essential to sight. Restricting the free flow of aqueous humor, as seen by narrowing, hardening, or constriction of the exit channels, can be a purveyor of glaucoma.

SIGNS AND SYMPTOMS OF GLAUCOMA

The symptoms of glaucoma differ depending upon the type of glaucoma diagnosed. In the majority of cases, especially in early stages, there are few signs of the impending disease. Some patients are without symptoms; others complain of a loss of side vision, followed by reductions in central vision, an inability to adjust the eye to darkened rooms, difficulty focusing on close work, and a frequent need to change eyeglass prescriptions. (Because glaucoma is sometimes missed in routine eye exams, symptoms should always be reported to the examining ophthalmologist or optometrist.)

Acute or Closed-Angle Glaucoma

Glaucoma may be classified into two types: acute (angle-closure, closed-angle, or narrow-angle) and chronic or primary (open-angle or wide-angle), the former being more severe but, fortunately, less common. About 10% of glaucoma is acute or closed-angle, and 90% is chronic or primary open-angle glaucoma. Closed-angle glaucoma represents a medical emergency. Unless the individual has treatment to improve the flow of fluid, the eye can become blind in as little as 2-5 days.

No discharge from the eye is apparent in acute or narrow-angle glaucoma. Symptoms commonly reported are extreme ocular pain, severe headaches, blurred vision, swollen upper lids, eyeballs that are tender and firm, and nausea and vomiting. Dilated pupils and a shallow anterior chamber are usually evidenced upon examination.

Closed-angle glaucoma can occur if the pupil in an eye with a narrow angle between the iris and the cornea markedly dilates, allowing the iris to assume a folded configuration, capable of blocking the exit of aqueous humor from the anterior chamber. Medicinally inducing a constricted pupil, by way of eye drops, is one treatment for acute (closed-angle) glaucoma. The constricted pupil draws the iris away from the cornea, allowing a larger exit chamber for the aqueous humor.

Osmotic agents, such as urea, mannitol, and glycerol, are used to reduce IOP. Acetazolamide, a carbonic anhydrase inhibitor, can be used to reduce fluid formation. Drugs to relieve pressure, in union with either a surgical iridectomy, a small opening in the periphery of the iris, or laser treatments to produce a filtration pathway, are commonly effective. About 60% of the individuals consenting to surgery consider the procedure successful. Approximately 15% of those having surgery report a decline in the quality of life.

Argon laser surgery is an innovation in glaucoma treatment. The laser, a device that produces a high-energy beam of light, is used to make about 100 small burns in the drainage meshwork at the edge of the iris. Scientists think that the scars from these burns help stretch open the holes in the meshwork, making it easier for fluid to filter out. Usually, individuals who have this surgery continue taking some glaucoma medication afterward, although the dosage may be lowered. The positive effects of the laser treatment may wear off eventually, requiring a second or third treatment session.

For those patients whose eyesight is severely compromised, Johns Hopkins Medical Institutes have developed a high-tech video headset that is helping individuals with significant visual impairment lead more independent lives.

Primary Open-Angle Glaucoma (POAG)

Primary open-angle glaucoma (POAG) is often a bilateral condition of genetic determination that develops slowly as the drainage canals gradually become clogged. In open-angle glaucoma, the angle where the iris meets the cornea is as wide and open as it should be. The intraocular pressure rises because the "ebb and flow" of the fluid has been disrupted and drainage out of the eye is impaired. The obstruction in POAG is thought to be within the canal of Schlemm, a tiny vein at the angle of the anterior chamber of the eye that drains the aqueous humor, funneling it back into the bloodstream. (See illustration on page 544.)

Cupping of the optic disc, a small area insensitive to light on the surface of the retina, is another determinant in glaucoma progression. Pale and cupped optic discs may be observed by ophthalmoscopic examination, even when the IOP has been stabilized.

POAG may be asymptomatic, except for a gradual loss of peripheral vision over a period of years. Symptoms may be mild and intermittent, perhaps only occurring while in a darkened room, watching television or a movie. Rest or sleep may appear to rehabilitate the eye for short periods of time. Headaches, blurred vision, and a dull pain in the eyes may be experienced. Halos around lights and central blindness are late manifestations of the condition.

Pilocarpine, a meiotic substance, can usually control POAG by inducing pupil constriction. It can reduce IOP in less than 15 minutes after application and maintain the lowered pressure for about 24 hours. Pilocarpine is actually derived from jaborandi, a tropical tree that grows in South America. Spanish naturalists accredited jaborandi with the ability to treat eye diseases as early as 1648.

Other conventional treatments for POAG include epinephrine, to increase the outflow of aqueous humor, and beta-adrenergic blocking agents, to decrease aqueous humor production. Beta-blocking eye drops are not without undesirable side effects. They tend to disorganize the ratio of HDL, the beneficial cholesterol, to LDL, a form of cholesterol considered extremely harmful when in excess and oxidized. The strength of the epinephrine drops is not great enough to induce a sympathetic nervous system response, which would be contraindicated in a glaucoma patient.

Symptoms of POAG can usually be controlled with treatment, but the treatment is considered lifetime. Vision is usually not impaired permanently if glaucoma is found early and treated.

STRUCTURES OF THE EYE

To understand glaucoma, it is necessary to comprehend the responsibilities of the various structures of the eye and their placement. Recall that the iris is the colored portion of the eye that contains smooth muscle and regulates the amount of light entering the eye. The pupil is the opening in the iris through which light passes to the lens and the retina. The cornea is the part of the eye that produces the greatest amount of convergence of light and composes one-sixth of the outermost tunic, referred to as the fibrous tunic, of the eye bulb. The retina or nervous tunic is the innermost tunic of the eye. The optic nerve passes through the retina at a point called the blind spot. This is an apt description, for the blind spot contains neither rods (photoreceptors that respond to dim light) nor cones (photoreceptors that respond to bright light and allow color vision). Nerve impulses initiated by the rods and cones are passed to the bipolar cells, which in turn pass them to the ganglionic cells. The fibers of these cells pass in front of the retina forming the optic nerve, which carries the nerve impulses to the brain.

WHO IS PRONE TO GLAUCOMA?

About 1 in every 30 people in America, age 40 or over, has glaucoma. This number includes the one-half who are not aware that they have the eye disease. According to the National Eye Institute, a person with diabetes is almost twice as likely to have glaucoma as other adults. The longer an individual has diabetes, the greater his or her risk of becoming a glaucoma victim. This form of glaucoma is referred to as neovascular glaucoma.

The incidence of glaucoma is four to five times greater among African-Americans compared to Caucasian Americans. In the Caucasian American, an increase in the incidence of glaucoma occurs after the age of 50. Hypertension and a family history of glaucoma place an individual at an increased risk.

The risk of glaucoma appears greater in individuals who suffer extremes of farsightedness or nearsightedness. Farsightedness is associated with a greater risk for closed or narrow-angle glaucoma. The individual displays a shorter eye and a shorter axial length. This condition alters the angle, the spongy meshwork of tissue located at the point where the cornea and iris meet, hampering drainage of the aqueous humor. In some individuals, an anatomical peculiarity of the eye, often inherited, makes the angle unusually narrow and easily closed off.

An extremely nearsighted individual has a greater risk association with POAG. The elongated eyeball, characteristic of nearsightedness, allows a larger optic channel, with the optic nerve fiber becoming more susceptible to pressure and injury.

Glaucoma can be congenital, for example, when the ducts responsible for fluid drainage fail to form completely. Some infants are born with defects in the angle of the eye that slow the normal drainage of aqueous humor, a condition most often correctable with surgery if done early enough.

Individuals who have either Ehlers-Danlos syndrome, a disorder of connective tissue, or Marfan's syndrome, a condition characterized by elongation of the bones, appear to have a higher association with glaucoma and other eye complications.

Secondary glaucoma can manifest as a result of a predisposing event, such as eye surgery, advanced cataracts, eye injuries, eye tumors, or uveitis (eye inflammation). Correction of the primary source may allow rectification of the secondary disease as well.

CAN DRUGS CAUSE GLAUCOMA?

According to Leonard Levine, Ph.D., certain drugs can "impair the biological health of the visual system." For example, the Physicians' Desk Reference lists 94 medications that can cause glaucoma, including antihypertensives, antidepressants, and steroids, such as cortisol, which can destroy vital collagen tissue in the eye. Both herbal ephedrine and pseudoephedrine have central nervous system (CNS) stimulating properties. Ephedrine is the stronger of the two, but both are considered stronger than caffeine. The glaucomatous person should avoid these substances, particularly Ma-huang, licorice, and belladonna.

Note: *Antihistamines can increase pressure within the eye. If using drugs for other conditions, always inform your doctor of an existing glaucoma condition to avoid prescribing drugs that might adversely affect the disease. Obviously, it behooves individuals relying upon prescription drugs to thoroughly acquaint themselves with the side effects.*

The use of certain medications that inhibit cholinergic response has been linked to a higher incidence of glaucoma. An anticholinergic drug blocks acetylcholine receptors, resulting in the inhibition of parasympathetic nerve impulses. This action would make stronger the sympathetic nervous system, an action that could dilate the pupil and relax the iris sphincter. Dilation of the pupil could make smaller the passage between the iris and cornea, complicating the exit of the aqueous humor.

DO ALLERGIES INFLUENCE GLAUCOMA?

Individuals who suffer either food or environmental allergies appear to be at a higher risk for glaucoma. Both causative and therapeutic factors appear to link allergies and glaucoma. Persons with nonresponsive or refractory glaucoma are occasionally asked to consult an allergist, in an attempt to lessen the endogenous stress load. Greater acceptance of the allergy/glaucoma hypothesis adds another dimension to treatment.

CALCIUM--PROS AND CONS

Calcium excesses can be redistributed in the body to soft tissues, contributing to the risk of glaucoma. The more soluble forms of calcium supplementation are usually well absorbed and utilized, such as calcium citrate, calcium bis-glycinate, or microcrystalline hydroxyapatite. The problem with soft tissue damage due to calcium deposition may be more appropriately seen as a consequence of calcium shortages. When calcium levels are in short supply, the parathyroid hormone participates in a cascade that eventually asks the bones to give up a share of their calcium stores. The host loses on two fronts: (1) too many withdrawals can eventually weaken the skeletal system and (2) the release of calcium from the skeleton is not well regulated. Excesses of calcium can tie up in soft tissues, exacerbating arthritis, arteriosclerosis, kidney stones, and glaucoma. Recall that vitamin K assists in keeping calcium in the bone and not in soft tissue. Considering this, adequate amounts of dietary calcium are absolutely essential to prohibit the activity of the parathyroid gland and the subsequent calcium withdrawal from the skeletal frame.

ODDS AND ENDS

The herb bloodroot (Sanguinaria canadensis) may contribute to glaucoma. Toothpastes occasionally contain bloodroot, because the herb is a strong adjunctive component contributing to gum health. Because toothpastes and mouthwashes are not ingested, the amount of bloodroot entering the system would be minimal, but individuals concerned about glaucoma should be aware of the caveat surrounding bloodroot.

Most vitamins and minerals are nonproblematic for the individual with glaucoma, but patients should restrict their intake of niacin to not more than 200 mg daily.

continue ▸

LOOKING BACK AT TREATMENT

- Vitamin C
- Bioflavonoids
- Coleus Forskohlii
- Minerals
- Melatonin
- Vitamin A
- Marijuana

Vitamin C

Fortunately, history provides significant therapeutics in regard to managing glaucoma. Conventional medications and interventions are the most widely used methods of treatment, but nutritional protocols have produced convincing evidence of benefit.

Vitamin C is an effective adjunct in stabilizing IOP. Some individuals respond to as little as 2 grams a day of vitamin C, although others respond to only extremely high doses, for example, 35 grams a day. Because of the variance in the amount of vitamin C required to exert a positive effect, careful monitoring by a physician is required. Intravenous administration of vitamin C results in an even greater initial reduction. The pressure-lowering action of vitamin C is long-lasting if supplementation is continued, frequently showing an average reduction of 16 mmHg. Nearly normal tension levels have been achieved in some patients using vitamin C, when acetazolamide and pilocarpine therapy failed. The beneficial mechanisms by which vitamin C lowers inner eye pressure include (1) increased blood osmolarity, a process that draws fluid from the eye and into the blood, (2) diminished production of eye fluid, and (3) improved fluid outflow.

Many of the benefits of vitamin C are likely attributable to collagen formation, an important function of this water-soluble vitamin. Collagen is the most abundant protein in the body, including the eye, giving strength and integrity to ocular tissue. Vitamin C helps preserve the collagen in the eyes' drainage tubes, the very tubes that malfunction in glaucoma. Credits directed to vitamin C appear justified when considering reduced IOP and the improved structural health of the eye.

Bioflavonoids: What Can They Accomplish?

All nutrients that support collagen metabolism, particularly at the back of the eye where the optic nerve exits and in the tissues that drain the eye, are important in glaucoma treatment. One such nutrient bioflavonoid, known as the proanthocyanidins (found in grape seeds and pine bark), cooperates with vitamin C in achieving collagen integrity. In the eye, collagen provides tensile strength and stability to the tissue. Another major function of vitamin C is the preservation of capillary integrity, a task made easier with the assistance of a bioflavonoid. The bioflavonoids work not only with vitamin C but also on behalf of vitamin C, preventing the breakdown of ascorbate. The proanthocyanidin bioflavonoids work by binding to collagen, increasing elasticity and flexibility. The proanthocyanidins are considered a powerful antioxidant, defending the collagen matrix against free-radical attack and guarding it against enzymatic breakdown through the enhanced delivery of oxygen and blood to the eye.

Rutin, a bioflavonoid from the citrus family, has demonstrated the ability to lower IOP when used in conjunction with standard drugs. Pansy (Viola) contains up to 23% rutin on a dry-weight basis. Naturopaths, for the treatment of glaucoma, often recommend sources of rutin, including pansy.

The genus Vaccinium comprises nearly 200 species of berries, all showing generous amounts of flavonoid/anthocyanidin compounds. Bilberry, Vaccinium myrtillus fructus, has historically been used in various eye conditions, including glaucoma, cataracts, macular degeneration, diabetic retinopathy, and retinitis pigmentosa. Although bilberry is not considered a curative herb in regard to glaucoma treatment, it appears to assist in halting additional damage by bringing a good flow of blood to the eyes.

Coleus Forskohlii

When Coleus forskohlii was applied directly to the eye, it was shown, in clinical studies involving both animals and humans, to reduce IOP, making it of significant benefit in glaucoma treatment. Forskolin represents a potentially useful class of antiglaucoma agents, differing in molecular mechanism and action from previously used drugs (Caprioli et al. 1984; Hartman et al. 1988). C. forskohlii appears to have a twofold approach that delivers benefit for glaucoma by increasing intraocular circulation and decreasing aqueous humor outflow. The outflow facility remains unchanged, but the ciliary blood in the vascular tunic increases. The benefits are observable about an hour after application and reach a therapeutic peak at 2 hours. The value of C. forskohlii remains significant for at least 5 hours after application. Because C. forskohlii eye drops are not yet available, oral administration may be considered, with the hope that similar results can be obtained. C. forskohlii appears to bestow its therapeutic values without risk of major side effect.

C. forskohlii has been used to advantage in the treatment of hypothyroidism. Interestingly, subclinical hypothyroidism, so mild that it produces no symptoms, has been noted as a cofactor in some patients with glaucoma.

Hydergine has some of the same biochemical advantages as C. forskohlii. Hydergine may be capable of lowering IOP by decreasing hypoxia (reduced oxygen supply) and preventing free radical damage to critical cells.

The Value of Minerals

Magnesium has long been recognized as nature's physiological calcium blocker. Previous studies had demonstrated that calcium channel-blocking drugs offer benefits for some glaucoma patients. Armed with this revelation, researchers at the University Eye Clinic in Basel, Switzerland, evaluated the effect of supplemental magnesium on glaucoma patients. Magnesium (121.5 mg twice daily) was administered to 10 glaucoma patients for 1 month. At the conclusion of the study, results substantiated that magnesium supplementation improved the peripheral circulation, with an accompanying beneficial effect on the visual field in patients with glaucoma.

Magnesium also has the ability to turn off the sympathetic nervous system. This is a reputation that has earned magnesium credit in cardiology, acting as an antiadrenergic. An antiadrenergic drug blocks the effects of impulses transmitted by the adrenergic postganglionic fibers of the sympathetic nervous system. This act would tone and modify the sympathetic response, soothing the "fight or flight" syndrome. Recall that among the many functions controlled by the sympathetic nervous system--those normally not under conscious control--are dilation of the pupils and a general stimulatory response. Stimulation of the sympathetic nervous system would be contraindicated in glaucoma control.

Minerals are absolutely essential to longevity and quality of life. Individuals can survive longer with a vitamin deficiency than with a mineral deficiency. The importance of minerals is becoming more evident as research data amass. The trace mineral chromium has won additional credit beyond stabilization of blood glucose levels by being able to improve focusing of the eye and lower IOP. Selenium benefits ocular function, and zinc supports healthy eye structure. Selection of a good multiple will provide these vital minerals, plus additional nutrients needed for ocular health.

Melatonin

Less than 1 mg of melatonin has lowered pressure within the eyes of healthy people, but studies have not yet been published on the effects of melatonin on people who have glaucoma.

Vitamin A

Many nutritionists regard vitamin A as the most important vitamin of all. Various naturopaths consider vitamin A vital to an effective glaucoma protocol. Considering ocular health, the eyes are obvious indicators of a vitamin A deficiency, often showing symptoms of dry, itchy, or inflamed eyeballs and night blindness. Vitamin A appears to counteract weak eyesight by encouraging the formation of rhodopsin or visual purple, a pigmented compound in the rods of the retina that adapts the eye to low-density light.

Vitamin A, a fat-soluble vitamin, may be accompanied by risk if it is used carelessly or if the liver is under stress. Lewith et al. (1996) reported that dosages of 25,000-50,000 IU might cause liver damage in select individuals (particularly persons with liver problems, those taking certain drugs, or heavy drinkers) if administered over a period of several months. Nonetheless, with judicious administration, such as under the supervision of a nutrition expert or physician, this underrated vitamin can perform outstanding feats.

Some individuals prefer to obtain their vitamin A by way of food sources or supplemental beta-carotene. The conversion of the provitamin beta-carotene to its active form takes place largely in the liver or during the intestinal absorption process. A healthy liver obviously makes the conversion process more of a surety, a process enhanced by the trace mineral zinc.

Marijuana

The National Eye Institute supported research from 1978-1984 to determine whether marijuana or any of its components could safely and effectively lower IOP. Findings substantiated that marijuana did, indeed, lower IOP when administered orally, intravenously, or by smoking. Topical application did not lower IOP. Marijuana passed the initial phase of the study, illustrating it could lower IOP, but the consensus held that the drug was not any more safe or effective than a variety of drugs already FDA-approved and easily available. The potential risk factors of increased heart rate and hypotension also negated enthusiasm associated with marijuana usage.

Research to date has not investigated whether marijuana offers any advantages over currently available glaucoma treatments or whether it could be considered useful when used in combination with standard therapies. The National Eye Institute stands ready to evaluate any well-designed study to consider the value of marijuana in glaucoma treatment.

LOOKING AHEAD TO TREATMENT

The current hypothesis regarding the causative factors of glaucoma leans toward the neurotoxicity/neuroprotection theory. Ophthalmologists refer to neurotoxicity as the "buzz word" in their profession (i.e., the focus of current glaucoma exploration). It appears to be more than a trendy, ungrounded approach to explaining the causative factors and therapeutic modalities of glaucoma. Research emanating from various prestigious universities converges when considering the neurotoxicity theory of glaucoma.

The opinions of Dr. N. N. Osborne, Nuffield Laboratory of Ophthalmology, Oxford University, echo those of many other scholars who are studying glaucoma. Dr. Osborne believes that the visual-field loss in glaucoma is due to the death of retinal ganglion cells. Reducing or slowing down the loss of ganglion cells, a concept known as neuroprotection, appears to be the "only way forward." Osborne proposes that the death of neurons (a process referred to as apoptotic cell death) in various diseases is fundamentally the same but varies in cause. Experimental data show that the death rate of neuronal populations is dependent upon the impact of the insult. Neuroprotectants are more likely to benefit a patient in which neurons die slowly, as in glaucoma. If a reliable neuroprotector can be administered in such a way that it reaches the retina in appropriate amounts and has insignificant side effects, it is likely to attenuate ganglion cell death and thus benefit the glaucoma patient. Providing a solution to neurotoxicity appears to be the therapeutic goal for future treatment.

Aminoguanidine may help preserve the vision of refractory glaucoma patients by inhibiting the build-up of nitric oxide synthase-2 (NOS-2), a substance believed to degrade neuroprotection. NOS-2 stimulates the emission of nitric oxide, a compound implicated in retinal nerve damage (Morgan et al. 1999). Reduction of nitric oxide through nitric oxide synthase inhibition provides partial but significant protection against the lethal effects of oxygen deprivation and the action of excitatory amino acids, such as glutamate and aspartate, upon retinal ganglion cells.

Interest in knowing exactly what aminoguanidine could accomplish in regard to glaucoma spurred researchers at Washington University to look at the drug more closely. Two groups of animals with glaucoma were selected for aminoguanidine research. All animals initially displayed elevated IOP, with cupping and pallor of the optic disc. One group remained untreated, and the other group was treated with aminoguanidine. At the conclusion of the 6-month study, the untreated group displayed the original benchmark symptoms, whereas the eyes of the aminoguanidine-treated group appeared normal but with continued elevations in IOP.

The Washington University study also quantified retinal ganglion cell loss in a group receiving aminoguanidine compared to a control group void of treatment. The untreated group displayed a 36% loss of retinal ganglion cells, compared to less than 10% in the treated group. To realize the importance of this latter finding, visualize the retina being composed of ten layers of various types of cells. Retinal ganglion cells are large, flask-shaped cells composing one of the ten layers. The degradation of the ganglion cells pathologically compromises the delicate nervous tissue membrane of the retina. The final consensus of the study was that aminoguanidine might prove useful as a pharmacological neuroprotector in the treatment of glaucoma, contributing to a healthier eye, with less neuronal death.

Some patients have normal (or low) tension glaucoma. Even though the eye pressure is within normal range, the optic nerve continues to be injured. Despite efficient control of IOP, retinal ganglion cell loss will continue, resulting in further visual impairment if the causative factor is not determined and treated. This revelation was considered valuable, for it exonerated IOP as being the sole antagonist in retinal degradation. Researchers at University Hospital of Wales determined that neuroprotective agents might play a role in patients with glaucoma who have progressive visual-field loss despite satisfactory control of IOP.

OTHER POSSIBLE CAUSES

- Glutamate's Role in Glaucoma
- Cell Death Apart from Glutamate
- Pigment Dispersing Syndrome

Glutamate's Role in Glaucoma

Agreement on the importance of preventing the death of retinal ganglion cells has been established, but the cause of ganglion cell death remains speculative. Present information supports the hypothesis that ganglion cell death may result from a form of ischemia (decreased blood flow to a body organ or part). During ischemia, glutamate is released in excessive amounts, initiating the death of neurons. Glutamate is a salt of glutamic acid, a nonessential amino acid occurring in a wide number of proteins. Glutamate is considered a good guy/bad guy. Because brain cells use glutamate as a neurotransmitter, it may rightly be termed a "great communicator" as signals leap from neuron to neuron. Effective communication also means the controlled release of glutamate, as precise amounts are delivered to the proper cells. It is when glutamate occurs in excessive amounts that trouble begins. Communication between cells fails, and exorbitant amounts of glutamate attach to cells having glutamate receptors. This bonding or attachment spells doom to the ganglion cell, resulting in eventual cell death. Excesses of glutamate have, in effect, poisoned the cell.

Elevated glutamate levels can also exist in the vitreous humor of patients with glaucoma (27 mM as compared to 11 mM in controls) (Vorwerk et al. 1999a). The vitreous humor fills the posterior compartment of the eye, assisting in holding the retina and lens in place. An increased concentration of glutamate in the vitreous humor is sufficient to induce retinal ganglion cell death (Vorwerk et al. 1999b). The rise in IOP is probably the initial insult, which enhances the increase or release of glutamate. Supplements that protect against glutamate toxicity will be discussed later in this protocol.

Cell Death Apart from Glutamate

Two other major causes of cell death are the influx of calcium into the cell and the generation of free radicals. Substances that prevent activation of the glutamate receptor, calcium entry, or free-radical damage may be regarded as neuroprotective agents. Recall that magnesium, in assessing nutritional pharmacology, is considered a calcium channel blocker. Broad-spectrum antioxidants have long been known to quench the harmful activity of free radicals. Ideally, for a substance to have a role as a neuroprotective agent in glaucoma, it should be delivered topically to the eye and used repeatedly.

back continue

Pigment Dispersing Syndrome

Another cause of glaucoma is considered to be the pigment dispersing syndrome (PDS) or pigmentary glaucoma. In PDS, the concavity (curving inward) of the mid-peripheral iris allows iridozonular contact, causing a shedding of the pigmented iris. Released pigment is then carried to the trabecular meshwork where it can reside benignly, not affecting the IOP, or it can malignantly elevate the IOP, as in pigmentary glaucoma. Flattening of the concave iris by mitotic therapy and laser iridotomy appears the key to current and future management. Studies confirm that PDS is inherited as an autosomal dominant trait, observed most frequently in young, myopic (nearsighted) men (Campbell et al. 1995). An autosomal dominant trait is one in which the inheritance of a dominant gene on an autosome, not a sex chromosome, causes the characteristic to be expressed.

***Note:** Primary juvenile glaucoma is a rare form of glaucoma that typically affects individuals from 3-20 years of age, and it, too, is an autosomal dominant trait (Wiggs et al. 1995).*

In some individuals, exercise causes pigment release and an increase in IOP, contributing to the complexities of PDS management. A study conducted at the Institute of Ophthalmology in Italy determined that exercise-induced pigment release temporarily obstructs the aqueous outflow channels, causing IOP increase in some patients with PDS. Pre-exercise treatment with dapiprazole, an alpha-adrenergic blocking agent, was useful in reducing IOP spikes and increasing outflow facilities after intensive exercise (Mastropasqua et al. 1995; Mastropasqua et al. 1996).

Scientists are one step closer to locating the gene responsible for PDS. The New England Medical Center in 1997 stated that the telomeric end of the long arm of chromosome 7 appears incriminated in PDS. Locating a gene responsible for this condition is the first step toward the isolation of the gene itself. Characterization of the responsible gene will potentially lead to new methods of diagnosis and treatment. PDS is one type of glaucoma, accounting for 12-15% of all cases of blindness each year.

TREATMENT OPTIONS

- Current Drug Therapy
- Supplements
- Diet
- Eye Drops
- Lifestyle Changes

Current Drug Therapy

Betaxolol, a beta-blocker presently used to reduce IOP, has calcium channel-blocking functions. Experimental studies show that betaxolol is an efficient neuroprotective agent against retinal ischemia in animals when injected directly into the eye or intraperitoneally. Betaxolol exerts its primary neuronal actions on retinal ganglion cells. Unfortunately, betaxolol has an aggressive list of side effects.

Interviews with hospital pharmacists revealed two prescription drugs being filled with more regularity than others for the treatment of glaucoma. Timoptic eye drops, a beta-adrenergic blocking agent, represents an older, but still popular, approach to treating glaucoma. Xalatan, a prostaglandin analogue, generically known as latanoprost, is a newer method of treatment. Its mechanism of efficacy deals with replicating the activity of prostaglandins, hormone-like unsaturated fatty acids that act in minuscule amounts on local target organs. Latanoprost reduces IOP by increasing the outflow of aqueous humor.

Research conducted at the University of Nebraska Medical Center involved 272 patients taking latanoprost for one year (Camras et al. 1996). Of those enrolled in the study, about 70 individuals withdrew before the end of the study. Withdrawals were caused in 1% by inadequate control of IOP; 5% because of increased iris pigmentation; 3% because of other ocular problems; and 17% because of unrelated medical and nonmedical reasons. The final consensus was that latanoprost safely and effectively reduces IOP for one year, evidencing its usefulness in POAG. However, latanoprost usage can cause a darkening of the pigment in the iris, which might aesthetically disappoint a unilateral glaucoma patient.

Supplements That May Lessen Neurotoxicity and Glaucoma Progression

Experimental studies have identified a variety of naturopathic substances that may prove useful in preventing the death of retinal neurons, particularly ganglion cells, induced by ischemia. It may be possible to protect cells against glutamate toxicity by taking methylcobalamin supplements, the biologically active form of B12 (Akaike et al. 1993; Kikuchi et al. 1997). Methylcobalamin is immediately active upon absorption, although cyanocobalamin must be converted to either methylcobalamin or adenosylcobalamin by the body, removing the cyanide molecule and adding either a methyl or adenosyl group.

Note: *The amount of cyanide produced in the conversion process is extremely small.*

Acetyl-L-carnitine is said to possess efficacy by attenuating age-related neural deficits. Acetyl-L carnitine has produced stunning results in protecting neurons in a wide range of disease processes.

The antioxidant activities of lacrimal fluid and blood plasma were studied in glaucoma, as compared to normal eyes (Makashova et al. 1999). The findings indicate that the progress of glaucoma is paralleled by a gradual decrease in the lacrimal fluid antioxidant levels. A broad-spectrum antioxidant is a recommendation frequently made by various national and international researchers with regard to glaucoma treatment. The antioxidant complex should provide 200-400 IU of vitamin E daily.

Alpha lipoic acid (ALA), both water- and fat-soluble, is a vitamin-like antioxidant, sometimes referred to as the "universal antioxidant." Dr. Lester Packer, a scientist who heads the Membrane Bioenergetics Group at the University of California, regards lipoic acid as a "free agent," meaning that it can substitute for the other antioxidants when they are in short supply. Primary evidence indicates that 150 mg of alpha lipoic acid, taken daily for 1 month, improves visual function and ocular hypertension in glaucoma patients (Filina et al. 1995).

Thiamine (vitamin B1) has been used to improve visual acuity (van Noort et al. 1987). This may be of particular advantage to glaucoma patients, for thiamine-deficient states are frequently associated with glaucoma (Asregadoo 1979).

Can Diet Make a Difference?

The watchful selection of foodstuffs appears to be another modality that impacts the control level of glaucoma. The value of vitamin C has been documented with regard to both lowering IOP and maintaining the reliability of ocular collagen (Pfister 1980; Pasquali et al. 1997; Head 2001). For this reason, glaucoma patients should acquaint themselves with foods rich in this essential vitamin and use them freely in meal planning.

Fresh fruits and vegetables are reliable sources of vitamin C. Select from kiwi, bell peppers, broccoli, cabbage, citrus fruits, Brussels sprouts, kale, parsley, strawberries, tomatoes, and cantaloupe to contribute to an adequate vitamin C intake. Remember to emphasize dark-colored berries (raspberries, blackberries, blueberries), grapes, raisins, and plums, which are sources of anthocyanoside antioxidants having a special affinity for the eye.

Try to plan a diet around whole, unprocessed foods, including whole grains, legumes, nuts, and seeds.

The omega-3 fatty acids have shown benefit in lowering IOP (Kulkarni et al. 1989). One tbsp of flaxseed oil (a source of alpha-linolenic acid) daily provides a good supply of omega-3 fatty acids. Because flaxseed oil is highly polyunsaturated, it should not be heated.

Evidence is mounting pertaining to excitatory neurotoxins encountered in our food supply. The most frequently encountered food excitotoxin is glutamate, which is commercially added to many foods despite evidence that it can freely penetrate certain brain regions and rapidly destroy neurons by hyperactivating glutamate receptors (Olney 1994). Avoidance of glutamate may be of particular advantage to individuals with glaucoma.

The herb oregano, from the mint family, may have a worthwhile place in the diet of a glaucoma patient. James A. Duke, Ph.D. (1997) suggests that of the 60 mints he investigated, all high in antioxidant value, oregano had the highest concentration of antioxidants. He suggests using 1-2 tsp of dried oregano per cup of boiling water. The therapeutic strength of this drink can be amplified with the addition of peppermint and rosemary.

Identify and eliminate the consumption of allergenic substances in ingested food materials. Allergies are individualized and impossible to distinguish universally, but milk, onion, eggs, and chocolate are among the most common in patients.

Drink at least 48 oz of clean water daily. This amount should be metered throughout the day, with at least 1-hour intervals, consuming only a few ounces at one time. Individuals who enjoy juice in their diets or support the healing benefits associated with juice may wish to combine bilberry, cranberry, and huckleberry, all of which are high in anthocyanosides. Avoid stimulating beverages, such as coffee and tea, which cause vasoconstriction and elevated blood pressure.

Topical Eye Drops

Research shows that orally taken antioxidants will effectively raise blood plasma levels of the nutrients, but the intake does not always correlate directly in eye tissues. In one study, oral antioxidant therapy normalized blood antioxidant levels in advanced glaucoma patients but did not help lacrimal antioxidant activity. Although further research needs to be conducted, this may indicate that topically applied antioxidant eye drops may be the preferred treatment in glaucoma patients (Makashova et al. 1999).

Lifestyle Changes

Glaucoma is considered to be a stress disease. Avoid emotional upsets and upheavals, for external pressure increases internal ocular pressure (Kaluza et al. 1996; Flammer et al. 1999). Try to develop a composed, peaceful lifestyle. Climates with great temperature variances are thought to be detrimental. More stable climates and temperatures appear to be better tolerated by the glaucoma patient. Don't smoke, for tobacco constricts blood vessels, reducing the blood supply to the eye. Avoid prolonged eye stresses such as long movies, excessive TV viewing, or excessive reading.

Discuss with your ophthalmologist your physical and sexual activity. Normally, after treatment, regular exercise and activities are resumed. Restraint should be observed to avoid fatigue. Sexual relations are usually permitted, when eye pressure is under control.

SUMMARY

Current glaucoma research appears to focus on providing neuroprotection to retinal ganglion cells (Osborne et al. 1999a; 1999b). This approach may benefit those displaying normal tension but still experiencing progressive visual-field loss. Recommendations to reduce IOP are also included. Glaucoma represents a serious eye condition, requiring monitored supervision by a qualified ophthalmologist. Best results might be obtained by working with a complementary physician who employs the best of orthodox and alternative wisdom.

Some of the following suggestions replicate the same mechanism and should be structured to individual needs:

1. Vitamin B12, methylcobalamin, is the choice of many wishing to delay the death of neurons observed in the aging process. Sublingual methylcobalamin supplementation is considered therapeutic for central and peripheral neurological damage, at dosages of 5 mg dispensed throughout the day so that the total intake amounts to 40 mg a day. Do not eat the tablet as one would candy. Let the B12 dissolve slowly under the tongue. This form of vitamin B12 is an alternative to weekly B12 shots and may be quite useful in the prevention of neurotoxicity.
2. Aminoguanidine (300 mg daily) has shown neuroprotective benefits. Aminoguanidine reduces nitric oxide, protecting against oxygen deprivation and decreasing the death of the retinal ganglion cells. Limited clinical experience involving aminoguanidine suggests it should not be used in doses greater than 300 mg a day.
3. Alpha-lipoic acid has attained favorable attention in the treatment of glaucoma. It appears to improve ocular hypertension and visual function. Current glaucoma research considers a daily dose of 150 mg adequate for glaucoma treatment.

Note: *Much larger dosages are used in diabetes and AIDS (300-600 mg daily) without significant side effects. (This information is included to illustrate the safety parameters of alpha lipoic acid.) Possible side effects include skin rash and hypoglycemia. Lipoic acid can worsen a B1 deficiency. Chronic usage of lipoic acid can interfere with biotin utilization, so make sure you are taking plenty of biotin and vitamin B1 when taking over 100 mg a day of alpha lipoic acid.*

1. Topically applied eye drops may be a more effective delivery system for antioxidant protection. Brite Eyes II contains nutrients that protect against free radicals. The formula also contains the antiglycating agent N-acetyl-L-carnosine, which helps prevent the formation of nonfunctioning protein crosslinks. A daily dose of 1-2 drops in each eye is suggested for general eye health.
2. The Life Extension Mix, 9 tablets or 14 capsules daily, or 1 tbsp. of powder daily provides a storehouse of nutrients, including magnesium, zinc, chromium, selenium, vitamin A, thiamine, vitamin C, bioflavonoids, grape-seed-skin extract, vitamin E, and bilberry, which could benefit ocular health. Some individuals may wish to emphasize additional amounts of the most beneficial of these herbs and nutrients, regarding glaucoma management.
3. Use vitamin C crystals or a powdered form of vitamin C, buffered with magnesium. (This type is added to a liquid and is considered highly absorbable.) The buffered form of vitamin C is easier on the stomach when large amounts of ascorbate are ingested. The magnesium will tend to act as a calcium channel-blocker and temper a sympathetic nervous response. The vitamin C may assist in lowering IOP and establishing healthy collagen. Some individuals will realize benefit from as little as 2 grams of vitamin C daily; others will need as much as 35 grams daily. Some practitioners use 500 mg of vitamin C per kilogram (2.2 lbs) of body weight, a dose that must be reached gradually. Vitamin C should be spaced throughout the day, allowing a continuous supply of ascorbate.
4. Grape-seed-skin extract, rich in proanthocyanidins, increases the effectiveness of vitamin C. Together they support healthy collagen and defend against free radicals. A therapeutic dose of proanthocyanidins is considered to be 150-300 mg daily. Usually this dose can be reduced after a month's saturation.
5. Select bilberry by evaluating its anthocyanosides content. (This is calculated by the percentage of anthocyanidin present,

typically 25%.) The dosage for bilberry, the "eye herb," is 100 mg, 2 times daily (or as directed by your health-care professional).

6. Acetyl-L-carnitine is an important adjuvant in neuropharmacology. A dosage of 3000 mg daily may be used. With most supplements, including acetyl-L-carnitine, gradual introduction of the supplement is advisable, allowing the body to adjust to the actions of the substance.
7. Individuals with healthy liver function may use 25,000-50,000 IU daily of vitamin A. (Some research indicates the emulsified form of vitamin A is less stressful on the liver.) Vitamin A from all supplemental sources should be calculated into the daily total, being watchful of the cumulative amounts. Although toxicity is not usually associated with low doses, people should acquaint themselves with the symptoms of vitamin A toxicity (see Appendix A). Pregnant women should use vitamin A only after careful consultation with their physician. The benefits of vitamin A include decreased dry, itchy, inflamed eyeballs and an increase in visual purple, a substance needed for night vision.
8. Select Coleus forskohlii standardized to contain 18% forskolin. Use 50 mg (9 mg of forskolin 2-3 times per day) to assist in lowering IOP.

Do not use C. forskohlii if prostate cancer is apparent. During C. forskohlii usage, monitor blood pressure, being alert for hypotension.

1. Hydergine's mechanism of efficacy appears similar to C. forskohlii. Hydergine reduces hypoxia and free-radical damage. A dosage of 3-20 mg daily is considered appropriate.
2. Attempts to reduce stress are valuable to the glaucoma patient. External stress begets internal stress, both of which equate to physical disruption. Unpleasant interactions with others, temperature extremes, and fatigue are not desirable for anyone, especially individuals with glaucoma.

The preceding pages have delineated many pharmaceutical drugs that have been efficacious in glaucoma control. Nutritional pharmacology offers choices, as well. It appears important to have a relationship with a physician who employs the best from all disciplines. Side effects and quality of life should impact the selection of an ongoing protocol. When contemplating the number of therapeutic agents available to a glaucoma patient, obviously the individual has many options.

FOR MORE INFORMATION

Contact the Glaucoma Research Foundation, (800) 826-6693.

PRODUCT AVAILABILITY

Methylcobalamin, Life Extension Mix, ascorbic acid (vitamin C) powder, grape-seed-skin extract, bilberry, forskolin, liquid emulsified vitamin A, acetyl-L-carnitine, and alpha- lipoic acid may be obtained by calling (800) 544-4440 or ordering online. Aminoguanidine and Hydergine can be purchased offshore. Contact the Life Extension Foundation at (800) 226-2370 for further information.

back