Glaucoma Research Society

DEFINITION OF POAG- Some provocative thoughts

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1. **Nature of POAG**. In the primary open angle glaucoma(s) ("idiopathic" = "primary"), typical cases have a slow progressive excavating atrophy of the optic nerve with corresponding coalescing patches of altered visual function in the visual field, with the risk of developing the atrophy (and rate of further atrophy) modified by the level of IOP. Thus some important etiologic or pathogenic features reside in the optic nerve in the naturally occurring human disease. This allows (a) for the existence of disease at IOP in the statistically normal range ("normal pressure glaucoma"), (b) for the hope of developing neuro-protective therapy, and (c) distinction in principle from "ocular hypertension".

2. **Context-related relevant features**. The essence from a pathogenic viewpoint is that there is interaction between IOP level and some pathophysiology in the optic nerve head or its vascular supply. The essence from an epidemiologic viewpoint is that some people have the fully manifest disease, and others have risk factors (ocular hypertension, family history of glaucoma, abnormal optic nerve physiology, etc.), but not yet the disease. The essence from genetics is that there may be separate genes controlling the physiology of the optic nerve head or is blood flow, the threshold for apoptosis, and the level of IOP that an eye carries. The essence from a clinician's perspective (and clinical trials) is that he must judge the presence of damage, the expected rate of further damage, and the risk of developing damage if not already present.

3. **Identification of cases**. We may define what we believe POAG is, but have trouble identifying whether an individual has it or is developing it. Moreover, the definition may need to differ in different contexts. For studying the risk of ocular hypertension, we must define when we will consider that the person has progressed to having POAG. For treatment trials we must define the manifestations that we consider minimal evidence of having the disease. For genetics, we may be interested only in knowing whether the IOP is elevated, or only whether the person inherits vascular dysregulation, or only whether a person inherits a tendency to develop inducible nitric oxide synthase, or only whether a person has genetic predisposition to apoptosis. In the clinic, we may not separate these components, but only measure the net rate of progressive injury, and whether it is changed by a particular therapeutic intervention.

4. **Non-POAG glaucoma**. Just as IOP alone will not define glaucoma, neither will characteristic excavation of the optic nerve with patches of visual dysfunction, as the same (or indistinguishably similar) optic nerve consequences may occur with abnormal IOP of distinctly different causes (trauma, angle closure, etc.) in humans or experimental

animals, whose optic nerve physiology seems normal.

5. **Pseudoglaucoma**? Unanswered is what we will call a disease that has all the manifestations of POAG except that the pathogenic process is not influenced by the level of IOP. That is, the final common pathway for nerve excavation and other clinical manifestations may be identical, but the process that leads to them is not accelerated when the IOP is high, nor slowed when the IOP is lowered by therapy. Do such cases exist? And if so, what will we call them?

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