

## GLAUCOMA

# The “New” Pressure for Glaucoma Specialists: Ocular Perfusion Arrives

BY MIRIAM KARMEL, CONTRIBUTING WRITER

INTERVIEWING DONALD L. BUDENZ, MD, JODY R. PILTZ-SEYMOUR, MD, KULDEV SINGH, MD, MPH, FOTIS TOPOUZIS, MD, AND ROHIT VARMA, MD, MPH

**F**or glaucoma patients, and the doctors treating them, it all comes down to one number: intraocular pressure.

Or does it?

Now there’s a new number on the block—ocular perfusion pressure (OPP), the relationship between systemic blood pressure and IOP. A growing body of epidemiologic literature supports OPP’s importance as a risk factor for open-angle glaucoma. That’s because low blood pressure lets OPP drop, and low OPP is incongruously similar to elevated IOP in that it has consistently and strongly been associated with OAG.

There are a number of ways to estimate OPP, but the most precise is possibly the one below, which appeared in a 2005 report in *Investigative Ophthalmology and Visual Science*, with MOPP being the mean ocular perfusion pressure, DBP the diastolic blood pressure and SBP the systolic:

$MOPP = \frac{2}{3} [DBP + \frac{1}{3}(SBP - DBP)] - IOP.$

That formula was followed by a much simpler medical advisory: “The perfusion pressure changes during the day, but the tissue blood flow should remain stable, to maintain metabolic activity.”<sup>1</sup>

### OPP Emerges as a Factor

OPP is making a splash in a pond where several theories are now competing for the title “Cause of Glaucoma.”

- The prevailing mechanical theory

postulates that elevated IOP alters the architecture so much that axons get compressed and die.

- The vascular theory, starring OPP, suggests that when perfusion pressure gets too low, not enough blood reaches the optic nerve.
- The fluctuation theory contends that single pressure readings taken months apart are far less concerning for optic nerve insults than dramatic, diurnal fluctuations.
- The neurogenic theory suggests that individuals have very different thresholds of vulnerability to all pressures, and true damage to the optic nerve occurs far in advance of the appearance of visual field defects, even in people with “normal” pressures.

The vascular theory hasn’t muscled out the other theories, but glaucoma experts say it’s time to take OPP seriously. “Unlike other risk factors, like age and CCT, here’s something we can actually modify,” said Donald L. Budenz, MD, professor of ophthalmology, epidemiology and public health at the University of Miami. But, he added, it’s still only an epidemiologic association.

The notion that one theory should be championed over all the others was dismissed by Jody R. Piltz-Seymour, MD, a glaucoma specialist in Bristol, Pa., and adjunct associate professor of ophthalmology in the University of Pennsylvania Health System. “It’s all interrelated,” she said. “It does not make sense to argue about which theory is correct. There are mechanical fac-

### Plumbing the Pressure



A sphygmomanometer and stethoscope may be at the ready in those glaucoma practices that want to monitor ocular perfusion pressures, especially in those patients on both ocular and systemic antihypertensive medication.

tors and vascular factors. In different people, the relative importance of each plays a different role. In some people there may also be inflammatory, autoimmune or other factors that we have not as yet identified. It’s not one or the other.” The general consensus is that glaucoma is a multifactorial disease.

### Will OPP Drive Practice?

So what is an ophthalmologist to do? Is OPP a treatable risk factor? Should it be modified?

There’s little consensus. Yet even those who say it’s too soon to incorporate OPP into clinical practice agree that with cardiologists tweaking target blood pressures to new lows, the impact of blood pressure on OPP is becoming more profound. “We need to increasingly become aware that blood

pressure is an important component of management of the patient,” said Rohit Varma, MD, MPH, professor of ophthalmology and preventive medicine at Doheny Eye Institute in Los Angeles. Dr. Varma headed the Los Angeles Latino Eye Study (LALES), a population-based study of over 6,000 adult Latinos, which recently reported a correlation between both high and low systemic blood pressures and the prevalence of OAG.<sup>2</sup> “When blood pressure is too low, you have a low perfusion pressure and less blood and less oxygenation, so the optic nerve gets damaged,” he said, referring to a diastolic blood pressure that falls below 60 mmHg. When blood pressure is too high—a systolic reading above 160 mmHg—the vessels become arteriosclerotic, he said, and this leads to low perfusion pressure, which prevents nutrition from reaching the optic nerve. “In our study, we found that both ends of the blood pressure spectrum are damaging to the optic nerve.”

**New relationship for cardiology and ophthalmology.** Such findings could certainly alter clinical practice. “We’re going beyond the eye to focus on the whole patient,” Dr. Varma said, noting that a similar comprehensive approach has already affected the management of diabetes patients who are at risk for diabetic retinopathy. “This is another disease where systemic conditions can impact the eye health of the patient.”

It’s one thing, though, to warn a diabetic patient about controlling blood sugar levels; it’s quite another to ask a cardiologist to raise your patient’s blood pressure. Yet that’s the situation ophthalmologists may face in patients with low blood pressure.

“I have patients saying, ‘My other doctors are thrilled that I have low blood pressure.’ For me, that’s no cause for celebration because once it gets low we know the risk of glaucoma really starts to rise,” said Dr. Piltz-Seymour. “The medical community is really striving for very, very low blood pressures. And there’s a risk in that.”

Dr. Budenz agreed. “Cardiologists don’t foresee any side effects from very

low blood pressure. But we feel there is a side effect, and that’s low OPP. And that puts our glaucoma patients at risk of worsening,” he said. “Our cardio colleagues are looking for lower and lower target pressures. Maybe they’re overdoing it. Maybe we don’t need 110/60.”

In fact, if a patient is on maximum ocular medication but is still progressing, and they’re on blood pressure medication, Dr. Budenz said it’s reasonable to ask the cardiologist or primary care physician to cut the dose.

### Preliminary Approaches

Before the ophthalmologist asks the cardiologist to change anything, four steps should be considered.

**1. Switch ocular medications.** “A possible way to modify perfusion pressure is to prescribe glaucoma drops that don’t lower OPP,” said Dr. Budenz. Since blood pressure goes down at night when IOP rises, you might avoid using beta blockers, which also lower blood pressure. “If blood pressure is lowest when sleeping, this is a perfect setup for glaucoma progression.”

**2. Minimize systemic absorption.** Dr. Piltz-Seymour teaches patients about punctal occlusion and three minutes of eyelid closure. “If you can decrease the amount of systemic absorption of the eyedrops, you can decrease the blood pressure–lowering effect of those drugs.”

**3. I could have had a V8!** The patient with naturally low blood pressure and so-called normal-tension glaucoma poses a special challenge. In such cases, “There’s nothing you can take away to make blood pressure higher,” Dr. Piltz-Seymour said. Some doctors recommend hydration or salt supplements to boost blood pressure. Fluid volume at bedtime is another way to help keep blood pressure from bottoming out during sleep. She recommends a glass of V8 at bedtime. “It has a lot of salt, plus fluid volume and other good nutrients.”

**4. Simply stay the course.** “We’re already modifying perfusion pressure by modifying IOP,” said Dr. Budenz. “Any time you lower eye pressure,

you’re improving perfusion pressure.” Besides, he said, “It’s easier to lower IOP than trying to raise blood pressure. If blood pressure is low in an individual patient, consider more aggressive IOP therapy.”

### Is Doing Nothing the Best Medicine?

Fotis Topouzis, MD, assistant professor of ophthalmology at Aristotle University of Thessaloniki, Greece, said there’s not enough evidence to warrant monitoring or actually modifying OPP. “While we know that BP and IOP are the main components of perfusion pressure, we do not know who is really playing the game among the two ‘players.’ It could be only IOP, only BP, or a combination of both.”

What’s more, incorporating OPP into the mix would require changing the existing target IOP algorithm, said Dr. Topouzis. Because studies conflict regarding the role of blood pressure in glaucoma, Dr. Topouzis called for further study. Until then, he said, the effect of systemic pressures on glaucoma progression is unclear.

Kuldev Singh, MD, MPH, agreed that while low perfusion pressure is a risk factor, the literature doesn’t conclusively support a general recommendation for increasing blood pressure in individual glaucoma patients. There’s little ambiguity with IOP, where most would acknowledge that lower is better, said Dr. Singh, professor of ophthalmology and director of the glaucoma service at Stanford University. But the relationship between blood pressure and glaucoma is likely more complex. “When it comes to ocular perfusion and glaucoma risk, we don’t have good evidence that increasing blood pressure, all other things being equal, is good for glaucomatous disease in every setting.”

That evidence will elude us, said Dr. Budenz, until glaucoma specialists have a device that directly measures tissue perfusion or OPP, thus revealing whether blood flow is low in glaucoma patients due to either high IOP or low blood pressure. “We can’t measure blood flow of the optic nerve. It’s a very, very difficult area to study.”

**Get out your sphygmomanometers (or don't).** For now, said Dr. Budenz, "All we have is IOP. If we had something else to modify, it would be exciting." He suggested a study designed to modify blood pressure in three groups: high-risk glaucoma patients, those with low blood pressure and those with progressive glaucoma. Increase the blood pressure in half the patients and maintain low blood pressure in the other half. "Over five years would you see a difference in progression? That's a difficult study," Dr. Budenz said, but that's what is needed. Barring further research, Dr. Budenz doesn't see the point in measuring blood pressure. "There's no evidence that any of this helps. We're talking about risk factors that haven't been tested clinically."

Yet the LALES convinced Dr. Varma to measure blood pressure on those patients who are getting worse despite low IOP. "In patients in whom IOP is well controlled, we need to assess other factors such as blood pressure, rather than just watching the patient progressively lose vision with a worsening of their quality of life."

Dr. Piltz-Seymour advocated measuring blood pressure in glaucoma patients. "It makes perfect sense in a glaucoma practice because of the interrelationship between blood pressure and IOP," she said.

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1 Mitra, S. et al. *Invest Ophthalmol Vis Sci* 2005;46(2):561-567.

2 Memarzadeh, F. et al. *Invest Ophthalmol Vis Sci* 2010;51:2872-2877.

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*Dr. Budenz is a consultant for Alcon, Allergan and Santen and receives speaking honoraria from Alcon, Allergan and Merck. Dr. Piltz-Seymour receives grant support from Alcon, Allergan, Pfizer and Merck. Dr. Singh reports no relevant interests. Dr. Topouzis consults for Merck and Pfizer, receives lecture fees from Alcon and Pfizer, and grant support from Alcon, Heidelberg Engineering and Pfizer. Dr. Varma consults for Alcon, Allergan, Aquesys, Bausch + Lomb, Genentech, Merck, Pfizer and Replenish; receives grant support from Allergan, Genentech, Optovue and Pfizer; receives lecture fees from Alcon, Optovue and Pfizer; and has equity in AqueSys and Replenish.*



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