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Glaucoma Diagnosis

From the Artisanal to the Defined

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Purpose: To chronicle the history of glaucoma diagnosis from its subjective ancient origins to the modern, formerly aspirational goal of objective, precise, accurate quantitative diagnostics.

Methods: A review of the literature was performed to assess the method of diagnosis of glaucoma and determination of glaucoma progression.

Main Outcome Measures: Glaucoma diagnosis, glaucoma progression detection, and the tools and techniques used for the same.

Results: Glaucoma diagnostics have progressed from simple observation to actual quantitative measurement. In the 19th and 20th centuries, accurate, precise measurement techniques were developed and used, and by the late 20th and early 21st centuries, the presence and progression of glaucoma could be determined not only quantitatively but also objectively, and with a high degree of precision and accuracy.

Conclusions: Over the past 3 millenia, glaucoma diagnostics have evolved from subjective observation to quantitative, objective, accurate, precise measurement. Applanation tonometry has replaced finger tension intraocular pressure measurement; automated perimetry and statistical analysis have supplanted subjective assessment of manual visual field (VF) assessment; and imaging technologies, such as OCT, have provided measurable, unbiased, correct, and reproducible alternatives to clinical observation and optic disc drawings. The net effect of this innovation has been a paradigm shift from dependence on subjective physician interpretation to incorporation of objective data for discerning the presence and progression of glaucoma from health and stability. Ophthalmologists are now able to detect glaucoma and its progression earlier than ever before, enabling precise and personalized clinical decision-making that ultimately serves patients by triggering escalations of treatment even before the development of grossly detectable damage. Further, the objective, quantitative, accurate, and precise measures allow expert diagnosis to occur without the necessity of an expert observer. This permits high-quality glaucoma care in nearly any setting. *Ophthalmology Glaucoma 2018;1:3-14 © 2018 by the American Academy of Ophthalmology*

Glaucoma is a chronic, irreversible optic neuropathy, frequently with a surreptitious course; it is the second leading cause of blindness globally. Advances in functional and structural measures of disease progression are transforming glaucoma diagnosis from an art to a science: Applanation tonometers have supplanted finger tension intraocular pressure (IOP) measurement; OCT and other imaging modalities have enabled in vivo objective, quantitative assessments of neural tissue loss; and rigorous statistical algorithms have replaced subjective visual assessments of perimetric and imaging results. These innovations have enabled earlier detection of glaucoma progression than ever before, contributing to more judicious use of the array of medical and surgical treatments that have evolved in parallel to diagnostic advances. The aim of this article is to review the history of glaucoma diagnosis, covering more than 2000 years of innovation.

Early History of Glaucoma

Hippocrates' *Aphorisms*, published in 400 BC, included the first known record of glaucoma. He referred to the entity as "glaucosis," a condition associated with dimness of vision and eventual blindness that was observed among the infirmities of age.[1] In his text *De Generatione Animalium*, Aristotle (384−322 BC) postulated that, in the same way that a shallow body of water exhibited a light, bright color and a deeper one appeared dark, the color of the eye depended on the amount of water within it.[2] Centuries later, Galen (129−216 AD) defined glaucoma as a condition in which the pupils became discolored because of changes in the fluids within the eye.[3] Aetius (482−565 AD) described 2 distinct categories of glaucoma: a curable defect of the lens and an incurable abnormality of the pupil.[4]

As Jacques Daviel began to describe the process of lens extraction for treatment of advanced cataracts in the 1750s, it became clear that cataracts and glaucoma were distinct entities.[4] In the 18th century, the majority of eyes diagnosed with glaucoma had advanced disease, characterized by a dilated, poorly reactive pupil and lens opacity that resulted in the observation of a greenish reflection. The contemporary ophthalmologic literature listed this as a prominent sign of glaucoma.[4]

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Table 1. Early Historical Events in the Evolution of Glaucoma Diagnosis

Date	Event
400s BC	Hippocrates' *Aphorisms* includes the first written record of glaucoma.
300s BC	Aristotle proposes that the color of an eye is dependent the amount of water within it.
100s AD	Galen defines glaucoma as a discoloration of the pupils due to fluid shifts in the eye; he draws the optic nerve as a hollow structure.
500s	Aetius describes 2 categories of glaucoma: a defect of the lens and a defect of the pupil.
1510s	da Vinci notes the cornea and aqueous bend light and the temporal VF extends 90° from fixation.
1626	Banister suggests the relevance of eye pressure to glaucoma.
1668	Mariotte describes the blind spot.
1673	van Leeuwenhoek draws first illustration of a peripheral nerve.
1752	Daviel presents results of more than 200 cataract extractions.
1755	Zinn contests the notion that the optic nerve is a hollow structure.
1807	Young specifies the dimensions of the VF.
1826	St Yves describes clinical features of advanced glaucoma in *Nouveau traité des Maladies des Yeux*.
1830	Mackenzie delineates 6 stages of glaucoma in *Practical Treatise on the Diseases of the Eye*.
1851	von Helmholtz invents the ophthalmoscope.
1851	Mueller describes depression of the optic disc in glaucoma.
1854	Jaeger illustrates swelling of the optic disc in glaucoma.
1855	Weber describes the glaucomatous optic disc as "cupped."
1856	von Graefe proposes incorporation of VF assessment into clinical practice.
1860	Schwalbe discovers anatomic connection between anterior chamber and ciliary veins.
1867	Weber invents the first applanation tonometer.
1870	Leber describes the aqueous pathway.
1879–1890	Priestley Smith suggests that glaucoma damage is due to vascular and metabolic changes in addition to mechanical forces; he later proposes that narrowing of the angle predisposes to glaucoma.
1907	Trantas promotes gonioscopy as routine diagnostic technique.
1920	Seidel refines Leber's filtration theory to account for colloidosmotic pressure of plasma proteins.
1945	Hans Goldmann invents the hemispheric bowl perimeter.
1950	Hans Goldmann introduces the Goldmann tonometer.

VF = visual field.

In his 1826 *Nouveau Traité des Maladies des Yeux*, St. Yves described this reflection and other clinical features of advanced glaucoma.[4] William Mackenzie soon thereafter delineated 6 major stages of the disease: a greenish reflex of the pupil marked the first stage, hardness of the eyeball occurred in the second stage, and by stage 6, the cornea had ulcerated and the eye had atrophied, the perceived final consequence of advanced glaucoma. Mackenzie also suggested a posterior sclerotomy as a means of relieving pathologic hardness of the eyeball.[5]

Historical Notions of Fluid and Pressure in the Eye

Banister first suggested the possible relevance of eye pressure to glaucoma in 1626 when he described an association between the resistance of the eyeball to indentation by the physician's finger and ocular disease.[4] It was not until the 19th century that the cause of this resistance to indentation became clear (Table 1). In 1860, Schwalbe injected dye into the anterior chamber and noted that it subsequently appeared in the veins on the surface of the globe, leading him to the conclusion that the anterior chamber was a lymphatic space in communication with the anterior ciliary veins.[4] In 1870, Theodor Leber described the aqueous outflow pathway, filtration through the trabecular meshwork, and flow through ciliary and vortex veins.[4] His work suggested that, with the exception of early fetal life, the rate of outflow was always proportional to the perfusion pressure.[4] Leber's filtration theory stated that to maintain a stable in vivo pressure, consistent formation of fluid must match and thus compensate for the steady loss of fluid via the outflow pathway.[4] Eric Seidel refined Leber's filtration theory in 1920 to account for the effects of the colloidosmotic pressure of the plasma proteins and the active transfer processes in the formation of aqueous.[4]

In the 1870s, Priestley Smith stated that the glaucomatous damage at the optic nerve head (ONH), known by that time as cupping, was a manifestation of not only mechanical forces but also a combination of vascular and metabolic changes in the eye. Furthermore, he suggested that these forces must be present chronically to alter the nerve in a detectable way.[6] Smith also proposed that narrowing of the circumlental space with age could predispose to glaucoma.[7] This narrowing was reliant on the anatomic principle that in states of hyperemia, the ciliary processes are pushed forward, pressing the iris against the anterior angle wall.[7] In a seminal animal study that contributed to this theory, Smith demonstrated that a small increase in vitreous chamber pressure caused sufficient anterior movement of the lens and suspensory ligament to close the angle of the anterior chamber.[6] This work underscored the importance of individual angle anatomy in determining glaucoma risk, prompting Trantas in 1907 (and later, Salzmann, Koeppe, Troncoso, and Barkan) to promote gonioscopy as a routine diagnostic technique.[4]