PRIMARY OPEN ANGLE GLAUCOMA

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Special Studies in Optometry

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April 4, 1994

The broad definition of glaucoma is an eye disorder in which the intraocular pressure becomes too high for the health of the eye. The term glaucoma actually encompasses a group of ocular diseases with various etiologies that ultimately result in a fairly consistent optic neuropathy. Although this unphysiologic IOP is produced by changes in the anterior segment of the eye, the ocular impairments are manifested in the posterior segment. Optic disc changes, nerve fiber layer irregularities, and visual field defects are associated with a disturbance of aqueous circulation and a constant or intermittent unphysiologic IOP. Susceptibility to glaucomatous optic neuropathy varies from person to person. Although several risk factors have tentatively been identified, little is understood about what makes one optic nerve susceptible and another resistant to damage. Boundaries between normal and abnormal IOPs, acquired or pathologic cupping of the disc, and normal or abnormal visual fields are not clearly defined.

The four basic areas that are assessed in order to make the diagnosis of glaucoma or glaucoma suspect are the appearance of the anterior chamber angle, intraocular pressure, the state of the optic disc, and the visual field. These areas are evaluated using biomicroscopy, tonometry, gonioscopy, and perimetry. The exact mechanism whereby elevated IOP inflicts damage on the optic disc is still not fully understood, although current research has made progress toward identifying the subcellular changes that occur as a result.

Classifying glaucoma is very important in order to effectively manage this disorder. The glaucomas are broadly classified as primary or secondary, and open-angle or closed-angle. Congenital, or developmental, glaucomas are generally classified separately and occur in the young as a result of abnormalities in the anterior chamber angle that happen during the gestation period. Primary glaucoma is associated with a direct or unknown disturbance of the aqueous circulation. Secondary glaucoma develops because of another ocular and/or systemic disorder. The terms open-angle or closed-angle refer to the manner in which aqueous outflow is impaired.

Some cases do not fit neatly into one category, and others are a mixed-mechanism glaucoma which is a combination of both open-angle and closed-angle. Also, some patients may demonstrate a change in their type of glaucoma over time which will influence the treatment plan. Many patients have high IOP with normal optic disc appearance and normal visual fields. Some of these people will develop optic nerve damage eventually, but most will continue to have normal optic discs and visual fields for the rest of their lives. These individuals have been labeled as "ocular hypertensives," "glaucoma suspects," or "early glaucoma patients."

Primary open-angle glaucoma (POAG) is the most common type of glaucoma seen in primary care optometric offices. POAG, also known as chronic open-angle or simple glaucoma, is typically characterized by (1) an IOP greater than 21 mm Hg, (2) an open anterior chamber angle, and (3) glaucomatous cupping and/or visual field loss. POAG is a chronic, slowly progressive disease, and is usually bilateral, although the disorder generally appears in one eye before the other. POAG is the most prevalent of all glaucomas and affects approximately 1 in 200 of the general population over 40 years of age,[10] and accounts for approximately 70% of all adult glaucoma cases.[11] Glaucoma is responsible for roughly 20% of all cases of blindness in the United States, affecting both genders equally.[10]

Both ocular and non-ocular risk factors have been identified, and the presence of multiple risk factors increases the likelihood of developing POAG. The non-ocular risk factors are age, race or ethnicity, gender, family history of glaucoma, and systemic and environmental health factors including diabetes mellitus, hypertension, use of cigarettes and/or alcohol, and working indoors. The prevalence of primary glaucoma significantly increases with age. Genetic factors have been implicated in primary glaucoma. Studies have shown that primary glaucoma is found from 5.5 to 13 times more often in close relatives of glaucoma patients and that the prevalence of a positive family history is 6 to 7 times greater on the maternal side than on the paternal side.[1] The prevalence of primary glaucoma varies in different racial groups. In blacks, the prevalence of POAG was found to be 2.59 times that in whites and it occurs at a younger age in blacks than in whites.[1] At the time of diagnosis of POAG in blacks, the mean C/D ratio was higher, the IOP was higher, and the visual field loss was greater.[1] Glaucoma appears to be a more severe disease in blacks since they appear to be less responsive to glaucoma therapy.

Ocular risk factors for POAG include elevated IOP, optic nerve head appearance, cup-to-disc asymmetry, nerve fiber layer appearance, myopic refractive error, glaucoma in one eye, and retinal vein occlusions.[11]

PATHOGENESIS OF DAMAGE

Although the ocular changes that produce the elevated IOP are located in the anterior segment, the primary site of damage caused by elevated IOP is in the posterior segment, in and around the optic nerve head. Studies of axoplasmic flow show vulnerability of nerve axons to increased IOP as they pass through the optic disc.

Two hypotheses currently exist concerning this mechanism of damage. The direct mechanical theory postulates that elevated IOP

directly damages retinal nerve fibers. The second hypothesis, otherwise known as the vascular or indirect ischemic theory, suggests that elevated IOP causes death of nerve fibers by interfering with the microcirculation to the optic nerve head. Therefore, the difference between IOP and intracapillary, or perfusion, pressure determines whether or not damage results. This theory is supported by evidence that areas of localized ischemia show localized blockage of rapid axonal transport. Fluorescein angiography has demonstrated a delay in the filling of intraocular vessels, filling defects, and leakage in glaucomatous eyes. Ischemia could induce focal endothelial damage to blood vessels accounting for this leakage. A rise in IOP or a lowering of the systemic blood pressure can increase susceptibility to glaucoma and cause progression of damage in patients who already have the disease. A decrease in blood flow to the optic nerve can occur from local embolic disease, arteriosclerotic plaques in small arterioles, or carotid artery stenosis. Anemia, diabetes, and migraine headaches are risk factors for glaucoma and support a vascular etiology. More than likely, though, both mechanical and vascular factors contribute to glaucomatous damage.

With age, there is progressive increase in the resistance to the outflow of aqueous humor accompanied by a concurrent decrease in aqueous production, and this may result in a slight increase in IOP. In a few persons, an imbalance between increased resistance to outflow and decreased production of aqueous results in a more significant rise in IOP. Of these persons, those with susceptible optic nerve heads will develop an optic neuropathy from the elevated IOP eventually leading to glaucoma.

Recent studies of histopathological specimens of glaucomatous eyes have demonstrated that both Schlemm's canal and the uveoscleral pathways are altered by the disease. The earliest changes in POAG were localized to the uveal meshwork, formation of a prominent scleral spur, hyalinization and/or atrophy of the ciliary muscle, and associated uveal meshwork. Late stage changes demonstrated marked atrophy of the uveal meshwork, ciliary muscle, and root of the iris along with obliteration of Schlemm's canal from proliferation of its endothelial lining. The changes affecting the uveoscleral outflow of aqueous occurred before those involving the juxtacanalicular tissue and Schlemm's canal.[11]

In POAG, the exact etiology of decreased outflow is not known, although the most likely causes involve biochemical or histological changes in both the conventional outflow pathway through Schlemm's canal and the uveoscleral pathway. Current research has led to the conclusion that many, if not all, of the pathological features associated with glaucoma are actually exaggerated and accelerated changes that occur with age in all eyes.[11]

CLINICAL FEATURES OF POAG

PATIENT SYMPTOMS

Because of its insidious onset, POAG is usually asymptomatic until significant visual field loss has occurred. Rarely the patient may complain of decrease visual acuity, visual field defects, or problems with mobility. In most patients, POAG is suspected by finding an abnormal disc on routine examination.

ANTERIOR SEGMENT

The anterior segment in patients with POAG differs from that in a normal individual. The anterior chamber is typically narrower, more iris processes are present, more pigment is located in the trabecular meshwork, and the iris root tends to insert more anteriorly. The presence of one or more of these signs indicates a need for further evaluation for the presence of open-angle glaucoma.

The presence of an afferent pupillary defect in patients with asymmetric glaucoma has also been reported in the literature. In patients with visual field loss, the depth of the pupillary defect was quantified with neutral density filters which correlated well with the visual field differences between the two eyes.[1]

INTRAOCULAR PRESSURES

The average IOP has been determined to be approximately 15.5 mm Hg with a normal "upper" limit of 21 mm Hg, which is two standard deviations from the norm. The distribution curve, however, is skewed to the right, which indicates that more patients have an IOP greater than 22 mm Hg than would be expected for a typical gaussian curve.[14]

Intraocular pressure is not directly correlated with optic nerve damage because of varying individual susceptibility to optic neuropathy. There is, however, a correlation between IOP and the incidence of glaucoma: the higher the IOP, the greater the probability of developing glaucoma. IOPs above 21 mm Hg increase the risk 7 to 22 times for the development of glaucoma.[11] According to one study by Pohjanpelto and Palva, the frequency of visual field loss increased sharply at 34 mm Hg while minimal visual field loss was present when IOPs were below 30 mm Hg.[1]

Intraocular pressures typically fluctuate from moment to moment because of a multitude of factors, both internal and external, and these normal deviations can be as large as 3 to 4 mm Hg. Most individuals have higher IOPs in the morning that gradually decline throughout the day only to slowly rise again during the night. In some POAG patients, variations of 10 mm Hg or more are not uncommon. Therefore, a suspicious reading should be rechecked during the day at varying times to establish a peak level and to record the amplitude of the diurnal variation.

Asymmetry of pressure between the two eyes is an important

factor to consider when evaluating an individual for glaucoma. Normally, the interocular difference does not exceed 3 to 5 mm Hg, with the usual variation falling between 0 and 3 mm Hg. Interocular differences greater than 5 mm Hg should be viewed with suspicion and careful follow-up is warranted even though the upper normal limit of IOP is not exceeded.[1]

OPTIC NERVE HEAD

The optic nerve head may be thought of as a channel through which retinal nerve fibers leave the globe. The optic cup therefore represents the volume of the channel not occupied by neural disc tissue. Four aspects of the optic disc are evaluated: disc topography, disc hemorrhages, nerve fiber layer changes, and peripapillary changes. The optic disc vessels also undergo rearrangement with the progression of glaucomatous damage.

DISC TOPOGRAPHY. Six aspects of the relationship between the optic disc and the optic cup must be evaluated: cup size, cup shape, cup position, cup depth, differences between the two eyes, and changes of these features over time.

In all eyes, the diameter of the cup can expressed as a fraction of the diameter of the disc both in the vertical and horizontal meridians. This cup-to-disc ratio is genetically determined and great individual variations exist. The cup size is slightly larger in myopes than in hyperopes, is slightly larger in blacks than in whites, and changes very little with age.[1] Most normal eyes have a horizontal C/D ratio less than or equal to 0.3; however, half of early POAG patients have C/D ratios greater than 0.3.[11] Therefore a ratio greater than or equal to 0.4 should be regarded with suspicion although it may not be pathological.

An approximate relationship exists between IOP and the C/D ratio and the C/D ratio and visual field loss. When IOP is higher, the C/D ratio tends to be larger. When the C/D ratio is larger, there is a greater probability for visual field loss.

Asymmetrical C/D ratios between the two eyes is a particularly accurate predictor of glaucomatous visual field loss. A C/D ratio with an asymmetry of 0.2 or greater that is not caused by unequal disc sizes or anisometropia should be considered highly suspicious for glaucoma, especially if the eye with the larger cup has the higher IOP reading.[1,11]

When evaluating a suspicious-looking disc it is essential not to confuse cup pallor with cupping. Cup pallor is defined as the maximal area of color contrast which is related more to the amount of glial tissue rather than to disc vascularity. Cupping is best evaluated by observing the bending of small blood vessels as they cross the optic disc. In some eyes, cupping and pallor correspond, whereas in others the area of cupping is greater than the area of pallor. In normal eyes, cupping increases slightly with age but

the area of cup pallor remains essentially unchanged. In glaucomatous eyes, both cupping and cup pallor increase, although not necessarily at the same rate. A progressive increase in cupping generally precedes a visual field defect.

Cup shape is generally round when it is present. One of the early reliable disc signs of glaucoma is vertical elongation of the cup. Neuroretinal rim loss in the optic nerve has been correlated with visual field loss. In fact, the loss of this rim tissue has a stronger association with POAG than does a large C/D ratio. These optic disc changes have been documented to occur before the development of visual field changes.[15] Sixty to seventy percent of early POAG patients demonstrate unequal intraocular C/D ratios of 0.1 or greater.[1,11]

The area, shape, and integrity of the neuroretinal rim must also be closely evaluated. A healthy, large, pink, evenly shaped neuroretinal rim suggests no visual field loss, while a small, unevenly colored, or unevenly shaped neuroretinal rim is often associated with a visual field loss, although this correlation is not always the case.

Focal notching is another reliable glaucomatous sign. As damage progresses, a selective loss of ganglion cell axons in the superior and inferior quadrants of the optic nerve may occur with relative sparing of the nasal and temporal portions until late in the disease process. The inferior temporal pole of the optic nerve head is the most frequent location for localized disc damage.

Because the optic cup is typically located in the center of the disc, displacement of the cup is another indicator of possible glaucomatous damage.

A change in the C/D ratio with time strongly suggests the presence of glaucoma. After a period of time, abnormal intraocular pressure will eventually cause damage to the optic nerve head which is clinically reflected as a loss of the retinal nerve fiber layer, and an increase in excavation of the surface of the optic nerve, and/or a loss of neuroretinal rim tissue. These changes result from a destruction of ganglion cell axons transmitting impulses from the retina to the thalamus because of a blockage of axonal transport at the level of the scleral lamina cribosa. Blockage occurs both in retrograde and orthograde movement of materials. The degree of blockage appears to be proportional to the level and duration of elevated IOP. Short intervals of increased IOP block axonal transport only in the most peripheral bundles of axons in the optic nerve. Progressive increase in IOP results in injury that extends both across and longitudinally along the axon bundles. Axonal transport depends on adequate blood supply to the axon as well as the presence of intact microtubules for movement of material.[11]

Early glaucomatous changes in the optic nerve head involve (1) compression and rearrangement of laminar sheets, (2) distortion and/or enlargement of laminar pores, (3) changes in composition of laminar tissue and extracellular matrix, and (4) loss of prelaminar tissue. In the more advanced stages of glaucoma there is additional compression of laminar sheets. The scleral lamina cribosa is outwardly displaced, and a bean-pot shaped excavation of lamina appears as an undermining of the neuroretinal rim. The posterior scleral foramen do not enlarge during the glaucomatous changes.

The most typical pattern of early optic nerve damage in glaucoma is progressive concentric excavation of the optic nerve head, or cupping. In actuality, there is a thinning of the neuroretinal rim tissue of the optic disc from atrophy of the ganglion cell axons. Saucerization is an early sign of glaucomatous damage and is the progression of diffuse, shallow cupping extending toward the disc margins without concurrent changes in cup pallor. This process is frequently overlooked without a stereoscopic view.

DISC HEMORRHAGES. Optic disc hemorrhages, also known as Drance hemorrhages, are not pathognomonic for glaucoma. They can also occur in association with a PVD, a resolving branch vein occlusion, anterior ischemic optic neuropathy, papillitis, papilledema, subretinal neovascular membrane formation, hypertensive or diabetic retinopathy, intracranial hemorrhaging, and other optic nerve and retinal diseases.[9,11]

Drance hemorrhages are located on or adjacent to the optic disc and are therefore commonly overlooked. The hemorrhage is flame-shaped if located off the disc in the nerve fiber layer, and blot-shaped if it is on the disc. The inferior pole is the most frequent location, and the location is often associated with a corresponding notch in the neuroretinal rim tissue and a visual field defect. The hemorrhages appear either because of an ischemic cause or a mechanical one due to the shifting of disc capillaries from the loss of the rim tissue. Patients with low-tension glaucoma are 5 times more likely to develop these disc hemorrhages than a high-tension glaucoma patient.[9,11]

Typically, the hemorrhages will resolve in about 10 weeks, with a reported range of 2 to 35 weeks.[9] Recurrences are common and will typically reappear in the same quadrant within 6 months of the original hemorrhage.

Disc hemorrhages are an early indicator of glaucomatous damage and may precede nerve fiber defects and structural changes to the optic disc. They are also associated with a substantially greater incidence of progression of visual field defects. POAG patients with elevated IOP and no visual field loss are more likely to develop visual field changes 2-7 years after disc hemorrhages are

first observed.[9] Disc hemorrhages also indicate progressive or advanced glaucoma damage. Their appearance in advanced glaucoma patients forecasts an unfavorable prognosis. If a glaucoma suspect presents with a disc hemorrhage, the practitioner should give strong consideration for medical therapy. Patients currently under medical management for glaucoma should have their medical therapy reevaluated and upgraded when an optic disc hemorrhage is discovered. The compliance of these patients should also be questioned.

NERVE FIBER LAYER (NFL). Evaluation of the NFL is a useful technique for identifying patients with early optic nerve damage since the NFL defects precede visual field loss and structural changes to the nerve head. In a 10-year incidence study of an ethnically mixed population, NFL defects were noted in 60% of the POAG eyes about 6 years before the visual field loss was detected.[11]

When evaluating the NFL with a red-free filter, it is important to concentrate only on the NFL within 1-2 DD of the optic nerve head. Outside this area, the NFL gradually thins. The normal appearance of the NFL should be bright in the superior arcades with gradual dimming in papillomacular area and gradual increase in brightness towards the inferior arcades. The pattern of brightness should be fairly symmetrical between the superior and inferior arcades and also between the two eyes.

Nerve fiber defects can occur focally in the form of slits or wedges, or diffusely around the optic nerve. The predominant pattern is diffuse rather than focal. Selective damage occurs to the NFL in the superior and inferior arcuate bundles with relative preservation of the papillomacular bundles until late in the disease process.

PERIPAPILLARY CHANGES. Peripapillary crescents or atrophy are associated with glaucomatous damage and occur with a mottling or ratty appearance to the RPE seen around the disc. This feature usually corresponds to a thinned neural retinal rim on the temporal aspect of the optic nerve in advanced optic nerve head damage. Peripapillary pigmentary changes are much more commonly found in normal-tension glaucoma than in high-tension glaucoma patients. These changes should not be confused with the normal peripapillary choroidal atrophy which is generally observed in individuals aged 55 years and older.

DISC VESSEL CHANGES. Changes to the neuroretinal rim topography from ganglion cell loss may cause secondary changes to the optic disc vessels. Shifting of disc vessels suggests progressive loss of neuroretinal rim tissue. Baring of circumlinear blood vessels may occur which is the suspension of an unsupported horizontally oriented disc vessel from the cup margin. In endstage glaucoma, optic disc vessels may disappear segmentally beneath the neuroretinal rim and follow the contour of the

laterally excavated cup. This is referred to as bayonetting of the vessels. It occurs as the lamina cribosa is displaced posteriorly, giving the optic disc the appearance of a bowl or a "bean-pot." Undermining of the disc margin is pathognomonic for advanced glaucoma.

VISUAL FIELDS

Disc topography can be correlated with visual field loss with a great deal of accuracy. The earliest loss of optic nerve fibers generally occurs at the superior and inferior areas of the optic disc. Therefore, early visual field changes in glaucoma are expected to be paracentral scotomas, nasal steps, and temporal wedges.[1,7] There is also a generalized depression of peripheral and central isopters.

Small paracentral scotomas located within the 20^0 meridian are typically the earliest visual field defects found in approximately 88% of all glaucomatous visual fields.[1] These scotomas are most commonly found in the superior nasal field. Initially the defects do not connect with the blind spot but with time they tend to elongate circumferentially along the distribution of arcuate nerve fibers.[10] A nasal step defect is a constriction of the visual field either above or below the horizontal meridian in the nasal field. This defect is rarely present by itself, although it is commonly associated with other defects. A temporal wedge is a sector-shaped defect of the visual field either above or below the horizontal meridian in the temporal field.

Progression of visual field defects can occur despite medical intervention and can occur in two ways. The initial paracentral scotomas in the Bjerrum area can gradually enlarge and coalesce to form arcuate-shaped defects that arch from the blind spot around the macula reaching to within 5^0 of fixation nasally. In the second way, new paracentral scotomas and sector defects may occur independently from any previous defect, and then both begin to enlarge. Damage to adjacent nerve fibers causes a peripheral breakthrough, and a ring or a double arcuate scotoma develops when defects arising in opposite halves of the visual field join together. The visual field loss gradually spreads peripherally and centrally so that eventually only a small island of central vision and an accompanying temporal island are left. The temporal island is usually extinguished before the central island.

DIAGNOSING AND EVALUATING GLAUCOMA

CASE HISTORY

Based on epidemiological studies, the practitioner should look more carefully for POAG in patients who are older, black, myopic, under stress, have relatives with glaucoma, or have diabetes, thyroid disease, or other chronic systemic disease.[1]

BIOMICROSCOPY (PREDILATION)

A careful examination of the anterior segment in glaucoma suspects can reveal indicators for all types of glaucomas. Certain anterior segment findings may suggest the need for additional slit lamp examination. The most likely ocular structures involved in abnormalities with glaucoma are the cornea, iris, and anterior chamber. The clinician should assess the cornea for the presence of edema and/or endothelial pigment. The anterior chamber should be checked for the presence of pigment, cells, flare, keratic precipitates, and/or hyphema. The iris should be inspected for pigment, defects in the pupillary ruff, exfoliation, flakes, transillumination defects, rubeosis irides, iris atrophy, and/or posterior synechiae. The crystalline lens should be assessed for thickening, pigmentation, or exfoliation flakes. Assessment of the angle either with a gonioscopic lens or using the Von Herrick technique provides information for diagnosis of open-angle or closed-angle glaucoma.

TONOMETRY

A measurement of IOP is an essential part of the evaluation of all glaucoma suspects. At present, the Goldmann tonometer is the most widely used and gives the most accurate readings. Diurnal variation in IOP is important to detect and manage glaucoma patients and glaucoma suspects. While elevated IOP is associated with POAG, well over 50% present on initial examination with IOPs in the normal range of 21 mm Hg or below.[11]

In states without glaucoma therapeutic privileges, the optometrist has the obligation to refer to an ophthalmologist, on diagnosis, any glaucoma patient for initiation of treatment, including persons who are glaucoma suspects, ocular hypertensives, those with visual field or optic nerve changes, or patients with an IOP greater than 30 mm Hg. An IOP of 30 mm Hg or more is used as the cut-off warranting referral since this IOP is considered excessively high and may in the long-term damage the optic nerve.[11]

GONIOSCOPY

The purpose of gonioscopy is to identify abnormal angle structures and to estimate the width of the anterior chamber angle and should be performed on all glaucoma patients, glaucoma suspects, and narrow angle patients. The anterior chamber angle size and configuration and amount of pigmentation in the trabecular meshwork should be recorded. Identify the abnormal findings and document the negative findings as well (no PAS, no angle neovascularization, no angle recess). The diagnosis of POAG is one of exclusion and gonioscopy is the key test to differentially diagnose the type of glaucoma which will in turn affect the management and treatment regime.

Gonioscopic findings are documented by drawing an X for each eye and entering the numerical grading classifications corresponding to the superior, inferior, nasal, and temporal

quadrants and recording the most posterior angle structure seen in that quadrant.

PUPILLARY DILATION

Pupillary dilation is the standard of care in assessing the optic nerve appearance with a stereoscopic view. The most common dilating agents used are 1 gtt 1% Tropicamide and 1 gtt 2 1/2% Phenylephrine instilled one minute apart in each eye. Patients who are diabetic, or who have darkly pigmented irides, or who have habitually miotic pupils tend to dilate poorly. It is considered appropriate to instill an additional 1 or 2 drops of each diagnostic agent to improve dilation.[11] Punctal occlusion will help minimize systemic absorption of the drops. Avoid using multiple drops of 2 1/2% Phenylephrine in patients with hypertension or significant cardiovascular disease. Patients who are being treated with miotic agents should discontinue them for several days prior to the dilated fundus examination unless such contraindications as narrow anterior chamber angles exist.

DIRECT OPHTHALMOSCOPY

Direct ophthalmoscopy to evaluate the optic nerve is not necessarily performed on each patient any more since 60 D, 78 D, and 90 D condensing lenses are being used for routine indirect fundus biomicroscopy.

BINOCULAR INDIRECT OPHTHALMOSCOPY (BIO)

BIO should be performed at the initial exam and at regular subsequent intervals thereafter. The peripheral retina should be carefully examined for chorioretinal scars, other indicators of previous traumatic incidents, and peripheral retinal disease. A patient with prominent lattice degeneration or atrophic retinal holes should have these prophylactically treated before miotic therapy is instituted because of the risk of developing retinal detachments.

BIOMICROSCOPY (POST-DILATION)

For optic nerve head examination, stereoscopic methods are far superior to monocular methods such as direct ophthalmoscopy which use color clues rather than topographical changes in evaluating the size of the excavated area on the surface of the disc.

Through the dilated pupil, assess the crystalline lens and stereoscopically view the optic nerve head with either a 60 D, 78 D, or 90 D auxiliary lens which provides an inverted and reversed image. The Hruby lens and the central portion of a three-mirror retinal contact lens may also be used to assess the optic nerve head and provide an upright image. The red-free filter of the slit-lamp will enhance any vascular and nerve fiber layer changes. Stereoscopic assessment of the optic nerve should include the integrity of the neuroretinal rim with respect to thickness and color, the size and shape of the cup, the symmetry of the optic nerve between the two eyes, and the integrity of the surrounding

retinal nerve fiber layer.

VISUAL FIELD ANALYSIS

Automated perimetry is essential to the diagnosis and management of glaucoma. The presence of a defect confirms the diagnosis of glaucoma even in the absence of a detectable elevated IOP. Progressive visual field loss may occur even with the apparent control of IOP. Therefore, documentation of arrest or progression of cupping, combined with perimetry, plays a vital role in assessing the efficacy of treatment.

Once a patient has been identified as a glaucoma suspect, a thorough visual field testing should be performed. Some practitioners advocate initially performing a screening test such as the Humphrey's Full-Field 120 to acquaint the new patient with the method of testing since a significant number of patients display a learning curve if they have no previous experience with the automated perimeter.

Of the threshold visual field tests, the Central 30-2 and the Central 24-2 are most commonly used. The Central 30-2 test is comprised of 76 points within 30^0, whereas the Central 24-2 tests 58 points within 24^0. Both tests have their advantages and disadvantages, and it is up to the practitioner to decide which test he or she will consistently use.

FUNDUS PHOTOGRAPHY

Fundus photography provides objective documentation of the optic nerve head and can be used to judge changes over time. Stereophotography is the preferred technique. Red-free photography of the peripapillary nerve fiber layer will record areas of dropout that are indicative of focal or diffuse optic nerve head damage, but is not routinely performed in most offices at this time because of technical complexities.

CO-MANAGING GLAUCOMA IN A PRIMARY CARE OFFICE

When the optometrist makes the decision to become involved in the co-management of glaucoma patients, he or she should carefully choose a glaucoma specialist who shares a similar treatment philosophy. Treatment protocols to be used by the co-management team should be developed and written down on paper, and should include the order of medications and dosages to be used, when surgery is to be considered, and agreeing upon the target pressure for each patient.

For medical-legal purposes and for completeness of records, written documentation is essential. A standard referral form devised by the two doctors should be used between the offices to facilitate communication.

In general, a glaucoma patient who is stable and whose IOP is well-controlled is followed every three months. Each visit should include a history, visual acuity, biomicroscopy, tonometry, and a stereoscopic optic nerve head evaluation, either through a dilated or undilated pupil. An annual dilated fundus examination with stereophotography of the optic nerve heads, visual fields, and gonioscopy should be performed at one of these visits. Some practitioners advocate testing visual fields every six months. Every fourth visit should be with the glaucoma specialist who will typically perform a dilated optic nerve evaluation.

For patients who are not well-controlled, this schedule will be different. More frequent visits will be required to the optometrist for tonometry, perimetry, and optic nerve evaluation, as well as to the ophthalmologist for changes of medications or dosages until the target IOP is achieved and maintained.

Certain changes noted by the optometrist will necessitate a referral back to the glaucoma specialist. These signs and symptoms include optic nerve head changes, visual field progression, elevated IOP above the target pressure, significant side effects to the medications, and other changes such as retinal vein occlusions and flame-shaped hemorrhages. The optometrist should also refer the patient when advanced medical treatment such as carbonic anhydrase inhibitors or strong miotics are required or when surgery is indicated.

ANTI-GLAUCOMA MEDICATIONS

Universal agreement exists that all eyes with POAG must be treated to prevent further damage. If a patient has POAG in one eye and ocular hypertension in the other, most doctors would advocate treatment in both eyes even in the initial absence of visual field loss in the second eye. The specific therapeutic regimen must be individually tailored to each patient, using currently available medical and possible laser or surgical modalities. It is important to assess the "risk-to-benefit ratio" for each patient when selecting the treatment regimen. The patient's ocular history and systemic conditions must be carefully considered when designing the drug regimen, and contraindications to certain drugs should be recorded in the patient's file.

The primary goal of glaucoma treatment is to increase outflow facility of aqueous and/or decrease aqueous production. Intraocular pressure is subsequently reduced which permits greater vascular perfusion through the prelaminar portion of the optic nerve, thus decreasing further optic nerve damage and visual field changes. Ideally, once the decision to begin treatment is made, uniocular trials are performed for a short period of time to assess the efficacy of the drug regimen and the medication's side effects. If the IOP is markedly elevated in both eyes treatment must be

initiated bilaterally immediately.

The clinician must educate and assure the patient, tailor the drug regimen to the patient's needs, reinforce applications, answer questions, communicate with other clinicians, and improve the clinician-patient relationship to achieve the best results. In glaucoma patients, compliance is often poor since the patient has no visual symptoms and therefore does not experience clinical improvement during therapy but may be bothered by adverse reactions to the medications. It is very important to explain the disease process and the importance of follow-up visits to monitor treatment. Side effects of the medications should be discussed in detail with the patient prior to their use. The patient must understand that the medications only control the disease but do not cure the problem. Too often, the patient takes the medicine for a period of time and then discontinue them because they feel they are cured of their glaucoma. The clinician should consider using written patient educational materials that describe glaucoma and its treatment modalities, and visual aids such as the eye model and patient photographs to help reinforce his/her explanation.[6,12]

The main drugs used to treat glaucoma are B-adrenergic blocking agents, adrenaline, guanethidine, miotics, and carbonic anhydrase inhibitors. Many of these drugs have mild to severe side effects that can be reduced by performing punctal occlusion for one minute after instillation of the drops.

BETA ANTAGONISTS

B-blockers decrease IOP by reducing aqueous secretion. Those topical B-blockers currently used in the management of glaucoma are timolol, betaxolol, carteolol, levobunolol, and metipranolol. With the exception of betaxolol, all are non-selective B-blockers. The B-blockers are generally administered two times daily, or every twelve hours. Several recent studies have monitored the efficacy of once-daily treatment with B-blockers and have reported favorable results, especially when nasolacrimal occlusion is performed.[4,16,17] A gel-forming solution of timolol called Timoptic-XE has recently been introduced and is instilled once per day.

Local side effects include superficial punctate keratitis and rarely corneal anesthesia. Systemic side effects include fatigue, disorientation, confusion, and depression. Bradycardia may occur as a result of the B-1 blocking action which leads to decreased cardiac contractility and systemic hypotension. Therefore, in patients with a slow pulse or heart block or pulmonary disorders including asthma and COPD, betaxolol is the B-blocker of choice because of its cardioselective properties.

TIMOLOL is a non-selective B-blocker which reaches maximum pressure lowering effects in 1-2 hours and lasts up to 24 hours. Timolol may initially cause a dramatic lowering of IOP although in some patients this effect wanes partially during the ensuing days

in a phenomenon known as "short term drift." After 2 to 4 weeks, IOP will stabilize, usually below pretreatment levels. "Long term drift" may occur after months or years of treatment and is marked by a slow steady rise in IOP. This phenomenon may result from a loss of efficacy of the drug or worsening of the glaucoma or both.

BETAXOLOL is a cardioselective B-1 blocker and is the B-blocker of choice in patients with cardiopulmonary problems. It is nearly as effective as timolol in decreasing IOP levels.

DIRECT ACTING ADRENERGIC AGENTS

Adrenergic drugs or agonists enhance sympathetic activity, hence the name sympathomimetic. Adrenergic receptors are subdivided into alpha-1 and alpha-2, and beta-1 and beta-2 receptors based on their tissue location. While alpha drugs act quite selectively on alpha receptors and beta drugs on beta receptors, the selectivity within each class is less pronounced.

Adrenergic drugs reduce IOP by stimulation of inhibitory alpha receptors at the ciliary epithelium, constriction of the blood vessels (alpha-1), diminishing fluid supply, and excitation of beta receptors in the outflow pathways. The beta receptors seem to be more important for aqueous production and regulation.

The use of epinephrine is contraindicated in patients with narrow angles because of its mydriatic effects through its a-agonist action which are enhanced by concurrent use of timolol. In aphakic eyes, cystoid maculopathy may result, especially with use of the 2% concentration, but this effect is usually reversible upon cessation of administration. It should not be used in patients suffering from cardiovascular diseases, diabetes mellitus, hyperthyroidism, or recent myocardial infarction, or those who are taking MAO inhibitors.

Local side effects may include stinging, headaches, allergic blepharoconjunctivitis, conjunctival hyperemia about 2 hours after instillation, nasolacrimal obstruction, and adrenochrome deposits in the conjunctive with long-term usage.

Systemic side effects may include premature cardiac contractions and occasionally other arrhythmias because of the B-1 agonist action.

EPINEPHRINE

Adrenaline or epinephrine is an A- and B-agonist and lowers IOP by constricting ciliary blood vessels (alpha-1) which reduces aqueous humor formation, and by increasing aqueous outflow through its alpha-agonist action at the trabecular meshwork. IOP falls within 1 hour with maximal decrease at three hours. Its pressure lowering effect lasts 12-24 hours after a twice daily administration.

This drug does not cause miosis or spasm of accommodation, and is useful for treatment of secondary glaucoma. It has an additive effect to pilocarpine, carbonic anhydrase inhibitors, and also probably to timolol. However, approximately 30% of POAG patients are unresponsive to this drug. It is also not as effective as timolol or pilocarpine in reducing IOP. A relatively high incidence of side effects results in discontinuing its usage in a significant number of patients.

DIPIVALYL ADRENALINE (0.1%)

Propine is the pro-drug form of epinephrine which is converted after absorption into the eye. It penetrates the cornea 17 times better than epinephrine, and its low concentration causes fewer side effects such as headaches and conjunctival hyperemia. It also appears to have a longer duration of action. Patients who are intolerant to epinephrine are sometimes able to use dipivefrin without complications.

APRACLONIDINE

Apraclonidine is an alpha-2 agonist and reduces sympathetic activity in the ciliary body, resulting in reduced inflow of aqueous and subsequently decreased IOP. This drug can lower IOP by about 25% with few adverse reactions, which makes it useful for minimizing pressure spikes after cycloplegia in eyes of open-angle glaucoma patients.

GUANETHIDINE

Guanethidine has a potentiating effect on adrenaline, and the two drugs are combined into a product called Ganda. It comes in several concentrations with either 1% or 3% guanethidine combined with 0.2% or 0.5% epinephrine.

DIRECT ACTING CHOLINERGIC OR MUSCARINIC DRUGS

In the eye, muscarinic receptors are located in the iris, ciliary body, and the trabecular meshwork. Stimulation of receptors in the iris causes contraction of the sphincter muscle leading to miosis which does not contribute to the therapeutic action in POAG. Stimulation of the ciliary body receptors causes a contraction of the ciliary muscle which pulls on the longitudinal fibers connected to the scleral spur. This action may open up the trabecular meshwork and increase aqueous outflow. Aqueous outflow may also be increased by direct stimulation of the receptors in the trabecular meshwork, although this effect is still debatable.

Cholinergic drug usage is contraindicated in the presence of neovascular glaucoma, uveitic glaucoma, or malignant glaucoma; ocular inflammations or acute ocular infections; cataracts; a history of retinal detachments; corneal abrasions; and aphakic or severe myopia. Asthma, ulcer, other GI problems, bladder dysfunction, Parkinson's disease, and cardiac irregularities constitute systemic contraindications.

Local adverse reactions to these agents include stinging and irritation, and allergic reactions are rare. Infrequently, persistent miosis with visual impairment or ciliary spasm may cause myopia and browaches that subside or disappear with time. Angle-closure glaucoma may be precipitated in certain eyes with narrow angles due to aggravation of pupillary block.

Potential systemic side effects include sweating, salivation, bradycardia, arrhythmia, dyspnea, gastrointestinal disturbances, and involuntary micturition.

PILOCARPINE

Pilocarpine in the solution form is administered up to 4 times daily and penetrates the cornea and rapidly reaches the iris and ciliary body. Within twenty minutes IOP starts to fall, and reaches its maximal reduction in 1.5-2 hours and lasts for 4 hours. Reduction in IOP is dose dependent. Although concentrations greater than 4% do not appear to be more effective in lowering IOP, they may have a slightly more prolonged effect. Pilocarpine is also available in wafer form called Ocuserts which are a timed-release delivery system lasting up to 7 days or longer which improves diurnal pressure variations and patient compliance. A gel form of pilocarpine is instilled at bedtime which is especially beneficial for patients suspected of poor compliance or those who suffer side effects from this drug.

CARBACHOL

This synthetic drug is used as the alternative to pilocarpine in resistant or intolerable cases. It does not penetrate the cornea as readily as pilocarpine although penetration may be enhanced with a wetting agent. It begins acting in 40 minutes and its effects last 8-12 hours. It is administered by instilling one drop in each eye three times daily. Carbachol 3% is closely equivalent to pilocarpine 4%.

ANTICHOLINESTERASE DRUGS

In the eye, anticholinesterases act indirectly to cause miosis, accommodation for near vision, and an increased outflow of aqueous through the trabecular meshwork by contracting the longitudinal muscles of the ciliary body. IOP is lowered both in normal and POAG eyes. The usage of these drugs has declined in recent years because of laser therapy and their cataractogenic property. Currently, they are employed in aphakic eyes when other drugs do not provide adequate reduction in IOP.

The drugs in this class bind either reversibly or irreversibly to the cholinesterase enzyme, thus the duration of action ranges from several minutes to several days. These drugs cannot be used with dipivefrin because dipivefrin requires esterase to convert it to epinephrine.

Ocular side effects include miosis, anterior subcapsular

cataracts, miotic pupillary cysts, irritation, conjunctival injection, lacrimation, and retinal detachment.

Systemic side effects may be rather severe. Repeated administration can depress serum and erythrocyte cholinesterase levels resulting in urinary incontinence, perfuse sweating, diarrhea, muscle weakness, abdominal cramps, apnea, and bradycardia. Persons receiving anticholinesterase drugs should avoid exposure to carbamate or organophosphate-based pesticides or insecticides, as well as succinylcholine which is a muscle relaxant given before or during general anesthesia. Prolonged respiratory paralysis may result from combining succinylcholine and an anticholinesterase.

Echothiophate 0.125% administered twice per day is the most commonly used anticholinesterase drug. Demecarium 0.125% solution and isoflurophate 0.025% ointment are also available but are rarely used for glaucoma treatment.

CARBONIC ANHYDRASE INHIBITORS

Carbonic anhydrase inhibitors (CAIs) inhibit the enzyme carbonic anhydrase and hence reduce the formation of carbonic acid and bicarbonate ions. If less bicarbonate ions are available, fewer bicarbonate and sodium ions will enter the posterior chamber. Consequently, less water from the plasma will move into the eye, causing a decrease in IOP. Additionally, the slight metabolic acidosis caused by the accumulation of hydrogen ions has been claimed to also reduce aqueous outflow. The CAIs produce their major effects by reducing aqueous inflow with little or no effect on outflow.

CAIs are among the most potent of all anti-glaucoma agents and are useful in all types of glaucoma although they are not typically the first drug of choice. They decrease IOP by 40-60% by acting on the secretory ciliary epithelium. The pressure lowering effect occurs within 1 hour, peaks at 4 hours, and wears off in 6-12 hours. The CAIs may be given at specific times of the day to flatten a daily spike in IOP.

The usefulness of the CAIs is often limited by their side effects. Ocular side effects such as transient myopia are minimal. Systemic adverse reactions are more frequent and severe and often necessitate discontinuing the drug therapy. Paresthesia, usually in the extremities, is a universal side effect and compliance should be questioned if the patient denies this symptom. Many persons will suffer from the malaise symptom complex, which includes malaise, fatigue, confusion, depression, weight loss, and decreased libido in males. This complex is associated with excessive levels of the drug in serum and with systemic metabolic acidosis. Fifty percent of the patients are helped with supplemental 2-week courses of sodium acetate. The GI symptom complex includes gastric irritation, abdominal cramps, diarrhea,

and nausea. These symptoms can occur independently of the malaise syndrome and are not related to changes in blood chemistry. Renal stone formation is related to decreased urinary citrate excretion without corresponding decrease in serum calcium levels. CAIs belong to the sulfonamide family of drugs, and may cause Stevens-Johnson syndrome and blood dyscrasias.

The use of CAIs is contraindicated in persons immediately after filtering operations, in patients with cardiac problems (hypokalemia), Addison's disease (loss of sodium and potassium), liver disease, and a sensitivity to sulphonamides.

Currently four agents are used to treat glaucoma. Acetazolamide, dichlorphenamide, methazolamide, and ethoxzolamide are administered orally and are usually well absorbed. Methazolamide is the CAI of choice because of its reduced frequency for kidney stone formation, and is available in 25 mg and 50 mg tablets. The initial therapy begins with one 25 mg tablet two times per day and is increased in 25 mg steps until IOP is satisfactorily controlled. The maximum dosage is 50 mg three times perday. Acetazolamide is reserved for those patients whose IOPs are not sufficiently reduced by maximum methazolamide treatment. It is available in 250 mg tablets and in 500 mg time-release capsules. The dosage may be increased up to 250 mg four times per day by tablet form or 500 mg twice per day in capsule form.

SPECIFIC MANAGEMENT PLANS

When treating glaucoma, it is desirable to use the fewest number of medications, the lowest concentration, and the fewest number of dosages compatible with acceptable control of IOP. This increases the likelihood of patient compliance, as well as reducing the number of unwanted side effects. Target IOP should be established based on the observed optic disc and visual field changes caused by the initial pressure.

When beginning treatment, the choice of drugs should be a B-blocker which usually allows for a significant reduction of IOP without the ocular side effects of the miotics. Dosages are typically twice daily which improves the chances of proper patient compliance.

Typically the patient returns to the office after two weeks for evaluation of the clinical effectiveness of the therapy and to determine how the patient is tolerating the medication. Based on this information, therapy can be increased, decreased, or otherwise modified to enhance the reduction of IOP and to minimize side effects.

When a patient becomes tolerant of the initial drug or requires additional medications, a step-wise approach detailed in

Figure 1 is typically followed. This flowchart is modified according to the individual patient's systemic health and to the side effects of the medications. The more potent medications are reserved for patients with the more advanced and resistant forms of glaucoma.

A variety of factors contribute to the failure of medical therapy to adequately control IOP and prevent further optic nerve and visual field damage. The IOP measurement may not accurately reflect pressure control because of diurnal variations. The target pressure may be underestimated, leading to progressive visual field loss. The patient may become tolerant to the drug regimen or suffer from side effects that necessitate discontinuing certain drugs, leading in some cases to the need for laser or surgical treatment. The development and treatment of other diseases can contribute to progressive optic nerve damage. Finally, noncompliance can significantly reduce the success of medical treatment.

When maximal medical therapy is no longer effective at controlling glaucoma, argon laser trabeculoplasty (ALT) is performed. Initially only 180^0 of the angle is "burned", reserving the rest for an additional treatment if indicated. This procedure produces an increase in aqueous outflow by opening the trabecular spaces caused by the mechanical shrinking of collagen at the burn sites. Although the initial results of ALT are impressive, its effectiveness gradually decreases with time, necessitating a re-treatment or the addition of medical therapy once again. This time, most patients can discontinue the use of carbonic anhydrase inhibitors or miotics.

When ALT and maximum tolerable medical therapy have failed, filtering surgery is indicated. The most popular technique is trabeculotomy with a peripheral iridectomy to create a filtering bleb. Other procedures are performed on the ciliary body in an attempt to functionally destroy this structure, resulting in decreased aqueous production. Cyclocryotherapy uses transcleral freezing of the ciliary body at multiple locations.[1] This procedure has generally replaced cyclodiathermy and cyclodialysis because it is less invasive. Other techniques are currently being developed including transcleral Nd:YAG laser cyclocoagulation, endolaser treatment of the ciliary body, and therapeutic ultrasound.[1]

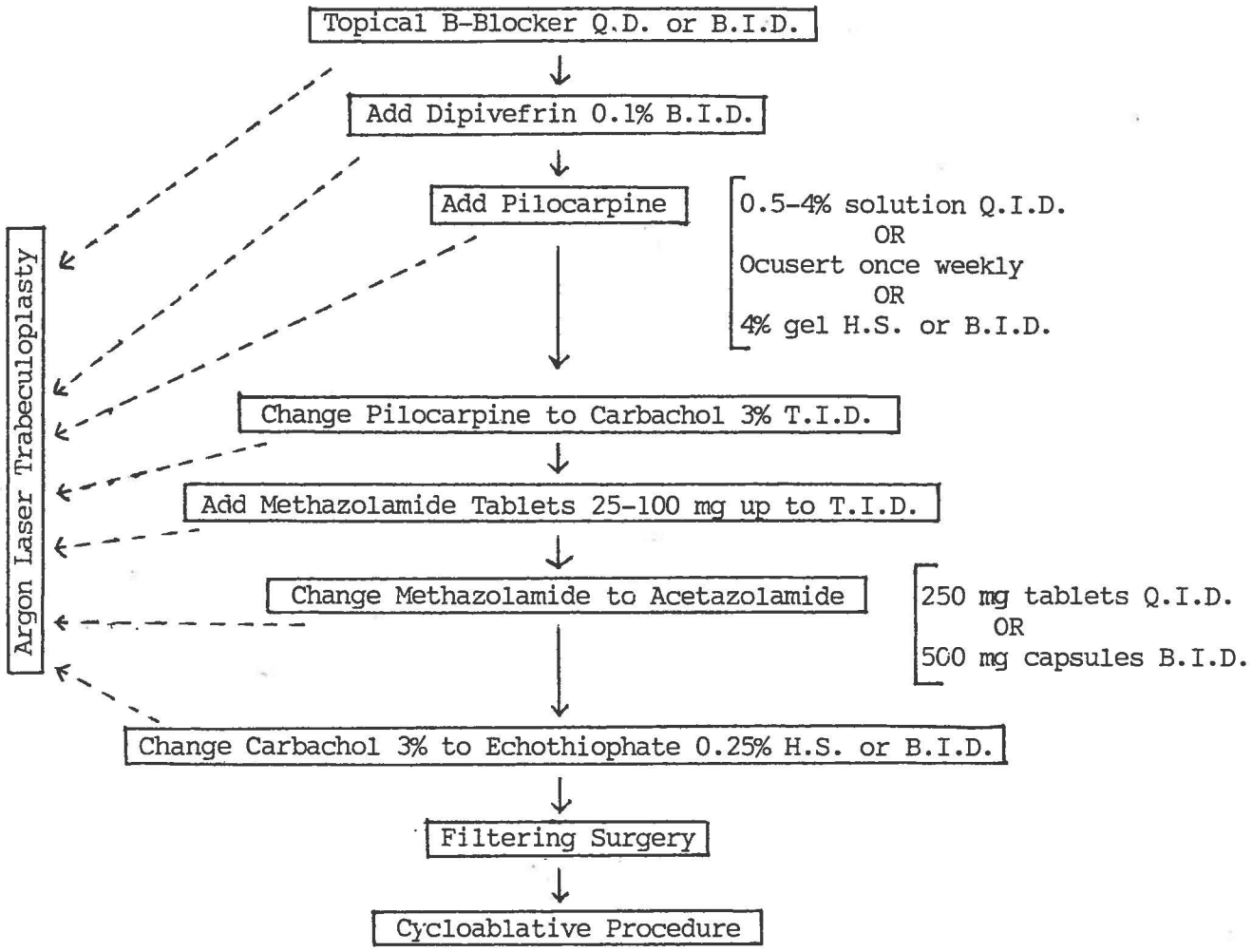

FIGURE 1. This flowchart for the management of POAG is a composite of the flowcharts presented in Lewis and Fingeret's Primary Care of the Glaucomas (page 267) and Bartlett and Jaanus' Clinical Ocular Pharmacology (page 766). It is essential that the practitioner design an individualized therapeutic plan that takes into account the patient's medical history, prior damage to the optic nerve and visual field, IOP level, target IOP, and ocular history along with other factors. Some ophthalmologists advocate the use of ALT as primary therapy but most favor using this procedure when patients cannot tolerate simple drug regimens or when noncompliance, drug tolerance, or advancing disease preclude the success of pharmacologic therapy.[1] Recent studies indicate that the majority of patients would prefer laser treatment or surgery because of the cumbersom drug schedule and the financial burden.

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