WORLDWIDE GLAUCOMA 2000

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Hosted by the Dana Center for Preventive Ophthalmology, Johns Hopkins University School of Medicine and School of Hygiene and Public Health, Baltimore, Maryland, USA

Co-Sponsored by the World Health Organization

Edited by Harry A. Quigley, MD, July, 2000

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1. EXECUTIVE SUMMARY

A group of those interested in blindness prevention were invited to a 2 day discussion co-sponsored by the World Health Organization (WHO) to evaluate the present status of glaucoma diagnosis and treatment in the world. The attendees represented academic and practicing eye care professionals, as well as representatives of non-governmental organizations and business firms interested in the subject. It is widely recognized that glaucoma is a major cause of blindness in the world, but its diagnosis and therapy have not been included in active eyecare programs in many developing countries. An initial meeting to discuss why this is the case and what might be done to improve the situation was held in Jamaica in 1993 ("Glaucoma in the Developing World").

At the Jamaica meeting, initial estimates of glaucoma prevalence and blindness were reviewed, and its disproportionately greater impact on the developing world was documented. Most of those affected were undiagnosed and treatments were considered both unproven in effectiveness, generally unavailable, and often unacceptable in major population groups. No successful screening approaches were available for either open-angle or angle-closure glaucoma. There were no existing examples of successful integration of glaucoma management into the health care systems of any developing country, and the models of glaucoma care in the developed world were too expensive and possibly inappropriate for the disease elsewhere.

From 1993 to 2000, a variety of developments improved the situation, providing hope that a second discussion would be valuable. More than a dozen, new population-based prevalence surveys had been carried out in North America, among Hispanic persons, in Europe, Australia, Africa, Mongolia, and Singapore. These gave better data for the number affected, their geographic distribution and type of disease. Treatment options began to be explored, with some clinical trials of trabeculectomy surgery and greater availability of more affordable eyedrop therapy in some countries. The FDT screening visual test was developed, inspiring hope for better identification of cases, and the definitive, threshold test made by Zeiss--Humphrey was improved by speeding its test algorithm. Field studies of the diagnosis of angle-closure glaucoma in Asia were completed to improve diagnosis of this condition.

At the Worldwide Glaucoma 2000 meeting, there were introductory presentations, followed by division into 5 working groups that discussed assigned areas and questions. These dealt with open-angle and angle-closure glaucoma, their diagnosis or therapy, and a group devoted to the role of glaucoma care in overall eye and health care programming. All attendees then participated in joint discussion of the findings from each working group and summaries were prepared. Action plans were developed that indicate areas in which progress could be made in the near future. This executive summary provides a synopsis of the findings and recommendations, followed by the detailed proceedings.

The **First Working Group dealt with Diagnosis of Open-Angle Glaucoma** (OAG). Their conclusions included reinforcement of the present concept that glaucoma

is a disorder of the optic nerve characterized by structural change at the optic disc and functional defect in the visual field. The structural defect that was favored was a cup/disc ratio whose size is large enough that it is found in only 2.5% of the population. The functional test considered the standard is threshold perimetry as now practiced on the Humphrey instrument--or any test that is shown by actual testing to be equivalent to deficiency on the Humphrey. They explicitly stated that these criteria may vary with the group being studied, hence, the criteria require validation in a test group of the population that is evaluated in each major world ethnic group. The level of the intraocular pressure (IOP) is not a defining feature of OAG, since many persons with this disorder worldwide have normal IOP. They felt that screening, perhaps using technology similar to the FDT instrument, should only be done if those who were identified to be treated had a significant chance of blindness in their lifetime. Hence, screening should attempt to identify only more aggressive or advanced cases to maximize its cost-effectiveness.

The **Second Working Group dealt with Treatment of OAG**. This discussion stressed that treatment should be assessed by evaluations that include the effect of the disease on quality of life. Agreeing with Group 1, they stressed the need to identify those who would more often progress to serious vision loss, and to single out these persons for treatment. It was recognized that factors motivating individuals to agree to therapy are not well known, especially in developing countries. A surgical approach to glaucoma was thought to have the most advantages at this time, though its risks were appreciated. In fact, the need to evaluate the risk and benefit of glaucoma treatment represents the highest priority in this area. One means to begin doing so immediately is to evaluate the addition of glaucoma surgery as a combined approach in the same eye to those presenting to cataract programmes with glaucoma.

The **Third Working Group dealt with Diagnosis of Primary Angle-Closure Glaucoma (PACG)**. This group began by defining the gonioscopic criteria and methods that denote a narrow angle (NA). Then, for those with NA who show signs of clinical abnormality preceding actual functional loss, the diagnosis of primary angle closure (PAC) is given. For PAC cases with functional loss in visual field testing, primary angle closure glaucoma (PACG) is diagnosed. For those with a symptomatic acute attack of high IOP due to PAC, the term acute attack is applied (AA). Specific criteria developed by this group have been initially tested in studies in Mongolia and Singapore, but the need for longitudinal validation of its concepts is recongnized.

The **Fourth Working Group dealt with Treatment of PACG**. The group made recommendations for developing and developed countries separately. For developing countries, NA cases would not be treated until controlled trials of laser iridotomy demonstrated its risk/benefit ratio. Those with PAC would receive iridotomy, while those with PACG would most likely benefit from trabeculectomy surgery, as iridotomy alone has shown a lack of long-term control. In addition, the blindness rates from this disorder exceed those of OAG substantially. When one eye is treated with iridotomy, the fellow eye should also be treated. Acute attacks should receive iridotomy, with immediate followup to determine if further surgery will be immediately needed. In

developed countries, NA patients may receive iridotomy where detailed study indicates higher risk, while PAC and PACG cases receive iridotomy first, reserving trabeculectomy for those who fail to be controlled on followup. The need for durable, inexpensive lasers to perform iridotomy was stressed.

The **Fifth Working Group dealt with Glaucoma in Overall Eyecare**. The immediate initiation of glaucoma programs was thought to be appropriate in target areas of the world where glaucoma is of public health importance and where existing resources exist to allow a broad-based program. Glaucoma services must be integrated into a comprehensive eyecare program, with specific training of delivery personnel, social marketing, and outcomes measurement. In the long-term, (by 2020) the hope is to extend treatment to those in danger of significant functional impairment through locally appropriate services in every region of the world. The rush to implement single-disease programs, outside the existing care system, should not occur. A variety of research areas were identified.

In response to these discussions, a series of **Action Items** were developed. These follow this Summary, along with the extended report of the proceedings, participants and related materials.

2. ACTION ITEMS FROM WORLDWIDE GLAUCOMA 2000

It was envisioned that a working group will be convened under WHO sponsorship to consider the action items presented below and to establish priorities for them. This process will suggest locations for data collection and investigations, who might conduct them, and how support for the projects could be obtained. These items are written in the form of **specific aims for research projects** that follow from the recommendations of the Working Groups.

A. OVERALL ACTION NEEDED

1. Develop by 2005 a comprehensive, evidence-based diagnosis and management program for angle-closure and open-angle glaucoma worldwide.

2. Define whom to treat, how to treat them, and training needed for the health care personnel who carry out the program.

3. Estimate costs related to treatment, visual impairment and blindness in present health care settings and after implementation of the 2005 program

B. ANGLE CLOSURE GLAUCOMA

1. DEFINING THE NARROW ANGLE

a. Compare methods of diagnostic gonioscopy (Goldmann 1 mirror, Posner 4 mirror, biometric method, and Koeppe) for usefulness, predictive power, ease of learning by ophthalmologists and non-ophthalmologists, and practicality in field settings.

b. Develop a surrogate method for primary angle closure (PAC) diagnosis that is validated against gonioscopy, with possible methods to include van Herick assessment, hand light test, ultrasound, and optical pachymetry.

2. NATURAL HISTORY OF PRIMARY ANGLE CLOSURE

a. Estimate risk of PAC progressing to primary angle closure glaucoma (PACG), with functional loss (including field loss and blindness), both in persons who have and have not undergone iridotomy through longitudinal study of relevant populations

3. TREATMENT OF PAC AND PACG

a. Determine the best method for performing iridotomy (neodymium:YAG versus continuous wave or both) in major ethnic groups; and evaluate the production of a better laser for developing country use that would be cheaper, capable of performing iridotomy, suturelysis, capsulotomy, laser trabeculoplasty, and

ciliodestruction.

b. In PACG, compare iridotomy to initial trabeculectomy as the most effective initial treatment, either through clinical trial or by longitudinal study (retrospective or prospective) of PACG treated by iridotomy with defined success rates.

C. OPEN ANGLE GLAUCOMA

1. DEFINING OPTIC NERVE DAMAGE

a. Test the utility of an operational classification of optic disc damage using criteria defined by the 97.5th percentile for vertical cup/disc ratio of each population. This would be tested using existing population-based prevalence survey data, comparing diagnosis of glaucoma used in a survey to the proposed classification scheme for each ethnicity. Evaluate differences among various ethnic groups. An associated issue is to determine how often a cup/disc ratio of 0.9 or greater is NOT glaucoma.

b. Determine what features of the optic disc other than the cup/disc ratio differentiate glaucoma damage from normal and non-glaucoma disease and develop practical methods to measure this attribute(s). E.g., what is it that “glaucoma experts” use to define glaucoma damage when they look at the disc and how can it be quantified and taught. Test whether scanning laser ophthalmoscopes should become the standard for identifying disc damage, replacing cup/disc ratio by features such as cup shape measure.

c. Evaluate the FDT technique for identifying those with glaucoma damage in population-based samples, validating its findings against threshold perimetry in each ethnicity. Develop a battery-operated, head-mounted, less expensive instrument using FDT technique

d. Develop screening guidelines that take into account the effectiveness of the methods and the age at which maximum yield of case identification and prevention of blindness can be achieved.

e. Determine the spectrum of visual field loss in each population and its functional consequence by assessment of a meaningful quality of life measure.

f. Determine the risk of blindness for PACG and open-angle glaucoma (OAG) in each population and factors identifying those at risk during their lifetime to define those in greatest need of treatment. Establish criteria for those in whom the risk of aggressive therapy is less than the risk of blindness.

D. TREATMENT OF OAG AND PACG

1. Survey present treatment methods in each major ethnic group, determining outcomes from present practice.

2. Conduct clinical trials of medical, laser and surgical methods of lowering IOP in various settings using either surrogate outcomes or optimal functional measures.

3. Develop a new (or test existing) simple filtering surgery devices or plugs.

4. Develop new outcome measures that are more relevant to those affected by glaucoma in world populations.

5. Engage those organizations with resources and societal responsibility to affect glaucoma blindness, including National Physician and Optometry Societies, Prevention of Blindness Committees, and NGOs.

3. PROCEEDINGS

8:00 AM

INTRODUCTION AND OVERVIEW OF MEETING GOALS: A DISCUSSION OF WORLDWIDE GLAUCOMA DIAGNOSIS AND THERAPY

HARRY A. QUIGLEY, MD
Director, Glaucoma Service and Dana Center for Preventive Ophthalmology
Johns Hopkins University School of Medicine

Until recently, **global glaucoma treatment has not been a priority**, finding itself relegated to footnotes and future considerations in international programs such as Global Vision 20/20. Glaucoma screening has been considered to be cost-ineffective and glaucoma therapy had not been proven conclusively to be beneficial in preventing blindness.

Increasingly, those dedicated to eye care recognize the need to address **glaucoma, the second leading cause of blindness in the world**. Resources are appearing for its care in developing countries. At vision care centers, families bring their affected mothers and fathers, often too late to prevent vision loss, but willing to provide the cost of care if it is judged to be of value. The model of cataract surgery delivery by the Aravind Hospitals of Madurai, India shows that self-sustaining programs can emanate from a care center of excellence to serve surrounding rural populations.

These eye care centers are now attempting to provide appropriate care for their populations and to evaluate their outcomes. **The benefit from eye pressure lowering therapy was recently validated** by the results of the Normal Tension Glaucoma clinical trial. Studies of glaucoma diagnosis and therapy in developing countries can have significant impact in developed countries as well. Substantial economic resources are now being devoted to glaucoma care and it would be prudent to determine which approaches are most effective and to prune those behaviors that are wasteful or harmful. At present, no one has definitive answers.

New **information is needed for every country** and we should use the strengths and opportunities that present themselves to conduct evaluations and research. Where high technology is appropriate, its advantages should be maximized. Less technical, cheaper approaches should be developed and evaluated by comparison to expensive techniques. Hence, there is no division of these questions into “first world” and “third world” solutions, but only a diversity of approaches that are interwoven.

Research must follow the same ethical standards regardless of location. This may require the alteration of present, local practices from those that are considered the “standard of care”. In controlled clinical trials, present clinical approaches may be judged unethical and cannot be evaluated. Much research will logically be performed in the developed world, since the infrastructure for its conduct is in place and subjects can and do willingly provide informed consent for participation. The usefulness of therapeutic options will be derived from well-designed clinical trials. It will be important

to re-evaluate these findings in the context of different populations and the variations in training and resources available to care delivery personnel.

At the 1993 conference in Jamaica, “Glaucoma in the Developing World”, a group of international experts in collaboration with the World Health Organization, the Interational Eye Foundation, and the Dana Center for Preventive Ophthalmology produced a report summarizing the state of knowledge on these issues. A series of proposals were made to generate progress for glaucoma therapy. These are presented below. In some cases, new information in the 7 years since that conference has clearly led to the need to re-evaluate, to focus, and to implement the recommendations.

In this two day conference, we will generate renewed interest in glaucoma treatment and plan substantive evaluation and research programs that will make an impact on visual impairment due to glaucoma in the near future.

8:05 **INTRODUCTORY REMARKS**

SERGE RESNIKOFF, MD
Coordinator, Prevention of Blindness and Deafness,
World Health Organization, Geneva, Switzerland

I am delighted to be here and to benefit from the discussions and, of course, from the inevitable debates that are not unusual when any forum discusses glaucoma. This to my mind is not an unhealthy sign, as debates arise when there is more than one point of view. As all of you are aware, in no field of ophthalmology is this truer than in the field of glaucoma, right from its pathophysiology through the whole gamut of patient care.

You all know that the Global Initiative for the Elimination of Avoidable Blindness by the year 2020, under the caption “VISION 2020--The Right to Sight”, was launched in Geneva in February last year. Since then, there have been regional and subregional launches in many parts of the world. VISION 2020 is a collective effort by a number of partners, both international and national, planning and working together in a phased manner towards the achievement of a common goal. We have also agreed upon priorities and strategies, setting specified, sometimes ambitious, targets.

The Global Initiative dos not include the prevention of blindness from glaucoma, and this has certainly raised many eyebrows and become the subject of FACS--frequently asked questions. The incontrovertible fact is that “glaucoma” causes irreversible visual disability, accounts for at least 15% of global blindness and, being also ageing-related, will therefore increase with the rapid increase in the ageing population globally.

Given these facts, there should be a reason why, through a consensus at various scientific planning meetings that preceded the Global Initiative, glaucoma was not included as a priority in the disease control component, at least early in the Initiative. This is one of the debatable points that I alluded to earlier.

Through intensive research over the years, we have a better understanding of glaucoma, and I know this meeting will give us an opportunity to be updated on this by many who are here who have, in fact, spearheaded these research efforts. Despite these advanced in knowledge, my understanding is that we still have major concerns relating to the definition of a case, the identification of cases, diagnostic criteria, treatments options--to name but a few--in the public health domain of blindness prevention efforts.

I trust that this meeting will elucidate at least some of these issues. We are living not only in an era where emphasis is on evidence-based practice, but also where, quite rightly, patient-centred care and outcomes, including quality of life, take precedence over profession-centred treatment modalities and outcomes. Moreover, the cost-effectiveness and cost-benefits of what we do are of major concern to the individual patient as much as to the governments and other institutions that pay for patient care. We also bear the responsibility to resist, to the extent possible, likely market forces that may not necessarily have the patient’s best interest in mind.

These considerations are very relevant when we discuss the management of glaucoma, particularly in a public health mode. On the other hand, we should be sure of the scientific basis underlying our recommendations and, perhaps, practice guidelines. Secondly, we should tailor our interventions in the best interest of the patient's quality of life. Lastly, attention must be paid to technology assessment and to the choice of appropriate technology, as far as is feasible, so that interventions are not only available, but also accessible and, most importantly, affordable to the populations in greatest need. There may not be simple solutions to meet these criteria.

I look forward to this meeting and believe the outcome would be a major step forward in at least finding some common ground on the issues before us. Even if we do not come up with answers to all the questions that we had before the meeting, we should be happy if the discussions also help define more precisely the questions for which we need to find answers in the future.

Finally, I would like to express our deep appreciation to Harry and his staff at the Dana Center for hosting this meeting.

8:15 **DEVELOPING WORLD PROBLEMS IN OPHTHALMOLOGY**

ALAN ROBIN, MD
Associate Professor of Ophthalmology and International Health
Johns Hopkins University Schools of Medicine, and Hygiene and Public Health

Glaucoma is the second leading cause of blindness worldwide, with 6.7 million persons estimated to be bilaterally blind, and over 2% of adults affected in European and Indian prevalence surveys. But, attitudes toward glaucoma have prevented its emergence into eye care programs. With the rapid aging of the world's populations, diseases like glaucoma that affect the most elderly will become more significant. Yet, in developed countries only 50% of those with glaucoma are diagnosed and in the developing world 90-100% of those affected are unaware that they have the disease and, when blind, do not know what has caused their disability.

The first problem is to define glaucoma, since we cannot treat a disease that is not characterized. We now know that glaucoma is not defined by a particular level of intraocular pressure (IOP), though the relative risk of disease rises with higher IOP. Ocular hypertension, or IOP above an arbitrarily defined normal range can represent 8% of adults in a population, yet most of these individuals will never develop glaucoma.

Glaucoma is now recognized to be defined as an optic neuropathy characterized by optic nerve head and visual field changes, with age, IOP, and family history representing important risk factors.

Increasingly, experts on glaucoma realize that the conservation of limited resources for caring for glaucoma should concentrate on those who are at greatest risk of going blind or losing visual function in their lifetime. This includes loss of visual field sufficient to affect quality of life--though studies to determine this linkage are just being performed.

Identification of cases (screening) cannot be done by measurement of IOP. The ideal screening tool should be easy to administer, easy to perform and easy to interpret. It must have high predictive power and be inexpensive, portable, and short in duration. The Frequency Doubling Technology approach appears to show promise to satisfy these attributes. Its sensitivity and specificity in identifying moderate and severe glaucoma have been shown to be high in recent clinic-based research.

The best mode of treatment has not yet been shown, with the cost of medications higher than most persons can afford in the developing world. Furthermore, there will need to be effective social marketing to induce those with glaucoma to self-administer medicines that have inevitable side-effects. The effectiveness of treatment in the developed world has just been shown, but variations in the quality of therapy in the developing world may not allow immediate translation of these results. For example, while cataract surgery has a remarkably high rate of restoring normal vision in the U.S., and in centers of excellence in India, reviews of results of general cataract surgery among Indians show disappointing returns of visual acuity.

It may be that approaches to therapy that are considered radical at present will be the best for many settings worldwide--for example, diode laser cilioablation as initial

treatment. In all discussions of therapy, the rate at which the average patient becomes worse must be taken into account to balance risk and benefit.

Once the best approaches are chosen, the training, equipment and teamwork needed to apply therapy must be found. The public will need to be educated to the need for treatment and will need to demand the highest quality of care. Education of health care personnel must receive a high priority. Outcome measurements to define success of any program is vital, from the perspectives of the patient, society and economic reality of each country.

8:30 **OPEN ANGLE GLAUCOMA--WHAT'S KNOWN AND UNKNOWN**

JAMES TIELSCH, PhD
Professor, International Health and Ophthalmology
Johns Hopkins University Schools of Hygiene and Public Health, and Medicine

Instead of reviewing facts about open-angle glaucoma (OAG) that are well-known to this sophisticated group, it will be useful to place a program for dealing with OAG in the perspective of epidemiological models for disease management. Such models include eradication and elimination. Examples of an eradication strategies are immunization for smallpox or and the SAFE strategy for trachoma is an example of an elimination of avoidable blindness. In this as in some other elimination models, the target is the endpoint of disease, not the disease itself. This is true for the W.H.O. 2020 Global Initiative program goals, which seek to eliminate blindness, not cataract or all trachomatous infection. Elimination is clearly impractical for glaucoma.

Other models are control programs, secondary prevention (such as cataract surgery), or tertiary prevention (for example, low vision rehabilitation for macular degeneration). Among these, the most applicable for glaucoma is the control model. It cannot be eradicated since its etiology is multifactorial and largely unknown, and its visual loss cannot be eliminated since the treatment is not 100% effective and not all cases can be readily ascertained.

A control model would attempt to reduce the level of disease to that which is considered acceptable to the community. This could vary substantially among regions of the world. Priority setting for control programs among various diseases can be complex and influenced heavily by political considerations. These include:

1) How big is the problem?
2) What are its social and economic consequences?
3) Are there substantial direct and indirect costs of care and blindness?
4) Is the community concerned about the problem?
5) Does treatment work and, if so, how well?
6) What is the added value of the program over present behavior?
7) Can public concern and confidence be maximized to improve acceptance?

It is important to recognize that control programs exist within the community, not within the health care system alone.

For a glaucoma control model, one must first decide what outcome is to be used to measure the success of the program. This will presumably be some measure of functional impairment. While visual field testing is the clinical standard, a more practical and applied measure of useful visual function is needed. This may be quite variable by locale, with the ability to care for cattle being a relevant level in rural communities, and the ability to read and drive representing a possible level in more urban settings.

Second, we must determine the level of the burden of visual disability that is acceptable to each community. We must determine the community's priorities and provide language that allows the community to make informed decisions. This might be related to prevalence or to impairment. The organization that certifies the definitions

also must be determined; candidates are W.H.O., non-governmental organizations, representative physician organizations, or the community itself. Disability is now graded using the unit “DALY” and this is well-established for other major eye conditions like cataract. Glaucoma might be graded by linkage to the already available cataract disability

Models can be represented as linear diagrams in which interventions and control program elements are illustrated in terms of their association with stages of disease.

Genetic susceptibility plus other risks
-----\>Development of OAG
(Screening acts here)-----\>Progressive worsening
(Treatment acts here) -----\>Life without severe impairment
or -----\>Life with severe impairment

Intervention opportunities in glaucoma appear to be mostly in the category of secondary prevention (primary prevention being equal to preventing the disease from happening in the first place and tertiary prevention equal to low vision rehabilitation for those blind from glaucoma). This would consist of two steps: 1) case finding at a stage prior to severe impairment and 2) an efficacious therapy that is accessible and used appropriately.

With respect to case finding, the development of the FDT instrument represents a possible improvement in glaucoma identification. The production of low technology versions of this instrument might be useful if they could be administered by relatively unsophisticated examiners.

Regarding therapy, no definitive determination has been made as to whether medical, laser or surgical treatment should be the approach of choice, and this may vary by region.

Importantly, we must consider how successfully glaucoma will compete for limited health care resources against other eye diseases and health issues in general. Combined programs that treat more than one eye disease with the same personnel or equipment should be sought. And, success criteria have to be chosen.

Finally, an applied research program is indispensable to any successful control program, to improve its components as it is implemented and to evaluate its success. It is not worth beginning a control program if funded research is not included in the costs.

9:15 **ANGLE CLOSURE GLAUCOMA IN INUIT AND ASIANS: OCULOMETRY, EPIDEMIOLOGY AND BLINDNESS PREVENTION THE MOHAMMED AZIZ LECTURE ON WORLDWIDE BLINDNESS**

POUL HELGE ALSBIRK, MD
Head, Eye Department, Hillerød Sygehus, Hillerød, Denmark

Dr. Alsbirk reviewed his personal experience with angle closure glaucoma (ACG) which he has studied among the Inuit people of Greenland and in recent research studies in Mongolia. He noted theories that ACG was likely to be common among people of the northernmost latitudes due to migration of the human population across the land bridge formerly present between Mongolia and North America/Greenland.

He proposed that iridotomy represents such a successful therapy for ACG that it might be considered at this time for inclusion in the W.H.O. Global Initiative. He based this recommendation in part on encouraging data to be published soon in the British Journal of Ophthalmology showing good control of ACG in most eyes of either suspects and those with primary angle closure without field loss and in at least one-half of those with ACG (with visual field loss).

The review touched upon the well-known risk factors for ACG, including female gender, age, and a variety of biometric measures implicating small ocular dimensions, especially shallow anterior chamber. Pachymetry, ultrasonic measures and gonioscopy all point to the association of smaller eyes and ACG. Eyes of those in Greenland show more eyes with smaller biometric properties. Heritability of small eye characteristics was shown in family studies in Greenland, with 70% of the age and gender independent ocular biometric properties being inherited. Interestingly, Eskimo persons who have lived in Denmark had deeper chambers (adjusted for age and gender) than Eskimos living in Greenland or Canada. In summarizing anterior chamber depth data by ethnicity, the chambers seemed deepest in African and European-derived persons, shallower in Burmese and Chinese, and shallowest in Eskimos.

The large burden of ACG in some regions of the world was illustrated by data from Greenland (a 1962 survey) with 0.25% of adults blind, 64% of these from glaucoma and 80% of the glaucoma blind being women. In addition, data from Burma (1982) were presented, where 28% of all surgery performed was related to glaucoma and 81% of the glaucoma surgery was for ACG. Among Eskimos, the prevalence of ACG in adults averages 3%, with the prevalence among Eskimo males of 2% and females of 10%, while it is typically less than 0.5% in Europeans

Unique longitudinal data on persons in Greenland with 10 and 20 year follow-up was collected by Dr. Alsbirk and shows that narrowing of the anterior chamber angle is an aging effect in all members of a population. These data support that the findings of several cross-sectional studies that the angle becomes narrower with age, and not due to a cohort effect.

His observations in a population-based survey of persons in Mongolia with collaborators from the International Centre for Eye Health, London, show that the van Herick method of estimating chamber depth can be effective in case finding for ACG. Using anterior chamber depth, measured either optically or ultrasonographically, he presented estimates of sensitivity and specificity for identifying ACG and normal subjects of approximately 85%/85% in this population with a high prevalance of occludable angles. With the van Herick method of limbal chamber depth, predictive power similar to that obtained with chamber depth measurement could be obtained. Mongolians had an age-specific prevalence of anterior chamber depth closer to that of Eskimos than that of Europeans.

In studying eyes that had undergone neodymium:YAG laser iridotomy among Mongolians,

iridotomies remained open in nearly all subjects 3 years after treatment, and no further glaucoma therapy was needed in nearly all those with primary angle closure who did not have optic disc and visual field damage. However, nearly one-half of those with field loss (ACG) required more than iridotomy. He spoke of the need for an improved, portable YAG laser that would be cost-effective in field delivery of iridotomy services. He proposed that anterior chamber depth should be further evaluated as a screening tool for ACG.

In closing he quoted the late Ronald Lowe, who said: "I believe that the big remaining problems of angle-closure glaucoma will be little assisted by further biometry, as they have a disturbed physiological basis."

REPORTS OF WORKING GROUPS

WORKING GROUP 1: DIAGNOSIS OF OPEN-ANGLE GLAUCOMA
FACILITATORS: Paul Mitchell and James Tielsch

Questions posed for discussion:

1. **What** diagnostic criteria can be defined from available examination findings-- is it disc alone, field alone, disc plus field, and when if ever does IOP play a role? What additional exclusionary features are included in definition, such as presence of an open angle, lack of secondary glaucoma features, etc?
2. **How** should the above definition be implemented, with what specific instruments and what exact criteria? For the disc is it clinical exam, photos, or imaging. For fields, what test/perimeter is the gold standard and which is practical for use widely? For tonometry, where that is included in definition, what tonometer and how to decide the cut-offs for various populations?
3. **Who** carries out the testing for each examination: lay employee, eye nurse, non-eye M.D., Optometrist, or Ophthalmologist. What are the relative training requirements for the persons chosen for this. What personpower is presently in place to carry out the testing.
4. **Screening**: should it be done, and if so, how are its methods distinct from the methods of definitive examination?
5. **Cost** estimates should be attempted for the features of diagnostic techniques that are chosen.

Summary of Discussion

The group unanimously felt that open-angle glaucoma should be diagnosed primarily from the **presence of structural glaucomatous optic neuropathy in combination with a glaucomatous visual field defect**. However, it was recognized that there would be circumstances in which one or other of these could not be documented. For example, a person who could not perform perimetry or in whom media opacity precluded a view of the optic disc. Hence, there would be need for a hierarchy of diagnostic criteria with ideal features and operational definition(s) that allowed identification of those likely to have the disease.

Diagnostic criteria for the optic disc should be defined for each ethnic group using data from study of a representative sample of that ethnicity. These data will differ among groups, such as European, various subgroups of African and Asian persons. Optic disc diagnostic criteria should be derived from data of already completed prevalence surveys, or from new studies as they are done. Vertical cup-disc ratio was considered the most useful parameter.

To determine what disc feature can be reproducibly measured by a wide variety of observers, yet at the same time be representative of glaucoma injury, **the operational standard that is suggested by this group is the 97.5th percentile for vertical cup/disc ratio**, determined by the distribution of disc findings in the relevant population. For example, the Rotterdam Eye Study, using both

ophthalmoscopy and Topcon ImageNet analysis found that the 97.5th percentile for vertical cup/disc ratio was 0.7. For the Blue Mountains Eye Study, however, the 97.5th percentile was ≥0.77. Taken alone, a disc with cup larger than this standard is, by definition, unusual in the population. Yet, simple statistical rarity should not be an identifier of disease, since there are eyes with cup/disc ratios above the standard that see normally and have no glaucoma. **Cup/disc ratio above the 97.5th percentile would then be a feature that made glaucoma "probable". When this finding is seen in combination with a defined visual field defect, the diagnosis could be considered "definite".** It was discussed in detail in the plenary session that the seemingly arbitrary choice of a statistical standard for a particular disc feature would not be universally accepted by the medical community as a definition of disease. However, the practical implementation of such a standard would be to identify with reasonable predictive power those at greatest risk of disease. Rather than awaiting some future ideally specific feature of glaucoma, it seems reasonable to use a standard that achieves a useful end. In doing so, it may be appropriate to admit that this is not a standard that "diagnoses" glaucoma, even if its operational value is appreciated.

For subjects in whom a reliable visual field finding cannot be obtained, the defining limit for disc abnormality in this operational scheme would be made more stringent, with definite glaucoma indicated by a cup exceeding the 99.5th percentile (≥ 0.9 in most populations). It is well-known that the larger the disc diameter, the larger the cup/disc ratio in normal eyes. The variation in disc size can account for as much as a 0.1 increase in cup/disc ratio from smallest to the largest quartile of disc diameter. This may or may not need to be taken into account. Cup-disc ratio asymmetry was also considered potentially useful as an identifier of glaucoma structural damage. The 97.5% rates for asymmetry of cup/disc ratio in the Rotterdam Study were ≥0.2, while for the Blue Mountains Eye Study the value was between 0.2 and 0.3. Similar values could be calculated for neuroretinal rim width, but these are not only likely to be duplicative of cup/disc ratios, but also more difficult to estimate numerically by observers without automated methodology.

The current full-threshold Humphrey 24-2 standard algorithm program was considered the defining standard for visual field loss. It is reasonable to use other threshold or suprathreshold methods, as long as their equivalence to the standard has been estimated by actual comparison testing in the population of interest. Tests must be considered reliable by current standards.

There was much discussion regarding whether IOP should be a diagnostic criterion for OAG. Overall, **members agreed that IOP should not be used to diagnose OAG**, though it is obviously important in determining appropriate management. It is now well-recognized that the distribution of IOP as measured by applanation tonometry differs by ethnicity, with the most striking finding being the lower IOP distribution of Asian populations.

Screening is only valuable in contributing to a control model if the available methods satisfy particular criteria, as defined by Dr. Tielsch above, including:

1. The disease must be of public health importance.

2. There must be an acceptable and accessible treatment for the disease once diagnosed. This treatment should be more effective if delivered earlier in the course of the disease.

3. There must be an acceptable screening test(s) with adequate sensitivity and specificity.

4. There must be a preclinical phase of the disease when it is normally not diagnosed during which time it is detectable with an appropriate screening test.

Open-angle glaucoma meets the above criteria in many respects, although we lack extensive evidence for the efficacy of IOP-lowering treatment, particularly with respect to its beneficial effects on vision-related outcomes of interest. In addition, access to appropriate and well-trained providers of eye care services must be assured prior to the initiation of population screening programs. Bluntly stated, **it isn't worth screening if one cannot expect better long-term visual function after treatment.**

Useful screening tests should identify a high proportion of true cases (high sensitivity), while limiting the number of false positives (high specificity). Glaucoma screening must have sensitivity and specificity of 90% to be useful. However, it is vital to consider the stage of disease that is to be identified and this will vary depending on the resources available and the goals of the screening program. For example, in developed countries it may be most appropriate to screen for the earliest detectable signs of glaucomatous optic nerve damage. **In settings where resources are more limited, screening should be targeted to the detection of moderate to severe disease**. The aim is to find those who will undergo severe vision loss in their lifetime.

To accomplish this aim, screening protocols could be devised to identify those with glaucomatous injury that was at least equivalent to that of the threshold perimetry standard, and that optimized the recognition of moderate to severe degrees of functional loss. This approach would maximize specificity. There was consensus that speed of testing is highly desirable, with ideal test time less than 3 minutes per eye. The frequency-doubling technology instrument is recognized to have promise in satisfying these criteria.

The group recommended that **glaucoma screening should be conducted as part of a comprehensive case-finding program for other treatable ocular diseases**. The measurement of visual acuity is a sine qua non of screening programs. Where resources are limited, screening could be limited to subgroups of the population with a disproportionate disease burden. There is little point in screening persons less than 40 years of age except among Afro-Caribbean populations. For Afro-American populations, the group suggested that screening may begin at age 40-50, depending on the yield expected and the resources of the program. For populations of primarily European decent, screening is of greatest value beginning at age 50-60. The best evidence to date on the OAG prevalence in the Indian subcontinent and in East Asia suggests that their age-specific rates are likely to be similar to European populations and that similar age criteria should apply to screening programs in these settings. Other risk factors for OAG could be used to target more specific populations for screening

when indicated by local circumstances. These factors could include diabetes, prior use of topical, systemic or inhaled steroids, and family history of glaucoma, especially among first degree relatives.

WORKING GROUP 2: OPEN-ANGLE GLAUCOMA TREATMENT
FACILITATORS: ALAN ROBIN, R. RAMAKRISHNAN

Questions posed for discussion:

1. **Which** treatment is the best: eyedrops, ALT, trabeculectomy (with or without antifibrosis), drainage device, diode laser, other surgery ?

2. **Who** should perform or administer the therapy? Lay person, eye nurse, non-eye M.D., Optometrist, Ophthalmologist? What are the relative training requirements for the persons chosen for this. What personpower is presently in place?

3. **What outcome measures** should be used to judge the success of the therapy? Visual acuity, IOP, disc change, field progression, quality of life measure, avoidance of blindness.

4. **What complications** are likely from treatment and what is the acceptable level of risk compared to potential benefit? Deal particularly with development of cataract and late infection after trabeculectomy.

5. **Cost** estimates should be attempted for therapeutic interventions for sample populations. If not possible, the information needed to make such estimates should be specified.

Summary of Discussion:

One important issue in considering glaucoma therapy is **what outcome should be used to measure the success of treatment.** Should IOP be used as the surrogate endpoint for therapy evaluation? The standard clinically applied outcome in developed countries--visual field loss--may be difficult to implement. There is as yet only a modest amount of information that lowering of IOP has an impact on blindness in glaucoma. We **need to determine who progresses most rapidly**. These persons could perhaps be identified using risk factors such as age, race, IOP level. If IOP is to be used as the surrogate endpoint, how low is the target, does this depend upon the degree of injury? Is the lower the better a good guideline? We should take into account the life expectancy.

Can a **health-related quality of life instrument specific to glaucoma be used in world populations** to supplement or to replace IOP as the endpoint of therapy? Or, should programs begin with much simpler outcomes: the prevention of legal blindness, the ability to carry out typical rural activities such as tending cattle, or the ability to retain employment in a usual occupation. In the developed world the goal may be considered to be no functional loss, no progression, or no measurable visual field defect, but the outcome level that is considered desirable will vary from culture to culture.

Are there ways to market the therapy of an asymptomatic disease to populations in which it has not been previously done? Some past successful programs should be evaluated, perhaps those dealing with hypertension, dental care, cholesterol lowering, and refractive surgery. A collaboration between pharmaceutical companies, NGO's and

clinicians may be needed, to utilize the motivations each has to increase therapy delivery. It would be **important to know the factors that influence patient behavior**, particularly cooperation with suggested treatment. Research into patient educational aids is needed; examples include visual representations of glaucoma damage for patients.

The decision to treat and the choice of therapy must depend critically on the resources available and committed to glaucoma. At the present time, the **surgical approach is generally agreed to be the most likely to be implementable** and to be efficacious. Methods to decrease complications and to simplify the procedure(s) are needed. Research is needed to test whether the expected success and complications that are seen in developed countries will be the same or different in the developing world with its different patient base and surgical setting and skill. Glaucoma surgery at this time has a number of complications that limit its acceptability. Glaucoma surgery has benefitted from the addition of anti-metabolites to decrease scarring, but safer agents in this class are needed. Simple “plug-in” devices are being studied that could make rapid glaucoma filtering surgery possible.

Ciliodestructive surgery has promise, though the optimal energy levels to achieve satisfactory IOP lowering with minimal complications have not been tested in representative populations. Data presented by Egbert on treatment in West Africa show a 50% rate of achieving a target IOP lowering with similar visual complications to those experienced after trabeculectomy.

Tube-shunt operations offer a possibly lower level of late infection risk due to the lack of a bleb. However, their use engenders a unique group of complications and the additional cost of the device would need to be accounted. Perhaps local manufacture, such as with the intraocular lens factory at Aravind Hospital, would function in this regard. A controlled clinical trial of tube-shunt surgery compared to trabeculectomy is being conducted in the U.S. at this time.

Argon laser (or diode) trabeculoplasty was considered by the group to have too low a success rate to be considered for a primary program. However, it was noted that this treatment has a very low risk, could be implemented more easily than operative surgery, and does have modest success. Even a modest lowering of IOP over a large number of persons could have a measurable impact on blindness rates.

Eyedrops are less available in the developing world. Research should concentrate on producing longer acting drugs with a higher degree of IOP lowering. Devices or drugs that would be implantable or injectable to treat glaucoma once per year, such as was attempted with ethnacrynic acid into the anterior chamber would be future prospects.

Where cataract is common and where cataract surgical programs are being conducted, **combined cataract/glaucoma surgery could represent initial approaches to test methods and outcomes**. It is recognized that the success of combined cataract/glaucoma surgery may be lower than that of glaucoma surgery alone with respect to IOP control, but the combined surgery would be expected to eliminate the frequent progression of cataract after glaucom surgery alone, which would either

ruin the value of the procedure or necessitate a second procedure.

To carry out any therapy program, extensive education of physicians is needed in most parts of the world. The socioeconomic benefits and burdens of blindness from glaucoma should be estimated to evaluate the appropriate place of a therapy program in the region of interest. Cost recovery in a therapy program is a desirable goal.

WORKING GROUP 3: ANGLE-CLOSURE GLAUCOMA DIAGNOSIS
FACILITATORS: PAUL FOSTER, DAVID FRIEDMAN

Questions posed for discussion:

1. **What** diagnostic criteria can be defined from available examination findings? Is disc and field loss required or appropriate as part of diagnosis? What method of angle evaluation is the gold standard and what are its quantitative properties? Is there a role for instrumentation to measure biometric properties for diagnosis or screening? Are simple methods good enough (hand-light, van Herick)? How to include those who have had an acute attack but are not disc/field damaged?

2. **How** should the above definition be implemented, with what specific instruments and what exact criteria? What gonioscopic equipment or biometric device(s)? Should the disc and field change be equivalent to open-angle glaucoma?

3. **Who** should do the diagnostic maneuvers: lay person, eye nurse, non-eye M.D., Optometrist, Ophthalmologist ? What are the relative training requirements for the persons chosen for this. What personpower is presently in place to carry out the testing?

4. **Screening**: should it be done, and if so, how are its methods distinct from the methods of definitive examination?

5. **Cost estimates** should be attempted for the features of diagnostic techniques that are chosen.

Summary of Discussion:

The diagnosis of angle-closure glaucoma presents inherently more complex questions than that of open-angle disease, since the past literature on the subject has given a variety of approaches. In defining open-angle glaucoma, we have stressed the primacy of optic nerve damage as a defining feature. It is the consensus of this group that the same principle should be applied to angle-closure glaucoma. However, it is clear that groups of **persons who share features of angle-closure or the potential for angle-closure are identifiable prior to suffering optic nerve damage**, but they also merit therapy, including laser iridotomy, prior to the stage of nerve damage.

As a result, there are 4 major categories of those with some form of angle-closure who are to be accounted in this classification scheme, including those with **narrow angle, primary angle-closure, primary angle-closure glaucoma, and acute attack**.

Narrow angle is defined as a bilateral condition in which the gonioscopic view of the angle with a Goldmann-type lens shows no view of the posterior (pigmented) trabecular meshwork through three-fourths or more of the angle. The gonioscopy is conducted with the eye in the primary position and without any attempted indentation of the cornea artificially to deepen the angle. In order to be classified as narrow angle ONLY, the person must not have an abnormal IOP, optic disc, visual field, nor have peripheral anterior synechiae or other signs of past acute attacks (iris atrophy, iris

spiraling of vessels, or anterior lens opacity). As defined elsewhere in the meeting, abnormality in IOP and cup/disc is defined as exceeding the 97.5th percentile value for the population to which the person belongs. Visual field abnormality is defined by the Zeiss--Humphrey threshold findings in Working Group 1's criteria (outside normal limits Hemifield Test or PSD with probability <5%) or a field finding equivalent to this with another instrument that has been standardized against the Zeiss--Humphrey in the population of interest.

Primary angle closure is defined as a person with bilateral narrow angle (as above) AND at least one of the following:

- IOP above the 97.5th percentile for the population
- peripheral anterior synechiae (with width of at least 1/12th of the angle)
- signs of past acute attack (iris atrophy, spiraling, anterior lens opacity)
- cup/disc ratio exceeding 97.5th percentile for population, but normal visual field.

Primary angle closure glaucoma is defined as a person with bilateral narrow angle and optic nerve damage as defined above for open-angle glaucoma (meeting cup/disc criterion for >97.5th percentile AND presence of Zeiss--Humphrey equivalent visual field defect in at least one eye).

Acute attack is defined as bilateral narrow angle with an episode of documented IOP more than twice as high as the 97.5th percentile value for the population in one eye, often but not necessarily associated with symptoms that include ocular pain, decrease in habitual vision, and conjunctival redness. Persons may be classified in this group either due to the active presence of an attack at the time of examination, or from records documenting the features in the past.

A variety of discussion of these diagnostic choices occurred at the meeting. With respect to the definition of narrow angle (and indeed all the angle-closure groups), there is **no present acceptable substitute for gonioscopy**. Other surrogate measures were considered, such as optical and ultrasonic anterior chamber depth measurements, “van Herick” slit lamp estimation of the space between cornea and iris, and biometry with Scheimpflug photography and ultrasonic biomicroscopy. Publications are now appearing in which some of these are evaluated (see Alsbirk lecture above). Furthermore, it was recognized that the choice of “three-fourths” of the angle to be narrow is presently arbitrary, and one-half or all of the angle were discussed as alternatives. Nor is it known whether there is greater risk from narrowness of the upper compared to the lower angle. A meta-analysis of available information in the literature might be performed or new clinical research carried out to evaluate these issues.

The ultimate best choice for what constitutes a “narrow angle” must be determined by features that are associated with the later development of disease. **Longitudinal studies are needed** to determine this. Yet, few such studies have been performed. Alsbirk followed a population on Greenland for 10 and 20 years with detailed gonioscopic evaluation (see above).

There was discussion of the merits of Zeiss (Posner) gonioscopy, a 4-mirror lens with smaller diameter contact on the cornea that allows dynamic forward pressure to deepen artificially the angle as an investigation for peripheral anterior synechiae. This

method is thought not to be in common usage worldwide and is considered to be more difficult to teach and to utilize, though it is recognized to provide more complete information.

WORKING GROUP 4: ANGLE-CLOSURE GLAUCOMA TREATMENT
FACILITATORS: GORDON JOHNSON, STEVE SEAH

Questions posed for discussion

1. **Which** therapy is appropriate? Discuss indications for iridectomy. Discuss treatment beyond iridectomy for those not judged permanently cured by iris hole. How many persons are helped by iridectomy alone, compared to those with continued episodic IOP attacks that continue (plateau iris) and those with chronic, moderate abnormal IOP after iridectomy? How many present with asymptomatic chronic angle closure? Are the treatments beyond iridectomy similar to those considerations for open-angle glaucoma? Which lasers are best in various populations? Can newer technology impact the ease of performing laser iridectomy?

2. **Who** should carry out the treatments: lay person, eye nurse, non-eye M.D., Optometrist, Ophthalmologist ? What are the relative training requirements for the persons chosen for this. What personpower is presently in place?

3. **What outcome measures** should be used to judge the success of the therapy? Visual acuity, IOP, disc change, field progression, quality of life measure, avoidance of blindness.

4. **What complications** are likely from treatment and what is the acceptable level of risk compared to potential benefit? Deal with iridectomy separately from post-iridectomy treatments.

5. **Cost** estimates should be attempted for therapeutic interventions for sample populations. If not possible, the information needed to make such estimates should be specified.

Summary of Discussion:

Recommendations are made here, though the group recognized the lack of definitive information to support many of the conclusions. In addition, the group wished to distinguish between treatment in developed and in developing countries, as a matter of realistic approach. The diagnostic groups defined in the angle-closure working group 3 are assumed here.

In **developing countries**, those with **narrow angles** would not presently be treated. There is a need for controlled clinical trial of iridotomy to determine its risk/benefit ratio in this setting. For those with **primary angle closure**, iridotomy is recommended. For those with **primary angle closure glaucoma**, one of two courses is to be followed. If only one encounter with the subject is likely due to distance and limited resources, then trabeculectomy surgery with or without lens extraction is suggested. If follow-up evaluations can be arranged, then laser iridotomy followed by medical treatment is suggested where IOP remains elevated after the laser treatment. For **acute attacks**, local medical personnel in high risk populations should be trained in the use of acute therapy with acetazolamide pills and pilocarpine eyedrops and rapid referral to an ophthalmologist should be possible. Determination will be made based on the estimated chronicity of the attack whether iridotomy alone, trabeculectomy alone,

or combined trabeculectomy/cataract extraction is appropriate. The fellow eye of acute attack cases should have laser iridotomy.

In **developed countries**, those with **narrow angles** may be followed or treated with iridotomy. Colleagues in Japan feel that determining features for those at highest risk can be seen on ultrasonic biomicroscopy, though no prospective trials have been carried out. For those with **primary angle-closure** or **primary angle-closure glaucoma**, initial laser iridotomy is typically performed, and where target IOP is not met, further treatment is applied with eyedrops or trabeculectomy. **Acute attacks** are treated with iridotomy after IOP is brought down medically, then further treatment as indicated. It has been recently recognized that those with primary angle-closure glaucoma (with visual field loss at diagnosis) are quite likely to require continued treatment after iridotomy, with more than 60% requiring trabeculectomy.

Areas of the world in which primary angle-closure glaucoma is a particular problem include China, Thailand, and Inuit populations. Acute attacks have been estimated to have an incidence of 12.2 per 100,000 per year in Singapore among Chinese adults over 40 years of age.

The role of iridoplasty in management of acute attacks of angle-closure is not settled. **Among those who suffer angle-closure glaucoma, mechanisms of disease are certainly not fully understood**. The relative role of pupil block, plateau iris, and malignant glaucoma are not elucidated. Nor is the role of provocative testing in decision-making settled.

The group discussed whether the primary angle-closure glaucoma subject, once an iridotomy has been performed, is effectively identical to the person with open-angle glaucoma in terms of appropriate treatment choices. It is well-documented that the **blindness rate with angle-closure is greater than that in open-angle glaucoma**.

The type of laser for iridotomy was also discussed. The **overall most useful instrument is the neodymium:YAG laser**, which has the advantage that it can also be used for capsulotomy in programs of cataract surgical delivery. In some populations in Asia, it is common to use the argon laser as an initial step to thin the iris prior to penetrating with the neodymium:YAG. This is less practical in developing country settings. Field trials with the latter laser in Mongolia showed that it is typically possible to penetrate the thicker Asian iris, though a second treatment session and higher energy levels may be needed.

Technological discussions suggested that it may be possible to “pump” the crystal of a neodymium laser to increase its portability.

It is recognized that non-ophthalmologists could clearly be taught to perform iridotomy, though the preference of the group was that each program should be overseen by an ophthalmologist.

Outcome measures for iridotomy in the short-term are patency of the opening and for acute attacks the relief of high IOP. An intermediate outcome unique to angle-closure is the prevention of (additional) peripheral anterior synechiae. Although it is recognized that no study has documented this as an outcome, it is an ideal to be

achieved. Otherwise, the outcomes are shared with open-angle glaucoma (see above).

Known complications of iridotomy treatment include failure to make a hole, reclosure of the hole, damage to the cornea or lens, bleeding, IOP rise, and posterior synechiae. Aqueous humor dynamics are altered by iridotomy, which theoretically may produce long-term complications such as more rapid development of cataract.

A unique cost for angle-closure is the purchase of the laser to be used, estimated at present from$US15,000 to$60,000 (for the Ellex and the Zeiss lasers, respectively).

As an estimate of the magnitude of the angle closure problem in one population, Nolan estimates that among 2.2 million persons in Mongolia there are 36,000 persons with occludable angles meriting laser iridotomy (about 15% of the population over age 50).

WORKING GROUP 5: GLAUCOMA IN OVERALL EYECARE
FACILITATORS: NATHAN CONGDON, SERGE RESNIKOFF, LALIT DANDONA

Questions posed for discussion:

1. **What** are the synergistic and antagonistic features of including diagnostic and therapeutic programs for glaucoma in present eye health care programs? How will patients respond to preventive programs that do not improve vision (compare to other preventive programs, such as trachoma, onchocerciasis)? What economies of scale would be achievable by doing glaucoma surgery together with cataract surgery programs? What technologies are available and which must be provided? What training programs will be most useful to implementing a program?

Summary of Discussion:

First, the group defined a short-term approach to glaucoma by **identifying target areas of the world where glaucoma is of public health importance OR where existing resources will allow a broad-based program to begin immediately**. These include China, India, the Caribbean, and sub-Saharan Africa due to the estimated high rate of disease, and North America and Europe for their resources and high rate of trained specialists.

The group validated the **concept that glaucoma services should be integrated into a comprehensive eye care program**, not a program oriented toward a single disease entity. In the short-term, glaucoma care should be delivered to those who present for care, rather than attempting broad-based screening or population-wide programs. This is a recognition of the intermediate stage of diagnostic and therapeutic knowledge of glaucoma at this time.

Priority should be given to the most severely affected persons, with emphasis on those who are young or most likely to become blind in their lifetime.

Training of eye care specialists to recognize glaucoma and to learn that its treatment is worthwhile must be a high priority to reverse historical behaviors.

Social marketing of glaucoma therapy must be developed to allow the acceptance of a treatment that stabilizes vision but does not improve it. Pairing glaucoma surgery with cataract surgery programs will help in this regard.

Institution of a glaucoma program within the overall eyecare programs will be expected to have a variety of impacts on present eyecare services: need for better ancillary services (visual field testing), need for better record keeping, more instrumentation (tonometers, goniolenses, direct ophthalmoscopes, field machines), need for eyedrop medicines, increased operating room utilization, requirement of lasers for iridotomy, and more consumables in operating room.

Outcomes-based assessment of glaucoma treatments are critical.

A more **long-term approach** was also discussed, envisioned to involve

programs extending toward 2020. It was felt that major scientific breakthroughs in detection and treatment of disease would need to occur before population-based screening and mass glaucoma programs would begin. Until that time, the most prudent approach would be to **extend treatment to those in danger of signficant functional impairment during their lifetime**. A second direction would be to improve public awareness of the need for periodic eye examinations, with the actual implementation of such messages dependent upon local glaucoma prevalence and public health resources to respond to generated need. **Locally appropriate glaucoma services should be integrated into eye care programs in every region of the world**. There should be a diffusion of skills in detection of glaucoma to all medical doctors and to ancillary eye care personnel. Most importantly, all ophthalmologists worldwide should learn the basic skills of glaucoma detection and treatment during their training or in post-graduate programs in areas where past training has been insufficient.

A number of short-term and long-term needs or areas in which information is needed were identified to achieve the goals described. These included:

1) the need for breakthroughs to simplify the diagnosis of glaucoma or to produce a safe, permanent cure.

2) treatment trials are needed to evaluate present therapies in the many world contexts.

3) surveys of present eyecare programs should be conducted to determine how many affected by glaucoma are now presenting to and being treated at the centers of care in developing countries (e.g. Aravind, L.V. Prasad).

4) it would be interesting to determine what proportion of those with severe glaucoma are detected by the present systems of care in various settings.

5) better identification of which individuals are at risk for significant blindness from glaucoma, as well as improved outcome measures that account for the effect on quality of life.

6) what is the true risk of vision loss from glaucoma surgery itself ?

7) more natural history information is needed, particularly for those with narrow angles.

8) how effective can non-ophthalmologists be in glaucoma detection and treatment?

9) calculations of real costs of glaucoma detection and treatment to health care systems are needed.

10) what training strategies for glaucoma care are effective?

11) what is the role of rehabilitation services for glaucoma?

12) what should be the role and timing of public service messages for glaucoma?

13) the efficacy and cost-effectiveness of different monitoring and treatment strategies should be estimated.

A group of other observations were made by this group. First, they noted that the **rush to implement vertical cataract surgery programs, often working**

outside the existing eye care provision and training programs, and with insufficient regard to outcomes, should not be repeated as glaucoma care is added to the system.

Second, there is a need to put serious thought into training in all of its aspects, including subject matter, methods, trainers, and how to foster dedication into the provision of glaucoma services. The role of paramedical staff in developing countries may be the same or different from the paradigms now in place in developed settings.

Third, there is a need to develop new glaucoma advocates, including non-governmental organizations dedicated to its treatment. A program to be implemented should consider its role in international meetings, specialty societies, and training programs.

4. ATTACHMENTS

A. MEETING AGENDA

GLAUCOMA WORLDWIDE 2000
SATURDAY, MAY 6, 2000
ARNALL PATZ LECTURE HALL, WILMER INSTITUTE

8:00 AM	Introduction and Overview of Meeting Goals	Harry Quigley
8:05	Glaucoma:The World Health Organization Perspective	Serge Resnikoff
8:15	Developing World Problems in Ophthalmology	Alan Robin
8:30	Open Angle Glaucoma--What's Known and Unknown	James Tielsch
9:15	Angle Closure in Inuit and Asians. Oculometry, epidemiology and blindness prevention	Poul Helge Alsbirk
10:00	Assignment to Working Groups	
10:15	BREAK: Reception for Aziz Lecture	
10:45	Working Groups Begin Discussion	
12:30 PM	LUNCH	
2:00	Working Group Discussions continue	
5:00	ADJOURN	
7:00 PM	RECEPTION AND DINNER: American Visionary Art Museum	

Sunday, May 7

8:00 AM	Working Groups Present Summaries in Plenary Session
10:00	BREAK
10:30	Working Group Summaries continue
12:00	LUNCH
1:30	Action Plans Formalized
3:00	ADJOURN

B. THE DEFINITIONS OF GLAUCOMA

A Synopsis of Concepts Discussed at an ISGEO Meeting, Amsterdam, 1998
Summarized by Harry A. Quigley, MD

Glaucoma is estimated to be the second most prevalent cause of worldwide blindness, yet glaucoma was not included in the World Health Organization's *Vision 2020* initiative. This reflects the fact that effective glaucoma detection and management approaches at the population level have not been defined and tested. Currently, comparison among different studies of glaucoma is hindered by differing methods of examination and diagnostic criteria. In addressing this problem, we should re-examine our assumptions and use all relevant data to derive a definition system for prevalence surveys and clinical trials. This essay is a synopsis of a report generated at the International Society for Geographic and Epidemiologic Ophthalmology 2 years ago. All participants in the Worldwide Glaucoma meeting in Baltimore may benefit from thinking about these issues prior to the meeting. Some may have data relevant to these issues, which we urge you to examine and to bring along.

Glaucoma Definition

Definitions should separate those with established disease from those who do not have the disorder. They may also aid in identifying risk factors for the disease. And, they might be useful as a means to follow the progress of the disease, so that treatment effects can be measured and compared.

The suggested approach proposes that the loss of visual function denotes disease; hence, glaucoma is defined by the presence of measurable abnormality in the structure or function of the eye. As the American glaucomatologist Robert Shaffer once wrote, glaucoma patients don't care what the eye pressure is, they care if they can see. An alternative approach, in which disease can be present when only the risk of injury exists, may be appropriate in disorders, such as diabetes mellitus, where the risk factor (hyperglycemia) is easy to measure, but end-organ injury is more elusive. A comparable risk-only approach for glaucoma would define its presence by abnormal intraocular pressure. This is known to include as diseased many persons who would never suffer significant visual disability in their lifetime. Public health policies should direct limited resources to those genuinely in danger of blindness. Disease definitions should facilitate such determinations.

In the public health context, glaucoma is an optic neuropathy associated with a characteristic form of visual dysfunction and optic disc appearance. These may result from various pathological processes. This characterization differs from the more academic concept that there are many types of glaucomas with varying clinical features and etiologies. This presentation will differentiate between open-angle and angle-closure glaucoma, but in the initial discussion of how to classify glaucoma damage, the two are considered together.

Structural damage

Glaucomatous optic neuropathy differs from other causes of visual morbidity by its characteristic damage to the optic nerve head. The vertical cup/disc ratio is a simple, robust index of glaucomatous injury. However, it has several weaknesses as a defining feature for glaucoma. The size of the cup/disc ratio does not specifically identify glaucoma damage, since the size of the optic disc varies considerably among individuals, thereby causing a consequent variation in the cup/disc ratio. There is also a substantial variation in the number of axons in the optic nerve, with larger discs having more axons. In addition, the size of the disc and number of nerve fibers differ by ethnicity. Correction for variation in disc size when assessing the cup/disc ratio has been suggested, and both clinical and instrument-based methods for doing so are available. The ideal method is to use a system that records a digital or photographic image for expert or automated analysis. Some persons with small cup/disc ratios can, therefore, have glaucoma and some persons with large cup/disc ratios have no disease at all.

To define glaucoma using cup/disc ratio, one might first define the range of cup/disc ratio among persons with normal visual field testing in a population. This fails to classify individuals with visual dysfunction affecting the field test due to causes other than glaucoma, but this is probably an acceptable compromise. The choice of where to place the division between normal and abnormal cup/disc ratio must be initially arbitrary, as there is overlap between in the range of cup/disc ratios in those who do and do not have glaucoma. A useful statistical convention is that those whose chance of falling within the normal cup/disc ratio distribution is less than 0.05 could be considered damaged. Deviations could occur at both extremes of the distribution. Thus, those with cup/disc ratios higher than the 97.5th percentile are to be defined as abnormal and, therefore, glaucomatous.

The use of this approach must account for the differences in cup/disc ratio due both to methodological variation and to differences among persons of various ethnicities. Among European-derived groups, a cup/disc ratio $\geq$ 0.7 occurred in from 1-5% of persons not defined as having glaucoma. Cup/disc ratio values that exceed the normal range may be larger in African-derived persons. In 3 recent studies among Asian persons, the 97.5th percentile for cup/disc ratio was 0.7. Hence, for each ethnic group, the precise value that is defined as abnormal could be determined empirically and that value would be used as the group-specific criterion. Furthermore, the 97.5th percentile value for asymmetry of cup/disc ratio could be a second criterion of abnormality.

It might seem a significant disadvantage that the suggested method for defining abnormal cup/disc ratio would seemingly provide an upper limit on the prevalence of glaucoma (at 2.5% if the 97.5th percentile were used). This is not necessarily the case, since some persons would be defined as glaucoma without a disc exam (see below). In addition, there are few reported populations in which the adult prevalence of glaucoma is greater than 2.5%; thus, in practical terms, the apparent limitation may only rarely occur. Existing prevalence data could be examined to compare the glaucoma rates with this structural criterion compared to those used in the original study.

Functional damage

While the authors of many published studies of glaucoma state that subjects had visual field defects that are described as characteristic or typical, one often finds no clear criteria for such abnormality. Glaucomatous field loss has these features: 1) it respects the horizontal midline; 2) it is often focal (abnormal points cluster together); and 3) it is located in the mid-periphery. Due to variability in testing, one should validate defects by repeating the test to demonstrate reproducibility. The occurrence of a defect on repeat testing in a similar location is good evidence for its reliability as a sign of glaucoma damage.

The most commonly used instrument for field testing in developed countries is the Zeiss--Humphrey Field Analyser. With the 24-2 or 30-2 threshold programs, the following findings have been suggested as valid measures of glaucoma damage:

1. Glaucoma Hemifield Test (24-2) rating of "outside normal limits"
2. Pattern Standard Deviation index abnormal (probability <5%)
3. A cluster of 3 contiguous points abnormal at the 5% level.

An individual with field loss meeting one or more of the stated criteria in one eye could be defined as having glaucoma if the optic disc is compatible with glaucoma and the remainder of the examination provides no alternative explanation for the defect. An optic disc finding would be assumed to be compatible with glaucoma if it exceeded the 97.5th percentile value.

There will be studies and situations in which visual field tests other than the Humphrey (or Octopus) machines are used. It would be possible to define findings that are comparable to these standards by performing pilot studies in the population of interest. For these, tests with the two instruments could be compared (e.g. Humphrey versus Friedman, Hensen, Dicon, or FDT). The findings in the alternative system would then be referenced to the standard Humphrey findings to yield equivalent criteria for field loss.

Practical Considerations in Diagnosis

In every study, the clear criteria for defining glaucoma collide with practical limitations. Subjects can have media opacity that prevents a view of the cup/disc ratio. Other subjects fail to perform reliable field tests. How can one deal with the situations in which either disc or field information is unavailable? These can be some of the most severely affected persons, hence, those in most need of care. In the Kongwa Eye Study (Tanzania), these situations were handled by classifying glaucoma using three levels of definition, depending upon the amount of available information. Other investigations have used similar graded definitional structures.

The highest level of certainty included persons who met criteria similar to those described above for both optic disc and visual field findings. At a second level, for those in whom a visual field test was not performed, a severely damaged optic disc was sufficient. To increase the specificity for this determination, the cup/disc or its

asymmetry had to exceed the 99.5th percentile for the population. Finally, if neither the disc exam nor the field test was possible, a high level of IOP (> 99.5th percentile for the population) combined with severe acuity loss might be taken as sufficient for a diagnosis of glaucoma.

Intraocular pressure

Intraocular pressure is no longer used as a defining feature of open-angle glaucoma, since a substantial proportion of those with typical disc and field abnormality often or always have IOP in the normal range. However, IOP level is still potentially useful in classifying angle-closure glaucoma, secondary glaucoma, and in situations such as those described above as criteria of level 3, in which high pressure and severe visual loss coexist with media opacity (disc exam and field test impossible).

Specific Issues Related to Definition of Angle-Closure Glaucoma

There has been even less consensus on the definition of angle-closure glaucoma than for that of open-angle glaucoma. While an acute angle-closure attack is dramatic, persons suffering this event are a minority of those with this form of glaucoma in most population-based surveys, whether among European, African, and Asian persons. The chronic, asymptomatic form of angle-closure glaucoma represents 75% of those with the condition. In 8 major population-based studies of glaucoma, only 3 used optic disc and visual field abnormalities as diagnostic criteria. In all 8 studies, IOP above a certain level combined with gonioscopic abnormality was sufficient to define angle-closure glaucoma. Symptoms compatible with a past attack or signs of treatment for a past attack may or may not be sufficient for inclusion.

It is useful to distinguish between the mechanism by which IOP becomes elevated and the resultant damage that is caused by angle-closure glaucoma. Persons with significant trabecular meshwork closure on gonioscopy could be denoted as primary angle-closure. Those with primary angle-closure and glaucomatous damage would be defined as primary angle-closure glaucoma. Thus, primary angle-closure includes both asymptomatic persons with occludable angles who have not had an acute attack and those who have had an attack that was treated promptly but suffered no detectable nerve damage. Up to 75% of those with an acute episode of angle-closure recover without optic disc or visual field damage. In this approach, those with angle-closure and those with angle-closure glaucoma share a mechanical mechanism, but are considered separately.

The gonioscopic findings that define primary angle-closure have not been validated by prospective, longitudinal follow-up of suspects for this disease. Without such evidence, one is left with empirical choices for those findings that most likely represent high risk for the disease. Furthermore, gonioscopy has significant variability among observers, with various systems of codification and a recent attempt to quantify gonioscopic angle depth. One approach has been to use the Goldmann one-mirror lens and to define the inability to see the portion of the meshwork that is typically pigmented as abnormal. When this meshwork zone is not visible over more than one-

half of the angle, primary angle-closure is defined. Primary angle-closure is typically bilateral, so that this finding must be present in both eyes. More sophisticated gonioscopic evaluation with the Posner 4-mirror lens allows the observer to press the lens forward to differentiate between areas that are narrow and those that are permanently closed. Such dynamic gonioscopy is a powerful technique, but the ability to use it in prevalence surveys or general practice may preclude its advantages.

An additional factor is the response of eyes with narrow angles to dilation of the pupil. It is necessary to dilate eyes for full evaluation, whether in a prevalence survey or during clinical management. It is not therefore useful to question whether we should do provocative testing to confirm the diagnosis of primary angle-closure or primary angle-closure glaucoma—we are dilating these persons, and if we measure the IOP after dilation, we have additional information about them. The questions are: 1) do we dilate everyone or do we avoid dilating some persons ? and 2) what response to dilation is considered corroborative evidence of angle-closure (if any) ?

In a study in which gonioscopy is performed, there will be persons whose findings are considered typical of angle-closure and immediate iridotomy without dilation is carried out. Criteria are needed to determine who receives such immediate surgery. Furthermore, if a narrow angle eye is dilated and the IOP increases to a high level (e.g. 70 mm Hg), angle-closure has been demonstrated and iridotomy is indicated. But, criteria are needed for how to proceed when the increase is less than dramatic. These questions are amenable to controlled clinical study in appropriate settings.

Secondary Glaucoma

Up to 20% of those with glaucoma damage in several surveys have a second, contributing ocular or systemic disease. Both open-angle and angle-closure mechanisms are detected among these persons. While IOP is not a defining feature of primary open-angle glaucoma (except in level 3 diagnostic situations, above), it is the most important element in many secondary glaucoma eyes that have opaque media, precluding optic disc and visual field examinations. A higher proportion of these persons is affected unilaterally, compared to those with primary glaucoma.

Integrating Structure and Function into Practical Definition System

In considering the practical situations in which glaucoma will be diagnosed worldwide, uniform definitions are needed. But, we must recognize that they might not always be practical. In some settings, quantitative optic disc imaging or threshold visual field testing are too expensive or unavailable. To account for this, we might propose that examination techniques be divided into two levels, tentatively called Basic and Ideal Methods. The Basic Method would be used in those settings without the more expensive technology and greater professional input of the Ideal Method.

Basic Method

- Assessment of best-corrected visual acuity with an ETDRS chart
- Intraocular pressure measurement (Goldmann, Tonopen, or Schiotz)

- Hand-light evaluation of anterior chamber depth
- Cup/disc assessment (ophthalmologist, dilated, direct ophthalmoscopy)

Ideal Method

- Assessment of best-corrected visual acuity with an ETDRS chart
- Intraocular pressure measurement (Goldmann or Tonopen)
- Slit Lamp evaluation (ophthalmologist)
- Gonioscopy with Goldmann one-mirror lens (ophthalmologist)
- Cup/disc ratio assessment (ophthalmologist, dilated pupil & image taken)
- Visual field test (Humphrey or a field test standardized to the Humphrey)

The Basic Method would not permit use of some of the definitions proposed above. Since no visual field test is used, for example, the highest level of the definitions for open-angle glaucoma could not be satisfied. However, by using level 2 definitions (99.5th percentile denoting glaucomatous cup/disc abnormality), the Basic Method could still identify many of those with glaucoma.

What differences might there be in prevalence estimates using the Basic compared to the Ideal Methods? This could be evaluated, both with existing data sets from past surveys and in future studies that use the Ideal Method. For example, in data from Bangladesh, the prevalence without field testing would have been 1.6%, compared to 3.4% with fields included. It is likely that prevalence would be higher when fields are included, presumably consisting of milder cases. But, one might speculate that the more severe cases would still be included in the Basic system. This could still accomplish the goal of identifying those most at risk for blindness

Since many previous prevalence surveys have used Ideal Methods (or could be reinterpreted now with these criteria in mind), their findings could be reduced to Basic findings and the outcomes of Basic and Ideal approaches compared.

Summary

This discussion was intended as a point of departure for discussions to be conducted at the Worldwide Glaucoma meeting, May, 2000. The intention is to stimulate thinking by participants prior to the meeting and to provide a context for initiation of discussion of diagnosis and treatment issues for open-angle and angle-closure glaucoma. The aim should be to devise definitions that identify persons at significant risk for blindness to prevent visual disability. Definitions should group persons with respect to appropriate therapies that might avert blindness—e.g., laser for diabetes, IOL for cataract, iridotomy and IOP-lowering for glaucoma. Any definitional scheme is a process of successive approximation, dependent on present and future technology. Its usefulness will be validated by subsequent research to determine which aspects are reasonable and to replace those that fail to achieve the stated goals.

C. CONCLUSIONS AND RECOMMENDATIONS, 1993 JAMAICA CONFERENCE "GLAUCOMA IN THE DEVELOPING WORLD"

THE SITUATION

1. Glaucoma is rapidly becoming the second most prevalent cause of blindness in the world, with over 5 million estimated to be blind.

2. The proportionate and absolute increase in older persons and others at higher risk in the world population will accelerate the rate of glaucoma blindness.

3. The visual impairment due to glaucoma is understated by blindness statistics that utilize visual acuity alone--estimates including field loss are 7 million blind from glaucoma by the year 2000.

4. Glaucoma is disproportionately more prevalent in the developing world. Africans are much more likely to suffer open-angle glaucoma, while Chinese and other Asian persons are predisposed to angle-closure glaucoma.

5. Prevalence surveys show that the majority of those with glaucoma are presently undiagnosed, even in developed nations.

6. Treatments for glaucoma may face poor patient acceptance due to the lack of symptoms from the disease until late in its course, and due to the failure of therapy to improve vision.

SCREENING

1. Screening by one method alone is ineffective.

2. More effective screening might involve limitation to the highest risk or highest priority persons.

3. The most practical screening combination at present is tonometry (Schiotz or TonoPen) combined with direct ophthalmoscopy.

4. An alternative screening method to gonioscopy for angle closure glaucoma is needed.

5. Visual field tests should be utilized in glaucoma screening to improve sensitivity; however, faster and cheaper methods need development.

6. An algorithm was developed to categorize the risk of blindness in individuals to be selected for glaucoma therapy. This needs refinement and field testing.

THERAPY

1. The most appropriate primary therapy for open-angle glaucoma is trabeculectomy, not only in the developing, but perhaps in the developed world.

2. Trabeculectomy with releasable sutures and anti-fibrosis agents as adjuncts needs clinical trial as primary treatment.

3. Surgical instruments for cataract and glaucoma surgery are similar and the production of robust, inexpensive tools for both can be a part of a combined ocular surgery program.

4. The diode laser needs evaluation as a modality for iridotomy, trabeculoplasty, cilioablation, suturelysis, and retinal photocoagulation.

5. Pharmaceuticals for glaucoma are too expensive in developing countries; local production and lower import duties may be solutions.

6. Outcome assessment should be an integral part of any therapy program, with length of follow-up appropriate for glaucoma.

PROGRAM DESIGN

1. A role for non-ophthalmologists and optometrists in glaucoma diagnosis, medical or surgical treatment, or follow-up is potentially important.

2. Traditional customs and medical practices should be taken into account and incorporated into glaucoma management programs.

3. To generate action by governmental bodies, programs must document the social impact of glaucoma blindness as compared to all health priorities, and the proposed programs must be demonstrably effective.

4. Cost recovery and sustainability are important features.

5. Programs for glaucoma must incorporate screening, initial treatment, and follow-up.

6. National blindness prevention programs may be appropriate vehicles for administration of glaucoma programs.

7. Glaucoma programs must be incorporated into overall health and ocular disease programs for maximum efficiency. The initial implementation of a glaucoma treatment program might best be accomplished in sites where cataract surgery is already being carried out.

8. External program implementation should take account of the impact on local care givers, should gain their pre-approval and cooperation, and should assure the positive long-term impact on follow-up care by indigenous personnel.

9. An international, non-governmental organization to implement the program envisioned here is needed.

10. The expectations of the population to be served must be kept appropriate for a glaucoma program.

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