Primary open-angle glaucoma (POAG) is a chronic ocular disease characterized by changes in optic nerve morphology and visual field loss without any secondary etiology or abnormal appearance of the anterior chamber angle. POAG is mostly seen in patients over 40 years of age. When the age at onset is between approximately 10 and 35 years, the condition is referred to as juvenile open-angle glaucoma (JOAG). JOAG is a rare condition that often results in more severe visual consequences than POAG, and, because of the age of onset, diagnosis can be delayed.\(^1\)

Elevated IOP is one risk factor associated with JOAG and POAG.\(^1\) Some individuals exhibit elevated IOP but no clinical evidence of glaucomatous damage, a condition known as ocular hypertension (OHT).\(^2\) Because teenagers with OHT are potentially at risk for developing JOAG, physicians must follow them closely in order to decide whether and when to begin treatment to prevent glaucomatous damage. This article reviews the clinical and genetic aspects of JOAG and discusses when and how to treat OHT in teenagers to prevent progression to JOAG and visual field loss.

**The Epidemiology of JOAG**

JOAG is a rare form of glaucoma that accounts for only approximately 0.2% of glaucoma cases.\(^1\) Teenagers with OHT should be monitored or, if their risk is high enough, should be treated for potential progression to JOAG. Risk factors include male gender, myopia, and a positive family history for glaucoma.\(^1,\(^3\)

**The Genetics of JOAG**

Although the majority of pedigree studies have reported an autosomal dominant inheritance pattern for JOAG,\(^4-\(^9\) the inheritance patterns and contributions of specific genes to glaucoma are complicated and not yet well understood. Two genes have thus far been shown to play roles in JOAG, MYOC and CYP1B1.

MYOC, also known as the trabecular meshwork-induced glucocorticoid response (TIGR) gene, was discovered in 1997 and was the first gene shown to be associated with open-angle glaucoma. Located on chromosome 1, this gene produces the myocilin protein, and myocilin is found in the parts of the eye that are thought to be involved in the mechanism of glaucoma as well as the aqueous humor. The exact function of the wild-type myocilin protein and how mutant forms are involved in glaucoma are currently unknown. MYOC mutations have been reported in JOAG cases, although not all cases of JOAG have been associated with MYOC mutations. Additionally, MYOC mutations have been
reported in POAG cases. The percentage of patients with JOAG and POAG who have MYOC mutations varies across the literature (2% to 4% in POAG and higher in JOAG), but the exact relation of these mutations to open-angle glaucoma is unknown.

CYP1B1 has also been shown to play a part in glaucoma. Located on chromosome 2, CYP1B1 encodes for the CYP1B1 protein, a mono-oxygenase that is part of the cytochrome P450 family and is involved in various metabolic activities. CYP1B1 has been associated with congenital glaucoma and is hypothesized to act as a modifier gene for MYOC in JOAG. Additionally, a primary role for CYP1B1 in JOAG has been suggested from certain pedigrees. As with MYOC, however, how mutations in CYP1B1 affect the manifestation of glaucoma is currently unknown. Genetic testing is available for both MYOC and CYP1B1, but its use has not been commonly incorporated into clinical practice.

The Clinical Signs of JOAG
As with POAG, JOAG usually has no alarming symptoms recognizable to the patient that may result in early detection. The characteristic signs of JOAG are similar to those of POAG and include optic nerve head cupping, visual field defects, and a normal-appearing anterior chamber angle. In JOAG, however, IOP tends to be higher (above 40 mm Hg) than in patients with POAG. Secondary causes for elevated IOP (eg, pigmentary glaucoma, steroid-induced glaucoma, uveitis, trauma) should be ruled out before a diagnosis of JOAG is made.

Physicians should perform visual field testing so that they may monitor changes over the course of follow-up. In teenagers, the authors use short wavelength automated perimetry (SWAP), which projects a blue stimulus onto a yellow background and may detect visual field changes earlier than testing with a conventional white-on-white background. Additionally, a reduction in the sensitivity of SWAP is less likely in teenagers than adults, due to the former’s lower risk of cataracts and, therefore, the lesser amount of artifact available to interfere with the test. It is also important to measure central corneal thickness (CCT), which can affect the accuracy of IOP measurements and an estimate of true risk. The authors recommend taking stereo photographs in order to monitor changes in the optic nerve during follow-up visits. Imaging can also be used to evaluate the optic disc and retinal nerve fiber layer. These measurements can be used as a baseline for damage to the retinal nerve fiber layer or optic nerve head, because a change may indicate a conversion to JOAG.

When to Treat OHT
When considering treatment for a teenager with OHT, physicians should take into account the risk factors for the development of JOAG and whether or not the patient exhibits any of them. The Ocular Hypertension Treatment Study (OHTS) investigated a group of patients aged 40 to 80 years with OHT. In the OHTS, the baseline factors that predicted the development of POAG within 5 years included a larger vertical or horizontal cup-to-disc ratio, higher IOP, a greater pattern standard deviation, and thinner CCT. Although there are no studies that specifically address these factors in teenagers, they should still be considered when treating a teenager with OHT.

“The decision of whether to treat OHT in a teenaged patient ... should be based on the probability of visual impairment as well as cost, the potential side effects of the therapy, quality of life, and other factors.”

The next point to consider is whether IOP-lowering therapy will effectively decrease the patient’s risk of conversion to JOAG. The OHTS found that lowering IOP with topical medications decreased the probability of developing POAG in the group treated with IOP-lowering medications compared with the control group (4.4% probability of developing POAG in the medication group vs 9.5% probability in the control group). Another study found latanoprost to lower IOP effectively in a small group of older children (ie, age range, 8.8 to 13.0 years). These children were significantly more likely to be diagnosed with JOAG as opposed to other conditions. The use of common IOP-lowering medications in teenagers, however, has not been the subject of formal trials, and, currently, there are no adequate studies of the long-term effects of IOP-lowering medications in this patient population. For these reasons, although such medications may be effective, their use should be accompanied by more than the usual care and close monitoring. Surgical intervention has also been shown to be effective and may be considered if treatment with topical medications is either ineffective or impractical due to noncompliance or other patient-specific factors.

Finally, the decision of whether to treat OHT in a teenaged patient is individualized. It should be based on the probability of visual impairment as well as cost, the
potential side effects of the therapy, quality of life, and other factors specific to the patient. If the initial decision is made not to start treatment and, during follow-up, there is evidence of glaucomatous conversion, treatment must be started immediately to prevent further loss of vision.

HOW TO TREAT OHT IN TEENAGERS
Extensive studies have not been completed as to the effectiveness of certain treatments in teenagers. Current standards of treatment that are used for adult POAG patients are generally used for teenagers as well, with close follow-up monitoring. After deciding to proceed with treatment, the clinician must set a target IOP. The OHTS set a target IOP reduction of 20% and less than 24 mm Hg. Owing to the longer life expectancies for teenagers than adults and the more severe nature of JOAG compared with POAG, however, physicians may wish to set a lower target pressure.

Physicians must choose the most appropriate treatment modality to accomplish the goal of treatment and the one that has the fewest ocular and systemic adverse effects. In almost all cases, topical medication is the first choice for the treatment of OHT. Because teenagers with OHT may have extremely high IOPs, however, topical medications may fail to achieve the desired reduction in pressure, and glaucomatous progression may be detected. In these cases, laser trabeculoplasty, trabeculectomy, nonpenetrating filtering surgery, or tube shunts may be indicated. Additionally, other patient-specific factors—such as poor compliance with or adverse effects from medical therapy—may necessitate choosing a more invasive surgical treatment.

CONCLUSION
Although OHT is uncommon in teenagers, it may precede JOAG, which can cause severe visual damage. The decision whether to treat a teenager with OHT should be individualized based on the patient’s risk factors. Treatment initially consists of topical medications. Rarely, surgical intervention may become necessary if the risk of developing JOAG is unacceptably high. With appropriate care, teenagers with OHT and even early JOAG may have a lifetime of useful vision.

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