Japan Glaucoma Society
Guidelines for Glaucoma
(2nd Edition)
# Table of Contents

**Introduction** .................................................................................................................................................. 5

**Flow-charts**.................................................................................................................................................. 6

I. Examinations for glaucoma diagnosis ........................................................................................................ 6

II. Automated static perimetry ...................................................................................................................... 7

III. Treatment of primary open-angle glaucoma (broad definition): General principles ................. 8

IV. Treatment of primary open-angle glaucoma (broad definition): Target intraocular pressure .... 8

V. Treatment of primary open-angle glaucoma (broad definition): Medical treatment ............. 9

VI. Treatment of primary angle-closure/primary angle-closure glaucoma ........................................ 9

VII. Treatment of acute primary angle-closure/acute primary angle-closure glaucoma ............. 10

**Section 1. Definition of Glaucoma** ........................................................................................................... 11

**Section 2. Classification of Glaucoma** ..................................................................................................... 13

I. Primary glaucoma ....................................................................................................................................... 13

   1. Primary open-angle glaucoma (broad definition) ............................................................................ 13

   2. Primary angle-closure glaucoma ....................................................................................................... 15

   3. Mixed glaucoma ................................................................................................................................. 16

II. Secondary glaucoma ................................................................................................................................. 16

   1. Open angle mechanisms in secondary glaucoma ........................................................................ 17

   2. Angle closure mechanisms in secondary glaucoma .................................................................... 17

III. Developmental glaucoma ......................................................................................................................... 17

   1. Early onset developmental glaucoma ............................................................................................ 17

   2. Late onset developmental glaucoma ................................................................................................ 18

   3. Developmental glaucoma with other congenital anomalies ......................................................... 18

**Section 3. Examination of Glaucoma** ...................................................................................................... 19

I. History taking ........................................................................................................................................... 19

   1. Eye pain ........................................................................................................................................... 19

   2. Headache ........................................................................................................................................ 19

   3. Blurred vision ................................................................................................................................. 19

   4. Visual field defects ......................................................................................................................... 19

   5. Hyperemia ..................................................................................................................................... 19

II. Slit-lamp microscopy ............................................................................................................................... 19

   1. Keratoconjunctiva .......................................................................................................................... 19

   2. Anterior chamber ........................................................................................................................... 20
Section 4. Principles of Treatment for Glaucoma

I. Principles of glaucoma therapy
   1. The objective of therapy is to maintain the patient's visual function
   2. The most reliable method of treatment is reduction of intraocular pressure
   3. Causal therapy must be provided for all treatable causal factors
   4. Early detection is vital
   5. Achieving the maximum effect with the minimum required drugs
   6. Selecting among drugs, laser treatment, and surgery

II. Current status of treatment
   1. Baseline data determination
   2. Target intraocular pressure
   3. Glaucoma and QOL
   4. Compliance with glaucoma drug treatment

III. Glaucoma treatment agents
   1. Classification of glaucoma treatment agents
   2. Selection of drugs
   3. Therapeutical trial
   4. Points to be borne in mind in drug combination
5. Combined treatment.......................................................................................................................................................................................... 28
6. Guidance in administration.............................................................................................................................................................................. 28

IV. Laser surgery............................................................................................................................................................................................................................. 29
1. Laser iridotomy..................................................................................................................................................................................................... 29
2. Laser trabeculoplasty................................................................................................................................................................................................ 30
3. Laser gonioplasty (laser peripheral iridoplasty).............................................................................................................................................. 31
4. Cyclophotocoagulation.................................................................................................................................................................................................. 32
5. Laser suturelysis........................................................................................................................................................................................................... 32

V. Incisional surgery.............................................................................................................................................................................................................. 33
1. Indications..................................................................................................................................................................................................................... 33
2. Surgical techniques......................................................................................................................................................................................................... 33

Section 5. Treatment for Each Type of Glaucoma.............................................................................................................................................................................. 37

I. Primary glaucoma....................................................................................................................................................................................................... 37
1. Primary open-angle glaucoma.............................................................................................................................................................................. 37
2. Normal-tension glaucoma.................................................................................................................................................................................................. 38
3. Primary angle-closure glaucoma......................................................................................................................................................................... 39
4. Mixed glaucoma......................................................................................................................................................................................................... 41

II. Secondary glaucoma....................................................................................................................................................................................................... 41
1. Secondary open-angle glaucoma......................................................................................................................................................................... 41
2. Secondary angle-closure glaucoma......................................................................................................................................................................... 42

III. Developmental glaucoma.................................................................................................................................................................................................. 43
1. Early onset developmental glaucoma................................................................................................................................................................. 43
2. Developmental glaucoma accompanying with other congenital anomalies............................................................................................ 44

APPENDIX 1..................................................................................................................................................................................................................... 47
1. Glaucoma prevalence rate in Japan................................................................................................................................................................. 47
2. Van Herick method......................................................................................................................................................................................................... 47
3. Gonioscopic classifications.................................................................................................................................................................................................. 47
4. Criteria for glaucomatous visual field defects............................................................................................................................................... 47
5. Classification of glaucomatous visual field defects............................................................................................................................................... 48
6. Glaucoma treatment agents.................................................................................................................................................................................................. 49

APPENDIX 2..................................................................................................................................................................................................................... 55
1. Methods of observing the fundus oculi................................................................................................................................................................. 55
2. Observation points for the optic disc and retinal nerve fiber layer.......................................................................................................... 55
3. Significance of glaucoma diagnosis using computerized image analysis techniques.................................................................................... 60
Preface

Glaucoma, found in approximately 5.8% of persons aged 40 and older, is a disease that causes a severe impairment of visual function and leads to blindness if untreated. In today's aging society, glaucoma is the second-leading cause of acquired blindness, and the question of how to appropriately diagnose, treat, and manage the disease is of vital importance not only in maintaining patients' quality of life, but also in stemming the increasing burden on society imposed by the disease.

Rather than constituting a single clinical entity, glaucoma should be understood as a syndrome, and in order to diagnose, treat, and manage this illness, one must possess the expertise and discernment needed to consolidate intricate clinical findings, frequently over a lengthy disease course.

In light of this background, the Japan Glaucoma Society has prepared the present guideline as an aid to ophthalmologists in providing everyday medical care for glaucoma, including appropriate diagnosis and treatment.

In the present guideline, we have attempted to systematically present the proper standards for current glaucoma treatment. In preparing this guideline, however, it has not been our intent to impose limitations on physicians in diagnosing various clinical conditions. It is our hope that the present guideline will serve as a reference for improving the level of care and reducing discrepancies among the various types of treatment provided. On the other hand, it would be improper to place excessive importance on this guideline, as this would restrict the physician's flexibility to introduce future progress in treatments by limiting his or her individual responses to various clinical situations.

It is the hope of the authors that the present guideline will contribute toward raising the standard of glaucoma treatment in Japan.

November 2003

Yoshiaki Kitazawa, Chairman, Japan Glaucoma Society
Preface to the 2nd Edition

The First Edition of the Glaucoma Treatment Guideline was prepared in 2003 and was widely read not only by the members of the Japan Glaucoma Society, but via the Journal of Japanese Ophthalmological Society and the internet, it was also widely distributed to ophthalmologists in clinical practice. Moreover, an English edition of this Guideline was prepared and has also become well-known abroad as a guideline published in Japan.

It has been over 3 years since the first edition was prepared, and in this short period of time, there have been great strides in both glaucoma treatment and glaucoma research, and at the same time, the disease concept of glaucoma has been radically transformed. For this reason, the Japan Glaucoma Society has now prepared a second edition of the Glaucoma Treatment Guideline in order to reflect these changes.

The main changes are as follows:
1. Glaucoma has been defined as glaucomatous optic neuropathy.
2. The concept of primary angle-closure (PAC) has been incorporated, and this term has been translated into Japanese as genpatsu heisoku gukakusho [primary angle-closure].
3. Appendices have been prepared, and citations had been simplified.
4. A guideline for assessing changes in the glaucomatous optic disc and retinal nerve fiber layer has been added.

In conducting this revision, we have received considerable assistance from the Glaucoma Treatment Guideline Preparation Committee, the Chairman and members of the Japan Glaucoma Society, as well as Akira Kondo of the Society’s Secretariat. We would like to express our heartfelt thanks for their assistance.

It is our sincere hope that this guideline will continue to play an important role in glaucoma treatment.

March 2006

Haruki Abe, Chair, The Japan Glaucoma Society Guidelines for Glaucoma Committee
The Japan Glaucoma Society Guidelines for Glaucoma

Committee Members
Haruki Abe, MD, PhD, Chair
Yasuaki Kuwayama, MD, PhD
Motohiro Shirakashi, MD, PhD
Shiroaki Shirato, MD, PhD
Hidenobu Tanihara, MD, PhD
Goji Tomita, MD, PhD
Tetsuya Yamamoto, MD, PhD

Authors and assistant author of Japan Glaucoma Society Guidelines for Glaucoma

Authors:
Haruki Abe, MD, PhD, Chair
Yoshiaki Kitazawa, MD, PhD
Yasuaki Kuwayama, MD, PhD
Motohiro Shirakashi, MD, PhD
Shiroaki Shirato, MD, PhD
Hidenobu Tanihara, MD, PhD
Goji Tomita, MD, PhD
Tetsuya Yamamoto, MD, PhD

Assistant author:
Kiyoshi Yaoeda, MD, PhD

Reviewed and approved by Japan Glaucoma Society Board of Trustees (September 2006)
Glaucoma consistently ranks among the leading causes of blindness in Japan, and it is also an extremely serious illness from a social standpoint. In a detailed epidemiological survey of glaucoma conducted from 2000 to 2002 (the Tajimi Study), the prevalence rate for glaucoma in subjects 40 years of age and older was estimated at 5.0% (see Appendix 1 [1]). Moreover, as the rate of newly-discovered cases of glaucoma in the epidemiological study was 89%, this clearly demonstrates that there are numerous latent cases of the disease in this country that have not yet been treated.

Optic nerve damage and visual field damage caused by glaucoma are essentially progressive and irreversible. In glaucoma, as damage gradually proceeds unnoticed by the patient, early detection and treatment is of paramount importance in arresting or controlling the progress of damage.

In recent years, progress in the diagnosis and treatment of glaucoma has been remarkable, with numerous new diagnostic and therapeutic aids being introduced in the clinical setting, and the diagnosis and treatment of the disease has become multi-faceted. What has not changed, however, is the difficulty of selecting appropriate diagnostic and therapeutic measures for the individual patient, conducting early diagnosis and treatment, and ensuring long-term patient management in order to improve both quality of life (QOL) and quality of vision. Moreover, even with a variety of diagnostic and therapeutic options at one’s disposal, there is still a considerable number of patients in whom the progress of the disease cannot be arrested or slowed, and this remains a major problem.

In particular, with recent technological innovations, increasing attention has been focused on maintaining and increasing therapeutic standards, and there has been an increasingly pressing need in recent years for glaucoma treatment guidelines in order to improve the quality of therapy. Moreover, guidelines are also needed in order to improve communication between patients and caregivers, facilitate the selection of treatment options, provide relevant information to all parties concerned, and facilitate team medical care. In addition, as a social background, it is necessary to reduce health care expenses by efficiently utilizing resources from the standpoint of globalization of health care and medical economics. Therefore, the need for a guideline as a standard has been pointed out.

The Japan Glaucoma Association has therefore prepared the present Glaucoma Treatment Guideline in light of these circumstance. In this guideline, we first present flow charts illustrating the main points of glaucoma diagnosis and treatment, followed by explanations in five sections and appendices, with sections entitled “Definition of Glaucoma,” “Classification of Glaucoma,” “Examination of Glaucoma,” “Principles of Treatment for Glaucoma,” and “Treatment for Each Type of Glaucoma.” Additionally we present “Guideline for Detecting Glaucomatous Abnormalities in Optic Disc and Retinal Nerve Fiber Layer” in appendix. We hope that the present guideline will be widely applied and will prove useful as an aid in everyday glaucoma treatment.

Medical care is first and foremost at the discretion of the treating physician, and the physician must conduct the most appropriate diagnosis and treatment tailored to the individual patient. The Japan Glaucoma Association assumes no responsibility for any legal problems arising in connection with health care provided based on the present guideline.
I. Examinations for glaucoma diagnosis

- History taking
- Visual acuity and refraction tests
- Slit-lamp microscopy
- Tonometry
- Gonioscopy
- Ophthalmoscopy
- Perimetry
- Other tests

Comprehensive assessment of test findings

Type of glaucoma

Assessment of glaucomatous optic nerve and visual field damage

Stage of glaucoma
II. Automated static perimetry

Initial test

Screening test

Threshold test

Retesting

Test reliability

Low
Normal

Visual field assessment

Normal
Abnormal

During follow-up

Threshold test

Test reliability

Low
Normal

Retesting

Visual field assessment

Stable/improved
Deteriorated

* Kinetic perimetry (Goldmann perimeter)
† Perimetry using other perimeters
III. Treatment of primary open-angle glaucoma (broad definition*):
General principles

Baseline
<table>
<thead>
<tr>
<th>Stage of glaucoma</th>
<th>IOP without treatment</th>
<th>Other risk factors</th>
</tr>
</thead>
</table>

Establish target IOP

Initial treatment

Target IOP achieved

Continue treatment

Deterioration of optic nerve and/or visual field

Yes

No

Change treatment

Change target IOP

IOP=Intraocular pressure
*See Section 2.

IV. Treatment of primary open-angle glaucoma (broad definition*):
Target intraocular pressure

Higher

Target IOP

Lower

Early

High

(−)

Stage of glaucoma

IOP without treatment

Other risk factors

Late

Low

(+)
V. Treatment of primary open-angle glaucoma (broad definition*): Medical treatment

Initial monotherapy → Target IOP achieved

Yes → Multi-drug therapy → Target IOP achieved → Continue medical

No → Change monotherapy

Change medication → Laser treatment and/or surgery †

IOP= intraocular pressure

*See section 2; † See section 4.

VI. Treatment of primary angle-closure/primary angle-closure glaucoma

Mechanism of angle closure

Relative pupillary block

- Laser iridotomy
  - Successful
  - Unsuccessful or not possible → Peripheral iridectomy

Plateau iris

- Laser iridotomy
- Miotics
  - Laser gonioplasty

IOP control

- Favorable → Follow-up
- Unfavorable → Additional treatment to lower IOP (medical treatment and/or surgery)

IOP= intraocular pressure
VII. Treatment of acute primary angle-closure/acute primary angle-closure glaucoma

Medical treatment

- Lowering IOP
- Opening chamber angle
- Reducing inflammation

Laser iridotomy

- Successful
- Unsuccessful or not possible

Peripheral iridectomy

IOP control

- Favorable
- Unfavorable

Follow-up

Additional treatment to lower IOP (medical treatment and/or surgery)

IOP=Intraocular pressure
Glaucoma is a condition that involves distinctive changes in the optic nerve and visual field. It is marked by functional and structural abnormalities in the eye in which optic nerve damage can ordinarily be alleviated and inhibited by sufficiently reducing intraocular pressure (IOP).
Introduction

Glaucoma can be classified according to anterior chamber angle findings and the presence or absence of disease (states) causing elevated IOP and accompanying factors. Basically, the disease can be classified into primary glaucoma, in which there is no other cause of elevated IOP, secondary glaucoma, in which the elevation in IOP results from other ocular disease, systemic disease, or drug use, and developmental glaucoma, in which the elevation in IOP results from developmental anomalies in the anterior chamber angle occurring during the embryonic period. Primary glaucoma is divided into primary open-angle glaucoma (broad definition) (a disease concept that encompasses both conventional primary open-angle glaucoma and normal-tension glaucoma) and primary angle-closure glaucoma.

In establishing a treatment method for glaucoma, classification according to the mechanism of IOP elevation is useful. It should be borne in mind that in secondary glaucoma, the mechanism of this elevation is not uniform, but depends on the disease type and stage.

The primary functional and structural abnormality involved in glaucoma is glaucomatous optic neuropathy. In recent years, the approach of including the presence or absence of glaucomatous optic neuropathy in the classification of glaucoma and related diseases has become internationally accepted. In the present guideline, we adopt the glaucoma classification shown in Table 2-1 based on the above considerations.

I. Primary glaucoma

1. Primary open-angle glaucoma (broad definition)

Primary open-angle glaucoma (broad definition) is a disease concept including both conventional primary open-angle glaucoma (in the following, this will denote the conventional concept of primary open-angle glaucoma unless “broad definition” is specified) and normal-tension glaucoma. The risk of the development and progression of primary open-angle glaucoma (broad definition) increases with increasing IOP.

Moreover, there are differences in the vulnerability of the optic nerve to IOP, and because primary open-angle glaucoma and normal-tension glaucoma cannot be distinguished based on specified IOP values, the term primary open-angle glaucoma (broad definition) was developed as a concept encompassing both disease types. Primary open-angle glaucoma (broad definition) can be conveniently subdivided in the clinical setting into an ocular hypertension group (primary open-angle glaucoma) and a normal IOP group (normal-tension glaucoma). It was reported in the Tajimi Study that the IOP was 14.6 ± 2.7 mmHg and 14.5 ± 2.7 mmHg (mean ± standard deviation) in the right eye and in the left eye, respectively, in Japanese. Thus, the upper normal limit is 19.9-20.0 mmHg when we define normal IOP as mean value ± 2 standard deviations. Accordingly, dividing this disease in Japanese subjects into the two clinical disease types of primary open-angle glaucoma and normal-tension glaucoma, taking IOP of 20 mmHg as a boundary, appears to be fairly reasonable. Primary open-angle glaucoma (broad definition) is characterized by chronic progressive optic neuropathy in which the optic disc and retinal nerve fiber layer show particular morphological characteristics (thinning of the optic disc margin, retinal nerve fiber layer defects), and it is a disease type in which other illnesses and congenital anomalies are absent and in which gonioscopy shows a normal anterior chamber angle (although the presence of functional anomalies of the anterior chamber angle cannot be ruled out). This is accompanied by progressive retinal ganglion cell loss and corresponding visual field defects.

In cases of discrepancies between optic nerve findings and visual field findings, if the optic disc is found to show pallor relative to the degree of cupping, the visual field and optic nerve should be retested, and brain imaging studies should be conducted in order to detect intracranial diseases, etc. Moreover, among cases of primary open-angle glaucoma (broad definition), genetic variations in myocilin or optineurin gene may be detected.

1) Primary open-angle glaucoma

In this subtype of primary open-angle glaucoma
### Table 2-1: Classification of glaucoma

<table>
<thead>
<tr>
<th>I. Primary glaucoma</th>
<th>A. Secondary angle-closure glaucoma due to pupillary block</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Primary open-angle glaucoma (broad definition)</td>
<td>Secondary angle-closure glaucoma: posterior form with pupillary block</td>
</tr>
<tr>
<td>A. Primary open-angle glaucoma</td>
<td>Examples: Glaucoma due to lens swelling, glaucoma accompanying microphthalmia, glaucoma due to posterior synechiae, glaucoma due to lens subluxation, glaucoma secondary to epithelial ingrowth, etc.</td>
</tr>
<tr>
<td>B. Normal-tension glaucoma, normal-pressure glaucoma</td>
<td>B. Secondary angle-closure glaucoma due to anterior movement of tissue posterior to the lens</td>
</tr>
<tr>
<td>2. Primary angle-closure glaucoma</td>
<td>Secondary angle-closure glaucoma: posterior form without pupillary block</td>
</tr>
<tr>
<td>A. Primary angle-closure glaucoma</td>
<td>Examples: Malignant glaucoma, glaucoma secondary to retinal photocoagulation, glaucoma secondary to scleral buckling surgery, glaucoma due to intraocular tumors, glaucoma due to posterior scleritis/Harada disease, glaucoma due to central retinal vein occlusion, glaucoma due to intraocular filling materials, glaucoma due to massive vitreous hemorrhage, glaucoma due to retinopathy of prematurity, etc.</td>
</tr>
<tr>
<td>B. Plateau iris glaucoma</td>
<td>C. Secondary angle-closure glaucoma: anterior form</td>
</tr>
<tr>
<td>3. Mixed glaucoma</td>
<td>Examples: Glaucoma secondary to flat or shallow anterior chamber, glaucoma secondary to uveitis, glaucoma secondary to familial amyloid polyneuropathy, glaucoma secondary to vitreous surgery, glaucoma secondary to uveitis and lens-induced glaucoma, glaucoma due to cataract surgery, glaucoma secondary to corneal transplantation, glaucoma due to intraocular foreign bodies, glaucoma due to intraocular tumors, Schwartz syndrome, pigmentary glaucoma, etc.</td>
</tr>
<tr>
<td>II. Secondary glaucoma</td>
<td>D. Secondary angle-closure glaucoma due to aqueous hypersecretion</td>
</tr>
<tr>
<td>1. Secondary open-angle glaucoma</td>
<td>Secondary open-angle glaucoma: post trabecular form</td>
</tr>
<tr>
<td>A. Secondary open-angle glaucoma characterized primarily by aqueous outflow resistance between the trabecular meshwork and anterior chamber</td>
<td>Examples: Neovascular glaucoma, glaucoma secondary to heterochromic iridocyclitis, glaucoma secondary to epithelial ingrowth, etc.</td>
</tr>
<tr>
<td>Secondary open-angle glaucoma: pre trabecular form</td>
<td>B. Secondary open-angle glaucoma characterized primarily by aqueous outflow resistance in the trabecular meshwork</td>
</tr>
<tr>
<td>Examples: Neovascular glaucoma, glaucoma secondary to familial amyloid polyneuropathy, glaucoma secondary to uveitis, lens-induced glaucoma, traumatic glaucoma, glaucoma secondary to vitreous surgery, ghost cell glaucoma, glaucoma secondary to cataract surgery, glaucoma secondary to corneal transplantation, glaucoma due to intraocular foreign bodies, glaucoma due to intraocular tumors, Schwartz syndrome, pigmentary glaucoma, etc.</td>
<td></td>
</tr>
<tr>
<td>2. Secondary open-angle glaucoma</td>
<td>Secondary open-angle glaucoma: trabecular form</td>
</tr>
<tr>
<td>A. Secondary open-angle glaucoma characterized primarily by aqueous outflow resistance in the trabecular meshwork</td>
<td>Examples: Steroid glaucoma, exfoliation glaucoma, glaucoma accompanying familial amyloid polyneuropathy, glaucoma secondary to uveitis, lens-induced glaucoma, traumatic glaucoma, glaucoma secondary to vitreous surgery, ghost cell glaucoma, glaucoma secondary to cataract surgery, glaucoma secondary to corneal transplantation, glaucoma due to intraocular foreign bodies, glaucoma due to intraocular tumors, Schwartz syndrome, pigmentary glaucoma, etc.</td>
</tr>
<tr>
<td>B. Secondary open-angle glaucoma characterized primarily by aqueous outflow resistance posterior to Schlemm’s canal</td>
<td>Secondary open-angle glaucoma: post trabecular form</td>
</tr>
<tr>
<td>Examples: Glaucoma accompanying exophthalmos, glaucoma due to increased pressure in the superior vena cava, etc.</td>
<td>Examples: Glaucoma secondary to flat or shallow anterior chamber, glaucoma secondary to uveitis, glaucoma secondary to familial amyloid polyneuropathy, glaucoma secondary to vitreous surgery, ghost cell glaucoma, glaucoma secondary to cataract surgery, glaucoma secondary to corneal transplantation, neovascular glaucoma, ICE syndrome, glaucoma accompanying iridoschisis, etc.</td>
</tr>
<tr>
<td>C. Secondary open-angle glaucoma characterized primarily by aqueous outflow resistance posterior to Schlemm’s canal</td>
<td>D. Secondary open-angle glaucoma due to aqueous hypersecretion</td>
</tr>
<tr>
<td>Secondary open-angle glaucoma: hypersecretory form</td>
<td>Secondary open-angle glaucoma: hypoergic form</td>
</tr>
<tr>
<td>2. Secondary angle-closure glaucoma</td>
<td>1. Early onset developmental glaucoma</td>
</tr>
<tr>
<td></td>
<td>2. Late onset developmental glaucoma</td>
</tr>
<tr>
<td></td>
<td>3. Developmental glaucoma accompanying other congenital anomalies</td>
</tr>
<tr>
<td></td>
<td>Aniridia, Sturge-Weber syndrome, Axenfeld-Rieger syndrome, Peters’ anomaly, Marfan syndrome, Weill-Marchesani syndrome, homocystinuria, neurofibromatosis, congenital rubella syndrome, Pierre Robin syndrome, persistent hyperplastic primary vitreous, congenital microcornea, Lowe syndrome, Rubinstein-Taybi syndrome, Hallermann-Streiff syndrome, congenital ectropion uveae, etc.</td>
</tr>
</tbody>
</table>
IOP exceeds the statistically determined normal range during the progression of glaucomatous optic neuropathy, and abnormally elevated IOP is strongly suspected to play a role in this optic neuropathy. As IOP is known to be subject to diurnal and seasonal fluctuations, when IOP is only measured a few times, there will be many cases in which abnormal IOP values are not detected.

Note) Disease types in which the characteristic morphologic changes in the optic nerve and visual field anomalies are lacking, while there are common characteristics with primary open angle glaucoma from the standpoint of aqueous humor dynamics, such as IOP, are referred to as ocular hypertension. Some see this subtype as a preliminary stage of primary open-angle glaucoma, while others see it as a type in which the resistance of the optic nerve to IOP is strong. Background factors such as family history of glaucoma, vascular factors, age, race, and refraction are known to facilitate the progression from ocular hypertension to glaucoma. Moreover, some researchers feel that IOP may be evaluated as high because of central corneal thickness, at least in some patients.

2) Normal-tension glaucoma, normal-pressure glaucoma
In this subtype of primary open-angle glaucoma (broad definition), IOP constantly remains within the statistically determined normal range during the development and progression of glaucomatous optic neuropathy. However, this does not necessarily mean that abnormal IOP does not play a role in the development of optic neuropathy in normal-tension glaucoma. In many cases, moreover, as another etiological factor, findings indicate that factors independent of IOP (such as circulatory damage) may also play a role. As IOP is known to be subject to diurnal and seasonal fluctuations, it is often quite difficult to establish that it is always within the normal range, and tests such as diurnal fluctuation measurements are frequently necessary.

2. Primary angle-closure glaucoma
In primary angle-closure glaucoma, elevated IOP results from closure of the anterior chamber angle rather than any other factors. In primary angle-closure glaucoma, relative pupillary block and plateau iris are the main angle-closure mechanisms. As the primary mechanism of angle-closure is relative pupillary block in the majority of cases, primary angle-closure glaucoma can ordinarily be defined as identical to primary angle-closure glaucoma with relative pupillary block. Even in this narrow definition of primary angle-closure glaucoma, however, the plateau iris mechanism frequently plays a role. Primary angle-closure glaucoma due solely to the plateau iris mechanism is referred to as plateau iris glaucoma.

Narrow-angle eyes that develop angle closure but do not develop glaucoma are defined as primary angle-closure. This applies to cases in which the anterior chamber angle shows peripheral anterior synechiae, suggesting the mechanism of angle closure, but there is no elevation of IOP or glaucomatous optic neuropathy, and cases in which IOP is elevated due to the mechanism of angle closure, but glaucomatous optic neuropathy has not yet developed. Primary angle closure is a preliminary stage of primary angle-closure glaucoma, and if left untreated, it will progress to primary angle-closure glaucoma. In the current literature in Europe and the U.S., there are cases in which primary angle-closure is used in the meaning of primary angle-closure alone and cases in which it is used as an overall term encompassing primary angle-closure and primary angle-closure glaucoma, or in the meaning of pathology or mechanism of the anterior chamber angle causing both, so this term should be interpreted with caution. In the present guideline, in order to avoid ambiguity, it is recommended that the term primary angle-closure be used only to denote primary angle-closure alone.

Note) Narrow anterior chamber angle refers only to a state in which the anterior chamber angle is narrow and does not mean that the angle closure mechanism is present. As the condition of primary open-angle glaucoma accompanied by a narrow anterior chamber angle is possible, the term “narrow angle glaucoma” should not be used.
1) Primary angle-closure glaucoma with relative pupillary block

From a clinical standpoint, primary angle-closure glaucoma with relative pupillary block is subdivided into the acute type and the chronic type.

In the acute type, extensive closure of the anterior chamber angle causes elevation of IOP within a short period of time, resulting in the clinical symptoms typical of glaucoma attacks, and in the chronic type, as closure occurs gradually or intermittently, elevation of IOP is mild and gradual. Some researchers specify a subacute or intermittent category as an intermediate form between the acute and chronic types.

(1) Acute primary angle-closure glaucoma

This disorder is characterized by the signs of rapidly elevated IOP, frequently reaching 40-80 mmHg, decreased visual acuity, and weakened or absent light reflex. On slit-lamp microscopy, findings include corneal edema, shallow anterior chamber, iris bombe, moderate pupil dilation, conjunctival hyperemia, and ciliary injection, and gonioscopy shows extensive angle closure. Ophthalmoscopic examination may show symptoms such as papilledema, venous congestion, and disc hemorrhage. The contralateral eye has a narrow angle or closed angle. Subjective symptoms include decreased visual acuity, blurred vision, iridopsia, eye pain, headache, nausea, and vomiting. There are also cases in which subjective symptoms are less pronounced and some of these symptoms are absent.

After remission of acute attacks, there are cases in which the optic disc is pale in color or shows glaucomatous cupping. This means a definite diagnosis of acute primary angle-closure glaucoma. In cases in which alleviation occurs before optic neuropathy is developed because of treatment, etc., it is frequently difficult at the time of the attack to assess whether or not glaucomatous optic neuropathy is present. For this reason, cases in which optic neuropathy is not observed even after remission of the attack are referred to as acute primary angle-closure.

(2) Chronic primary angle-closure glaucoma

In this subtype of primary angle-closure glaucoma, subjects do not show and have no history of the signs or symptoms of the acute type.

In addition to a shallow anterior chamber and narrow anterior chamber angle or angle closure, the signs and symptoms are similar to those seen in primary open-angle glaucoma. IOP is not necessarily elevated.

2) Plateau iris glaucoma

The mechanism in which, as a result of morphological anomalies of the iris root, the anterior chamber angle closes due to pupillary dilation without iris block is referred to as the plateau iris mechanism. Glaucoma occurring due to the plateau iris mechanism is referred to as plateau iris glaucoma. Cases in which optic neuropathy is not observed even though angle closure occurs due to this mechanism are considered to be cases of plateau iris. Nevertheless, in primary angle-closure glaucoma, there are many cases in which there is a combination of the plateau iris mechanism and the pupillary block mechanism. In these cases, following laser iridotomy, despite flattening of the iris, the root of the iris takes on a specific configuration (the plateau iris configuration), and partial angle closure is seen as a result of pupillary dilation.

Note) In Europe and the U.S., glaucoma resulting from the plateau iris mechanism is referred to as plateau iris syndrome.

3. Mixed glaucoma

The term mixed glaucoma refers to cases in which primary open-angle glaucoma and primary angle-closure glaucoma appear in combination.

In making a diagnosis of mixed glaucoma, the possibility of chronic primary angle-closure glaucoma and primary open-angle glaucoma developed in eyes with a narrow anterior chamber angle must be borne in mind.

II. Secondary glaucoma

Secondary glaucoma is glaucoma in which elevated IOP is caused by other ocular diseases, systemic diseases, or drug use. The approach of defining secondary glaucoma only as cases in which glaucomatous optic neuropathy is present is an interpretation consistent with the definition
of glaucoma in the present guideline. It, howev-
er, is difficult to assess morphological changes
and functional changes due to glaucomatous
optic neuropathy in some of these cases because
of the presence of the underlying disease or oth-
er diseases. For this reason, as a step taken over
time, in accordance with the conventional inter-
pretation, cases showing secondary elevation of
IOP are included under secondary glaucoma.
Secondary glaucoma can be classified from sev-
eral standpoints, including etiology, mechanism
of IOP elevation, and means of treatment.
However, these classification methods have both
advantages and drawbacks. For example, in
classification according to etiology, it is difficult
to express the concept that neovascular glauco-
ma begins as open-angle glaucoma and then pro-
gresses while the mechanism of IOP elevation
changes, becoming angle-closure glaucoma.

In classification according to mechanism
of IOP elevation, as the approach used in this
guideline is considered highly useful as an aid in
determining etiology and optimum treatment
method, we have followed this approach here.
Caution is required because there may be cases
in which conditions having the same etiology
show differing mechanisms of IOP elevation,
and the mechanism of IOP elevation may change in
one and the same eye. In diagnosing secondary
glaucoma, gonioscopic examination is essential
in order to confirm the mechanism of IOP eleva-
tion.

1. Open angle mechanisms in secondary glauco-
ma
1) Characterized primarily by aqueous outflow
resistance between the trabecular meshwork
and anterior chamber
Abnormal aqueous outflow resistance occurs
due to fibrovascular membrane, the conjunctival
epithelium, etc.

2) Characterized primarily by aqueous outflow
resistance in the trabecular meshwork
Abnormal aqueous outflow resistance results
from pseudoxfoliative material, inflammatory
material, macrophages, iris pigment deposition,
etc.
3) Characterized primarily by aqueous outflow
resistance posterior to Schlemm’s canal
These are cases resulting from increased epis-
cleral venous pressure with accompanying eleva-
tion of IOP and increased pressure in the superior
vena cava.

4) Cases resulting from aqueous hypersecretion

2. Angle closure mechanisms in secondary glau-
coma
1) Cases due to pupillary block
Pupillary block is caused by factors such as
lens swelling, lens luxation, goniosynechiae, etc.

2) Cases due to anterior movement of tissue pos-
terior to the lens
Causes include anterior movement of the lens,
ciliary edema, etc.

3) Cases caused due to goniosynechiae without
pupillary block or anterior movement of tis-
sue posterior to the lens
These cases are unrelated to anterior chamber
depth, but are caused by peripheral anterior syn-
echiae.

Ⅲ. Developmental glaucoma

Glaucoma resulting from malformation of the
anterior chamber angle is treated in this guideline
not as congenital glaucoma but as developmental
glaucoma. Developmental glaucoma can be eas-
ily understood when classified into early onset
developmental glaucoma, in which morphologi-
cal anomalies are limited to the anterior chamber
angle, late onset developmental glaucoma, and
developmental glaucoma accompanying other
congenital anomalies. Early onset developmental
glaucoma is equivalent to what was formerly
named primary congenital glaucoma.

1. Early onset developmental glaucoma
In this disease type, congenital anomalies are
limited to the trabecular meshwork. Frequently,
however, this is combined with mild hypoplasia
resulting from developmental anomalies of the
iris. Moreover, pathologies such as increased
corneal diameter, conventionally referred to as
buphthalmos, and corneal opacity are also fre-
quent.

2. Late onset developmental glaucoma
   Such cases involve hereditary abnormalities in anterior chamber angle formation, but the onset is delayed because the abnormalities are minor.

3. Developmental glaucoma with other congenital anomalies
   This category encompasses a wide variety of conditions, including aniridia, Marfan syndrome, Axenfeld-Rieger syndrome, Peters' anomaly, Sturge-Weber syndrome, and neurofibroma.

References
Section 3

Examination of Glaucoma

1. History taking

The initial interview is of essential and fundamental importance in the treatment of glaucoma. A detailed interview is indispensable in diagnosing glaucoma and determining the proper course of management. In order to take into account the possibility of secondary glaucoma, in addition to taking a history for ocular trauma, inflammation, surgery, infection, etc., it is also important to determine the patient's history of systemic disease and medication. Moreover, it is also important to interview the patient concerning subjective symptoms, with symptoms such as blurred vision, irisopsia, eye pain, headache, and hyperemia indicating a possible history of acute glaucoma attacks. Moreover, it is also important to ask about the patient’s family history, and patients with a family history of glaucoma in particular should be asked about visual function damage in blood relatives. If information from other physicians is available concerning diagnosis and treatment with respect to IOP, the eye-grounds, or the visual field, such information should be used whenever possible.

1. Eye pain

In cases of markedly elevated IOP due to acute glaucoma attacks, etc., the patient will frequently experience sudden and severe eye pain. Generally speaking, the patient will experience severe eye pain when IOP rises markedly from a normal value to a high value. Eye pain may also be caused by factors such as irritation to the ciliary body resulting from corneal epithelial damage or uveitis.

2. Headache

In acute glaucoma attacks, accompanying sudden elevation of IOP, the patient may experience headache accompanied by nausea and vomiting, as well as symptoms such as reduced visual acuity, photophobia, and irisopsia.

3. Blurred vision

The patient may experience blurred vision in the event of secondary glaucoma resulting from corneal edema and uveitis accompanying a marked increase in IOP.

4. Visual field defects

In the initial stage of glaucoma, even in cases where anomalies have been detected by visual field testing, the patient frequently has no subjective symptoms of such anomalies. If a patient complains of visual field anomalies, this frequently means that optic nerve damage or visual field damage has already progressed to a considerable degree.

5. Hyperemia

Bulbar conjunctival hyperemia is experienced not only in acute glaucoma attacks, but also in various forms of secondary glaucoma such as glaucoma secondary to uveitis, neovascular glaucoma, and phacolytic glaucoma.

II. Slit-lamp microscopy

Slit-lamp microscopy is of fundamental importance in the treatment of glaucoma. In this examination, the conjunctivae, anterior chamber, iris, lens, etc., are observed, but an auxiliary lens may also be used in combination in order to observe the anterior chamber angle and ocular fundus.

1. Keratoconjunctiva

Corneal edema is observed in cases of markedly elevated IOP, such as acute glaucoma attacks, but it is also seen in secondary glaucoma accompanying corneal endothelial damage, such as iridocorneal endothelial (ICE) syndrome, in which IOP is within the normal range. Following laser treatment (particularly laser iridotomy) or surgery, the complication of bullous keratopathy may occur, and this possibility should be borne in mind. In early onset development glaucoma, ocular swelling accompanying elevated IOP may cause breaks in the Descemet membrane referred to as Haab’s striae, which appear as meandering raised lines on the corneal endothelium. In addition, pigmentation on the posterior corneal surface and spindle-like pigmentation (Krukenberg spindle) may be observed in glaucoma resulting from uveitis and in pigmentary glaucoma or pigment dispersion syndrome, respectively.
2. Anterior chamber

In diagnosis of primary angle-closure glaucoma, screening for shallow anterior chamber by slit-lamp microscopy is a simple and useful procedure. Japanese patients are known to show a higher frequency of shallow anterior chamber than Caucasians. In the van Herick method (see Appendix 1 [2]), the width of the anterior chamber angle is estimated by comparing corneal thickness and peripheral anterior chamber depth. In plateau iris syndrome, despite the fact that anterior chamber thickness is largely normal, as narrow anterior chamber angle and anterior chamber angle closure are observed, assessment of anterior chamber depth by a slit-lamp microscopy is not sufficient to diagnose this condition, and gonioscopy is therefore necessary.

3. Iris

Ordinarily, the iris is flat or bulges slightly in an anterior direction. In cases where the iris bulges markedly in an anterior direction, the presence of pupillary block is suspected. Abnormal findings in the iris include anterior synechiae to the iris and cornea or trabecular meshwork, posterior synechiae to the lens, neovascularization of the iris, iridial atrophy, and iridial nodules.

4. Lens

Abnormal lens findings associated with glaucoma include abnormal size or shape of the lens (lens swelling, spherophakia, etc.) and abnormal lens position (lens luxation, lens subluxation, etc.). Abnormalities of the ciliary zonule (congenital anomalies, trauma, exfoliative glaucoma, etc.) may play a role in abnormal positioning of the lens. Abnormal lens position and increased lens thickness due to the progression of cataracts may result in angle closure. In the case of mature or hypermature cataracts, the complications of accompanying outflow of lens material and phacolytic glaucoma may occur. Observation of the anterior surface of the lens is also important, and following laser iridotomy and peripheral iridectomy, posterior synechiae may occur. In exfoliative glaucoma, characteristic deposits of white matter are observed on the anterior surface of the lens and the pupillary margin.

III. Tonometry

1. Intraocular pressure

Results of studies conducted in large numbers of subjects have shown that the distribution of IOP is skewed towards higher values and does not show a fully normal distribution. Average normal IOP (± standard deviation) is in the area of 15.5 (± 2.6 mmHg), and the statistically determined upper limit value of normal IOP is approximately 21 mmHg. However, these values are based on the results of studies conducted on Western subjects. Looking at the distribution of IOP in the subjects of the Tajimi study, IOP in the right eye was 14.6 ± 2.7 mmHg (mean ± standard deviation), and in the left eye the figure was 14.5 ± 2.7 mmHg (same). Defining normal IOP as mean value ± 2 standard deviations, the upper normal limit is 19.9-20.2 mmHg. There are diurnal fluctuations in IOP, with this pressure frequently being higher in the morning, but the pattern varies among individuals. Furthermore, IOP also shows seasonal variations, with pressure being higher in the winter and lower in the summer. Factors playing a role in IOP include age, gender, refraction, race, posture, exercise, blood pressure, eyelid pressure, and ocular movement. Moreover, a variety of drugs may affect IOP.

2. Tonometers

As the Goldmann applanation tonometer is the most clinically accurate device, this tonometer is used on a standard basis in the diagnosis and treatment of glaucoma. The Goldmann applanation tonometer, unlike applanation tonometers such as the Schiötz tonometer, has the advantage that measurement values are not affected by ocular wall hardness. The Tono-Pen and the Perkins applanation tonometer are portable tonometers in which IOP measurements can be conducted with the patient seated or supine. Non-contact tonometers involve simple measurement procedures and should ordinarily be used only for screening purposes. It is known that the physical properties of the cornea have an effect on measurement values. For example, it is known that when the cornea is thin, IOP is measured low, and when it is thick, IOP is measured high. Accordingly, the physical characteristics of
the cornea must be taken into account in interpreting IOP values. In particular, this factor should be borne in mind in interpreting IOP measurement values taken following laser surgery, such as photorefractive keratectomy (PRK) and laser-assisted in situ keratomileusis (LASIK).

IV. Gonioscopy

1. Anterior chamber angle

Gonioscopy is indispensable in the treatment and diagnosis of glaucoma. In gonioscopy, it is important to properly recognize the various structures composing the anterior chamber angle, such as Schwalbe’s line, the trabecular meshwork, the scleral spur, and the ciliary band (see Appendix 1 [3] with respect to the method of recording anterior chamber angle). Pathological gonioscopic findings include ocular ischemic findings such as diabetic retinopathy, retinal vein occlusion, and internal carotid arterial occlusion, and neovascularization may also occur in the anterior chamber angle. From a physiological standpoint, neovascularization may be observed in the anterior chamber angle, with these blood vessels following a concentrical or radiating regular course. Pathological neovascularization involves an irregular curved course, with multiple bifurcations in many cases, and may also be accompanied by peripheral anterior synechiae. In the case of active uveitis, nodules may also be observed in the form of inflammatory exudates in the anterior chamber angle, and this may also be accompanied by peripheral anterior synechiae.

1) Schwalbe’s line

Schwalbe’s line is located in an area equivalent to the ending portion of the Descemet membrane and extends into the anterior chamber.

2) Trabecular meshwork

The trabecular meshwork and Schlemm’s canal are located between Schwalbe’s line and the scleral spur. From the center of the trabecular meshwork, the scleral spur side is equivalent to the functional trabecular meshwork and is observed as a pigment band. In diseases such as exfoliative glaucoma, pigmentary glaucoma, and pigment dispersion syndrome, a pronounced pigmentation is frequently observed on the trabecular meshwork. In exfoliative glaucoma in particular, marked wavy pigmention may be seen posterior to Schwalbe’s line, and these are referred to as Sampaolesi’s line.

3) Scleral spur

The scleral spur is observed as a white line between the ciliary band and the trabecular meshwork. Iridal protrusions are frequently seen on the surface thereof. In eyes with developmental glaucoma, the iris shows synechiae anterior to the scleral spur, and the scleral spur cannot be observed.

4) Ciliary band

The ciliary band is equivalent to the anterior surface of the ciliary body, and it is observed as a grayish-black band.

2. Gonioscopic observation methods

Gonioscopy may be conducted either directly or indirectly, and gonioscopes can be classified as either direct and indirect. An example of a direct gonioscope is the Koepe lens, and examples of indirect gonioscopes include the Goldmann gonioscope and the Zeiss 4-mirror gonioscope.

3. Compression gonioscopes

Compression gonioscopes are useful for distinguishing between a simple narrow anterior chamber angle or functional closure and organic closure due to peripheral anterior synechiae. In a compression gonioscope, the area in contact with the cornea is small and flat, and the anterior chamber angle is observed by lightly pressing against the center of the cornea and pressing down on the lens and iridial surface. In the case of eyes with a simple narrow anterior chamber or functional closure, this procedure widens the anterior chamber angle, and in the case of organic angle closure, the angle is not widened at the closure site. Compression gonioscopy is useful in accurately determining the pathology of angle-closure glaucoma.

4. Test equipment used in auxiliary diagnosis

Ultrasound biomicroscopy is a diagnostic
procedure that allows sectional observation of the microstructure of the anterior ocular tissue, including the anterior chamber angle, and this technique has been reported to be useful in the diagnosis of glaucoma.

V. Ophthalmoscopy

1. Optic disc and retinal nerve fiber layer

In diagnosing glaucoma, the detection of morphological changes in the optic disc or retinal nerve fiber layer is extremely important. Although pathologic findings of the optic disc or retinal nerve fiber layer are related to the disease stage of glaucoma, they are frequently detected prior to visual field anomalies. In normal-tension glaucoma in particular, the disease is frequently discovered when optic nerve damage is detected by ophthalmoscopic examination. Observation of optic nerve findings by ophthalmoscopic testing can be conducted by 1) ophthalmoscopy, 2) slit-lamp microscopy using an auxiliary lens, 3) funduscopic photography, and 4) non-red funduscopy. In the case of observation using an ophthalmoscope, a direct ophthalmoscope should be used. In ophthalmoscopic observation of the optic nerve, the recommended technique is stereoscopic examination, with three-dimensional observation of optic disc cupping, and the method of using a slit-lamp microscope and an auxiliary lens (non-contact lens or Goldmann 3-mirror gonioscope, etc.) is convenient and useful.

The above four methods of observing the fundus oculi are used as appropriate in order to evaluate whether or not there are glaucomatous changes in the optic disc and retinal nerve fiber layer.

For further details on this subject, please refer to Appendix 2, "Guideline for Detecting Glaucomatous Abnormalities in Optic Disc and Retinal Nerve Fiber Layer."

VI. Perimetry

1. Visual field

The normal visual field has an elongated elliptical shape, and with respect to the fixation point, it measures 60 degrees superiorly and medially, 70-75 degrees inferiorly, and 100-110 degrees temporally. The two means for measuring the visual field are dynamic and static measurement. Perimeters express the brightness of the target in units of apostils (asb). 1 asb is equivalent to 0.3183 candela/m² (0.1 millilambert).

2. Goldmann perimeter

The Goldmann perimeter is in standard international use. Its background luminance is set at 31.5 asb, and the distance between the target and the test eye is 30 cm. Target sizes are 0 (1/16 mm²), I (1/4 mm²), II (1 mm²), III (4 mm²), IV (16 mm²), and V (64 mm²), and target brightness ranges from 1a (12.5 asb) to 4e (1,000 asb). Measurements are ordinarily conducted using the settings of V/4e, I/4e, I/3e, I/2e, and I/1e. In dynamic visual field measurement using this perimeter, the technician moves the target along several isopters. Experienced technicians can obtain quite accurate results using this method.

3. Static visual field

Generally speaking, static visual field measurement is more sensitive in detecting visual field anomalies in the early stages of glaucoma than dynamic visual field measurement. The most commonly-used perimeters for this purpose are the Humphrey and Octopus perimeters. Static visual field sensitivity is expressed in decibels (1 decibel (dB) = 0.1 log Unit). In these static visual fields, precise measurements are mainly carried out within 30 degrees from the center. The measurement program consists of screening tests and threshold value tests. In detecting glaucoma, screening is useful, but threshold value tests are essential in observation over time. Measurement results are affected by factors such as blepharoptosis, refractive error, opacity of the intermediate transparent tissue, pupil diameter, and aging. Fixation status, frequency of occurrence of false-negatives and false-positives, and short-term fluctuations are useful indicators in evaluating the reliability of measurement results. The subject’s degree of experience is also important, with first-time test results generally being
less reliable than subsequent test results. Test results are expressed using threshold values, Gray scale (shades of grey of actual threshold values), total deviation (deviation from normal values according to age), and pattern deviation (deviation from the predicted normal visual field of the test subject).

4. Other visual field measurements
   It has been reported that techniques such as blue on yellow perimetry (SWAP), frequency doubling technology, and flicker perimetry are useful in the very early stages of glaucoma diagnosis.

5. Assessment criteria and severity classification for glaucomatous visual field abnormalities
   See Appendix 1 [4, 5]
Principles of Treatment for Glaucoma

I. Principles of glaucoma therapy

1. The objective of therapy is to maintain the patient's visual function
   The purpose of glaucoma therapy at the present time is to maintain the patient's visual function. Visual function damage severely impairs patients' QOL. However, in providing treatment, one must not only bear in mind possible adverse effects and complications of treatment, but also the social and economic burden imposed by hospital visits and/or hospitalization and the impairment to QOL caused by worry about blindness.

2. The most reliable method of treatment is reduction of intraocular pressure
   At present, based on the evidence, the only reliable treatment for glaucoma is to decrease IOP. Improvement of ocular blood flow and direct neuroprotection have attracted attention as new therapeutic methods involving factors other than IOP, and these may become innovative therapeutic options in the future.

3. Causal therapy must be provided for all treatable causal factors
   If it is possible to treat a causal factor in elevation of IOP, this factor must be treated in conjunction with therapy to reduce IOP. Types of causal therapy include iridotomy in types of glaucoma in which pupillary block causes elevation of IOP, such as primary angle-closure glaucoma, antiinflammatory treatment in glaucoma due to uveitis, retinal photocoagulation in neovascular glaucoma, and discontinuation of steroid administration in steroid glaucoma.

4. Early detection is vital
   At present, once visual function has been lost in glaucoma, there is no way to regain it. It is also known that in the late stages of glaucoma, the disease may continue to progress even when treatment is provided. Accordingly, early detection and treatment of glaucoma are of primary importance.

5. Achieving the maximum effect with the minimum required drugs
   There are many antiglaucoma drugs available, but the principle of drug treatment of the disease lies in obtaining the maximum effect with the minimum required drugs and the minimum adverse effects. For this reason, the mechanism of action, adverse effects, and contraindications of the drugs used must be understood. In addition, factors such as QOL, treatment costs, and compliance must also be taken into consideration.

II. Current status of treatment

As glaucoma follows a chronic course in the majority of cases, the treatments discussed here are used in primary open-angle glaucoma (broad definition), primary angle-closure glaucoma following iridotomy, chronic secondary glaucoma, etc.

1. Baseline data determination
   Patient status prior to treatment is important as a baseline. This baseline IOP will cause optic nerve damage, and this is thought to be a level at which damage will continue to progress. In assessing therapeutic effect as well, it is necessary to determine baseline IOP. Determining optic disc findings and visual field findings at the baseline is of major importance not only in determining the therapeutic approach, but in detecting the progression of damage at an early stage and rapidly revising and modifying treatment. Therefore, unless treatment must be begun urgently, such as in late-stage cases, it is preferable to determine baseline data such as IOP, optic disc findings,
and visual field findings before beginning treatment.

2. Target intraocular pressure

Although the final objective of glaucoma treatment is the maintenance of visual function, in view of the fact that optic nerve damage is irreversible and assessment of therapeutic effect takes long periods due to the gradual course of the illness, it is rational to treat glaucoma by setting an IOP at which it is expected to prevent further glaucomatous damage (target IOP) (see flow charts III-V).

1) Setting of target IOP

Although it is difficult to accurately assess in advance the IOP level at which further progression of optic nerve damage can be prevented, in beginning treatment, factors such as those shown in Table 4-1 are taken into account, and a target IOP should be established for each case (see Flowchart IV). Generally speaking, the later the stage of glaucoma, the easier it is for visual field damage to progress, and as any further damage may be a major effect on QOL, the target IOP should be low. Moreover, the lower the IOP level at the baseline, the lower the target IOP must be set. In addition, one must take into account various risk factors such as the patient’s age and life expectancy and the advantages and disadvantages of therapy, the condition of the contralateral eye, and the patient’s family history in order to set a target IOP tailored to the individual case.

Table 4-1: Factors to be considered in setting target intraocular pressure

- Glaucoma stage
- Intraocular pressure level prior to treatment
- Age/life expectancy
- Status of fellow eye
- Disease history
- Other risk factors

As an example of target IOP values, it has been proposed to set this pressure according to glaucoma stage at 19 mmHg or below for the early stage, 16 mmHg or below for the middle stage, and 14 mmHg or below for the late stage. Moreover, based on the results of various randomized comparative studies, it is recommended to set a target rate of decrease in IOP from the baseline, such as a 20% or 30% decrease.

2) Revision of target IOP

A limitation on a target IOP approach is the fact that the validity of the initially set value can only be assessed after certain period of time. In other words, the target IOP can only be confirmed to be appropriate when the progression of optic nerve damage is halted. The target IOP is not an absolute value; just as there are cases that progress even when the target IOP has been achieved, there are also cases that show no progression even though this target has not been achieved. Accordingly, the target IOP must periodically be evaluated and revised. For example, in cases where progression of visual field damage is occur, the target IOP must be revised downward. On the other hand, if treatment is found to cause adverse effects or influence QOL, one must evaluate whether or not it is necessary to maintain the target IOP. Moreover, in cases where long-term progression is not observed, one must reconsider whether or not the current target IOP is necessary. It must never be forgotten that the target IOP is merely a therapeutic means rather than a therapeutic objective. Accordingly, it is important not to adhere too strictly to a given target IOP.

3. Glaucoma and QOL

QOL is one of the most important factors for the patient. It goes without saying that damage to visual function due to glaucoma has an enormous effect on QOL, but there is the possibility that being diagnosed with an illness that is chronic and may lead to blindness, even when properly diagnosed and explained, may cause anxiety and fear in the patient and his or her family. Moreover, QOL may also be adversely affected by adverse effects or economic and time burdens imposed by treatment.

In order to preserve the patient’s QOL, we must consider not only treatment of the disease, but the effect that diagnosis and treatment have on the individual. The patient should be
questioned about his or her awareness of the current situation and course and what difficulties he or she is experiencing in everyday life. If treatment is impairing the patient’s QOL, we should discuss the possibility of discontinuing treatment with the patient.

4. Compliance with glaucoma drug treatment

Glaucoma is a chronic, progressive disease, requiring long-term administration of eye drops and periodic follow-up of the patient, and as there are no symptoms in many cases, it is essential to secure the patient's cooperation in order to achieve therapeutic success.

Compliance in glaucoma drug treatment has been reported to be far worse than physicians believe. Non-compliance is an important factor in the progression of glaucomatous visual field damage. Therefore, compliance issues must be taken into account when the type of treatment is selected, and when visual field deterioration is observed, compliance issues must be verified before changing medications.

Moreover, the following are vital in improving compliance: (1) providing thorough explanations of the disease, treatment, and adverse effects; (2) keeping treatment to a minimum; (3) tailoring treatment to the patient’s lifestyle; and (4) providing proper administration guidance.

III. Glaucoma treatment agents

1. Classification of glaucoma treatment agents (Table 4-2)

1) Sympathomimetics
   (1) Nonselective
   (2) α₂-selective

2) Sympatholytics
   (1) β-blockers
      i. Nonselective
      ii. β₁-selective
   (2) α-β-blockers
   (3) α₁-blockers

3) Parasympathomimetics

4) Prostaglandin analogues

5) Carbonic anhydrase inhibitors
   (1) Systemic
   (2) Topical

6) Hyperosmotics

2. Selection of drugs

   In primary open-angle glaucoma (broad definition), prostaglandin analogs and beta-blockers are used as first choice because of their outstanding IOP-lowering effects and favorable tolerability. However, in patients in whom the use of β-blockers and prostaglandin analogues is unsuitable because of adverse effects, eye drop preparations such as carbonic anhydrase inhibitors, α₁-blockers, nonselective sympathomimetics, and parasympathomimetics have been used as the drugs of choice.

3. Therapeutical trial

   There are individual differences in drug effect, and IOP also varies both day-to-day and diurnally. In introducing eye drop, one should begin with one eye only if possible and determine the IOP-lowering effect and adverse effects (one-eye trial), and then after the effect has been confirmed, begin administration in both eyes. In evaluating β-blockers, however, it should be borne in mind that these drugs also exert a slight IOP-lowering effect in the untreated fellow eye.

4. Points to be borne in mind in drug combination

   • In cases where the drug is not effective or not effective enough, or if tachyphylaxis occurs, change the initial therapy rather than adding an additional drug.
   • The additional drugs should be used only if the effect of monotherapy is insufficient.
   • Increasing the recommended dosage will not enhance, the IOP-lowering effect and will increase adverse effects.
   • Taking into account the IOP-lowering effect, adverse effects, and compliance, when three or more drugs are required, the option of using other therapeutic methods, such as laser therapy or invasive surgery, should be considered.
5. Combined treatment

When monotherapy with glaucoma treatment agents does not produce a sufficient effect, these agents may be combined with other drugs. Although combinations of β-adrenergic blockers and sympathomimetics or combinations of prostaglandin analogues, which increase the uveoscleral outflow, and pilocarpine, which decreases uveoscleral outflow, appear to be unsuitable either from a pharmacological standpoint or from the standpoint of lowering IOP, these combinations frequently do reduce IOP in actual use. The combined effect of such administration has been confirmed in actual trial use. However, drugs which belong to the same pharmacological group such as concomitant use of two beta-blockers or combined topical and oral carbonic anhydrase inhibitor should not be used in combination.

6. Guidance in administration

In order to increase efficacy by improving intraocular penetration, while minimizing adverse effects by reducing systemic absorption of eye drops, and also in order to improve compliance, it is important to guide patients in the proper administration method as follows.

- Wash hands prior to administration.
- Be careful not to allow the tip of the eye drop bottle to touch the eyelashes.
- Administration should be conducted one drop at a time.
- After administration, gently close the eye and compress the lacrimal sac.
- Wipe away any eye drops that have overflowed around the eye and wash off any
eye drops adhering to the hands.
• When multiple eye drop are used, the administration interval should be 5 minutes or longer.

### IV. Laser surgery

#### 1. Laser iridotomy

1) **Purpose**
   - To relieve pupillary block, equalize pressure differential between the anterior and posterior chambers, and open the anterior chamber angle.

2) **Indications**
   - This procedure is the first choice therapy in primary or secondary angle-closure glaucoma due to pupillary block. It may also be performed in patients with suspected plateau iris syndrome in order to eliminate the factor of pupillary block.

#### 3) Preoperative preparation

1. In order to stretch/tighten the iris and facilitate perforation, 1%-2% pilocarpine is instilled one hour before surgery.
2. In order to prevent postoperative elevation of IOP spike, apraclonidine is instilled one hour before and immediately after surgery.
3. If the cornea is edematous, drugs such as carbonic anhydrase inhibitors or hyperosmotics are administered to make the cornea transparent prior to surgery.
4. The procedure is carried out under topical anesthesia.

#### 4) Contact lens

Contact lenses such as the Abraham or Wise...
contact lens for iridotomy are used.

5) Technique/surgical site
A contact lens for iridotomy is used, and irradiation is conducted on the periphery of the iris on the superior temporal and superior nasal sides under the eyelid (in order to prevent monocular diplopia). However, a transparent site on the cornea is selected, taking care to avoid areas of arcus senilis.

6) Laser settings
(1) Nd-YAG laser iridotomy
1. As the plasma generation energy differs depending on the unit used, the energy must be selected according to the model used.
2. The beam is focused not on the surface of the iris, but on the stroma of the iris.
3. In order to prevent iridial hemorrhage, the planned penetration site is pre-irradiated using an argon laser, etc.

(2) Thermal laser iridotomy using an argon laser, etc.
1. Stage I (peripheral irradiation of the planned perforation site in order to stretch the iris)
   - Spot size: 200-500 μm
   - Power: 200 mW
   - Duration: 0.2 seconds
2. Stage II (perforation irradiation)
   - Spot size: 50 μm
   - Power: 1000 mW
   - Duration: 0.02 seconds

As the pigment rises up from the irradiation site like gun-smoke when perforation is achieved, further irradiation is carried out in order to expand the hole so that it will be sufficiently large to relieve the pupillary block (100-200 μm).

(3) Concomitant use of an argon laser/Nd-YAG laser
   After irradiation with a thermal laser such as an argon laser, a penetrating wound is made using an Nd-YAG laser. Compared to use of an argon laser alone, the total energy is low, and hemorrhaging is reduced compared to the use of an Nd-YAG laser alone, so this method is recommended.

7) Complications
The following complications may occur in laser iridotomy. Among these, bullous keratopathy is serious, and this complication has been reported to occur frequently in Japan. The occurrence of bullous keratopathy is thought to be related with factors such as the condition of the corneal endothelium and the total laser irradiation energy. One must be careful to determine the status of the corneal endothelium prior to surgery and to avoid excessive irradiation.

Corectopia
Anterior chamber hemorrhage
Corneal opacity
Bullous keratopathy
Postoperative keratopathy
Focal cataracts
Transient elevation of IOP
Posterior synechia
Late closure of the iridotomy
Unintended retinal irradiation

8) Postoperative management
(1) IOP is monitored for 1-3 hours after surgery in order to determine whether or not transient elevation has occurred.

(2) Carbonic anhydrase inhibitors or hyperosmotics are administered as needed.

(3) Postoperative inflammation is usually self-limiting, but depending on the extent of the inflammation, it may be necessary to administer topical steroids.

2. Laser trabeculoplasty
1) Purpose
The trabecular meshwork is irradiated with a laser in order to improve aqueous outflow.

2) Indications
Primary open-angle glaucoma (broad definition), exfoliation glaucoma, pigmentary glaucoma, primary angle-closure glaucoma following laser iridotomy, mixed glaucoma, etc.

However, it is known to be difficult to normalize IOP in eyes in which this pressure is 25 mmHg or above. Rather than a replacement for invasive surgery, IOP should be considered an adjunct to drug treatment. Moreover, the IOP-lowering effect of this procedure is known to
recede over time.

3) Preoperative preparation
   (1) In order to prevent postoperative IOP spike, topical apraclonidine is given one hour before and immediately after surgery.
   (2) The procedure is carried out under topical anesthesia.

4) Contact lens
   Gonioscopy lens

5) Technique/surgical site
   An argon laser, diode laser, etc., is used. Approximately 25 applications are placed per quadrant at uniform intervals along 90° to 180° of the trabecular pigment band. In selective laser trabeculoplasty (SLT) using a 532 nm Q switched frequency doubling YAG laser, laser burns placed on trabecular meshwork non-overlapping manner over 180° to 360°.

6) Laser settings (argon laser)
   Spot size: 50 μm
   Power: 400-800 mW (allows transient blanching without small bubbles formation)
   Duration: 0.1 seconds

7) Complications
   Anterior chamber hemorrhage
   Peripheral anterior synechia
   Postoperative iritis
   Transient IOP elevation

8) Postoperative management
   (1) IOP is monitored for 1-3 hours after surgery in order to determine whether or not transient elevation has occurred.
   (2) Carbonic anhydrase inhibitors or hyperosmotics are administered as needed.
   (3) Postoperative inflammation frequently resolves spontaneously, but depending on the extent of the inflammation, it may be necessary to administer topical steroids.

3. Laser gonioplasty (laser peripheral iridoplasty)
   1) Purpose
      To contract the periphery of the iris by laser thermal effect in order to open the anterior chamber angle.

2) Indications
   Performed in cases of plateau iris glaucoma, cases where laser iridotomy cannot be carried out due to corneal opacity in angle-closure due to pupillary block, cases of primary open-angle glaucoma (broad definition) with a narrow angle approach as a preparation step to laser trabeculoplasty, or in eyes following goniosynechiolysis in order to prevent postoperative recurrence of synchiae.
   However, this procedure is ineffective in sites where peripheral anterior synchiae has already developed. Moreover, in performing this procedure in glaucoma due to pupillary block, laser iridectomy should be performed as early as possible.

3) Preoperative preparation
   (1) In order to prevent postoperative IOP spike, topical apraclonidine is given one hour before and immediately after surgery.
   (2) The procedure is carried out under topical anesthesia.

4) Lens
   A gonioscope or contact lens for iridectomy is used.

5) Technique/surgical site
   Coagulation is carried out on the peripheral iris with a width of 1-2 rows over 180° or 360°, with approximately 15 applications per quadrant.

6) Laser settings
   Spot size: 200-500 μm
   Power: 200-400 mW
   Duration: 0.2-0.5 seconds

7) Complications
   Transient elevation of IOP
   Postoperative iritis
   Corectopia

8) Postoperative management
   (1) IOP is measured 1-3 hours after surgery in order to determine whether or not transient
elevation has occurred.
(2) Carbonic anhydrase inhibitors or hyperosmotics are administered as needed.
(3) Postoperative inflammation frequently resolves spontaneously, but depending on the extent of the inflammation, it may be necessary to administer topical steroids.

4. Cyclophotocoagulation
1) Purpose
   The cyclodestruction with a laser in order to suppress aqueous production and thereby reduce IOP.

2) Indications
   Indicated when other glaucoma surgery such as filtering surgery has failed, or feasible.
   As serious complications may occur, this procedure is to be considered a last resort for reducing IOP.
   May be carried out using approaches such as the transscleral, transpupillary, or transvitreal route.

3) Preoperative preparation
   Retrobulbar anesthesia is carried out.

4) Technique/surgical site (transscleral diode laser cyclophotocoagulation)
   A cyclophotocoagulation probe is placed 0.5-2.0 mm from the limbus and the ciliary body is coagulated, with 15-20 applications over 180º-270º of circumference in each session.

5) Laser settings (transscleral diode laser cyclophotocoagulation)
   Power: 2000 mW
   Duration: 2 seconds

6) Complications
   Pain
   Prolonged inflammation
   Reduced visual acuity, loss of light sense
   Sympathetic ophthalmia
   Phthisis bulbi

7) Postoperative management
   (1) Antiinflammatory analgesics are administered for pain relief.
   (2) Topical steroids are administered for postoperative inflammation.
   (3) Although one-time irradiation frequently causes elevation of IOP, multiple repeated irradiations will usually bring about IOP control.

5. Laser suturelysis
1) Purpose
   To enhance filtration following trabeculectomy.

2) Indications
   Cases in which aqueous filtration via the scleral flap following trabeculectomy is insufficient and it is assessed that filtration will not become excessive.

3) Preoperative preparation
   (1) During surgery, the scleral flap is sutured with nylon.
   (2) The procedure is carried out under topical anesthesia.

4) Lens
   Laser suturelysis lens.

5) Technique/surgical site
   Thermal laser (a red laser is preferred in order to prevent conjunctival burn). Slight pressure is applied to the conjunctiva using the laser suturelysis lens, and the beam is focused on the visualized suture thread.

6) Laser settings
   Spot size: 50 μm
   Power: 100-300 mW
   Duration: 0.1-0.2 seconds

7) Complications
   Conjunctival burn, perforation
   Over filtration

8) Postoperative management
   IOP and filtering bleb status are to be confirmed.
V. Incisional surgery

1. Indications

Generally speaking, incisional surgery is indicated in cases in which sufficient reduction of IOP cannot be achieved by other therapeutic means such as medical treatment or laser treatment, cases in which other appropriate means of treatment cannot be used because of adverse effects or non-compliance, and cases in which it is thought that sufficient reduction of IOP cannot be achieved by other therapeutic means. The indication for surgery must be made for each individual patient based on a comprehensive assessment of type of glaucoma, stage of glaucoma, the patient's disease awareness, compliance, and the patient's social background (Table 4-3).

Moreover, not only surgery, but all treatments must be carried out after thoroughly explaining to the patient the treatment method and symptoms/complications associated therewith and then obtaining his or her consent.

Table 4-3: Factors to be studied in determining indications for glaucoma surgery

<table>
<thead>
<tr>
<th>Factors to be studied</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Glaucoma status</td>
</tr>
<tr>
<td>Type of glaucoma</td>
</tr>
<tr>
<td>Stage of glaucoma</td>
</tr>
<tr>
<td>Intraocular pressure</td>
</tr>
<tr>
<td>Previous history surgery</td>
</tr>
<tr>
<td>● Prognosis for nonsurgical treatment</td>
</tr>
<tr>
<td>IOP-lowering efficacy of treatment</td>
</tr>
<tr>
<td>Adverse reactions, complications</td>
</tr>
<tr>
<td>Compliance</td>
</tr>
<tr>
<td>Prognosis for visual function</td>
</tr>
<tr>
<td>● Prognosis for surgical treatment</td>
</tr>
<tr>
<td>IOP-lowering efficacy of treatment</td>
</tr>
<tr>
<td>Surgical complications</td>
</tr>
<tr>
<td>Prognosis for visual function</td>
</tr>
<tr>
<td>● Factors on patient side</td>
</tr>
<tr>
<td>Social factors such as work and home environment</td>
</tr>
<tr>
<td>Awareness of disease</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Ophthalmologic disease other than glaucoma</td>
</tr>
<tr>
<td>General condition</td>
</tr>
</tbody>
</table>

2. Surgical techniques

The following is a summarized explanation of various surgical techniques used in glaucoma. In addition to these, new techniques such as viscocanalostomy are being tried out in some cases, but the results for these techniques have not yet been sufficiently studied. At the present time, the most widely used surgical technique for the majority of glaucoma types, beginning with primary open-angle glaucoma (broad definition) is trabeculectomy. However, in selecting the surgical technique to be used, one must first investigate factors such as the mechanism of effect of the various techniques, long-term results, complications, and the disease type, disease stage, and surgical history of the individual patient.

1) Filtrating surgery

In this surgery, a small hole is made in the corneal limbus in order to create a new aqueous outflow pathway between the anterior chamber and subconjunctival space. The most serious complication is late infection of the filtering bleb. Patients undergoing filtration surgery such as trabeculectomy should be given sufficient explanations concerning the risk of late infections.

(1) Full-thickness filtrating surgery

In this surgery, a small hole is made in the corneal limbus in order to create a new aqueous outflow pathway from the anterior chamber and subconjunctival space. Compared to filtrating surgery in which a scleral flap is prepared, such as trabeculectomy, it is difficult to control filtration volume, and complications such as a shallow anterior chamber are frequent, so this technique is currently indicated only in a few extremely refractory cases.

(2) Trabeculectomy

In this procedure, a scleral flap is prepared, the limbal tissue is incised under the scleral flap, and the scleral flap is then sutured in order to regulate filtration volume. This is currently the most common type of glaucoma surgery. In order to prevent scarring at the filtration site, antimetabolites have come to be used concomitantly, resulting in a marked improvement in trabeculectomy outcomes. Moreover, the introduction of laser suturelysis has made it possible to regulate IOP after surgery, thus decreasing complications due to excess filtration such as ocular hypotension. Although additional surgery and other treatments are required in some cases, long-term
IOP control is achieved in most cases.

(3) Nonpenetrating trabeculectomy

In this technique, a portion of the tissue is incised underneath the scleral flap to form an aqueous outflow pathway without penetration of the anterior chamber. Compared to trabeculectomy, this procedure has been reported to show few early postoperative complications and to show high postoperative IOP. Long-term results for the procedure have not yet been studied to a sufficient degree.

(4) Implantation surgery

In this procedure, an aqueous outflow pathway is created between the anterior chamber and the outside of the eye using a special implant. This procedure is used in patients in whom trabeculectomy with antimetabolites has been failed, patients with excessive conjunctival scaring due to previous ocular surgeries, patients with risk factors for a poor result with trabeculectomy, and patients in whom filtrating surgery is going to be technically difficult. The specialized implant is not approved in Japan.

2) Aqueous outflow pathway reconstruction surgery
(1) Trabeculotomy

In this procedure, a trabeculotome is inserted into Schlemm’s canal under the scleral flap and is rotated in the anterior chamber in order to incise the trabecular meshwork from outside so as to promote aqueous outflow via Schlemm’s canal.

(2) Goniosynechiolysis

In this procedure, goniosynechia in eyes with angle-closure glaucoma are lysed and aqueous outflow via the physiological pathway is promoted in order to reduce IOP. This procedure is more effective if carried out concurrently with cataract surgery.

(3) Goniotoomy

Under observation with a gonioscopic lens, a knife inserted via the cornea is used to incise the anterior chamber angle from the anterior chamber side. This procedure is indicated in developmental glaucoma.

3) Surgery to relieve pupillary block

(1) Peripheral iridectomy

This procedure is conducted in glaucomas caused by pupillary block, such as primary angle-closure glaucoma, in order to equalize the pressure difference between the anterior and posterior chambers by incising the periphery of the iris. With the increasingly widespread use of laser iridotomy, invasive peripheral iridectomy has become rare.

4) Cyclodestructive surgery

In this procedure, the ciliary body is coagulated by means of a cryocoagulation device or diathermy in order to reduce IOP by inhibiting aqueous production. This procedure has become largely obsolete since laser units came into use for this purpose. Because the procedure causes considerable pain and complications such as phthisis bulbi, it is indicated only in refractory cases where other treatments are ineffective.

References


Section 5

Treatment for Each Type of Glaucoma

Introduction

For effective treatment of glaucoma, building trust with patients is of prime importance in every aspect of treatment (including decision on treatment plan, change, initiation, and follow-up).

Benefits and adverse reactions (complications) of each treatment should be carefully considered in order to choose a method that provides benefits that outweigh the adverse effects on a patient’s visual function, systemic condition, and quality of life. Follow-up intervals may be shortened or extended depending on the individual patient’s IOP, and status of the optic nerve and visual field. They should not be based on a standardized schedule. Follow-up examination should include IOP measurement, visual field testing and optic nerve imaging. Optic nerve photography is also recommended.

I. Primary glaucoma

1. Primary open-angle glaucoma

The target IOP is determined based on the individual patient's disease stage and pathology (see Flow Chart IV, Section 4). However, the target IOP is merely a standard. Clinicians should not be satisfied or neglect treatment once the target IOP has been reached. Conversely, clinicians should avoid excessive treatment, worrying too much about IOP not reaching the target.

1) Medical treatment

(1) Medical treatment is the first choice for primary open-angle glaucoma.

(2) Medical treatment is initiated with topical ocular hypotensives as monotherapy. When the drug is ineffective, it is replaced by another drug. If IOP is not satisfactorily controlled by monotherapy, multi-drug therapy is used.

(3) For confirmation of IOP-lowering effect, if possible, the IOP of the treated eye should be compared to that of the fellow eye that is not given the drug. Or, diurnal variations in IOP at baseline and during follow-up are compared to determine stability of therapeutic effect.

2) Laser trabeculoplasty

(1) The advantage of laser trabeculoplasty is that although it is an invasive procedure it can be performed under topical anesthesia on an outpatient basis.

(2) The IOP-lowering effect tends to diminish over time, and is maintained in only 10-30% of patients at 10 years postoperatively.

(3) Who will respond to this procedure and who will not is unpredictable. In addition, the procedure may damage the trabecular tissue and reduce outflow facility over a prolonged period, and eventually elevate IOP. Therefore, laser trabeculoplasty should not be performed as an alternative when patients are not candidates for invasive surgery or refuse to undergo invasive surgery.

(4) When patients still maintain IOP higher than 25 mm Hg despite medical treatment, it is difficult to lower it by laser trabeculoplasty.

(5) Since some patients develop IOP elevation following laser irradiation, they should be monitored for IOP for several hours postoperatively. If IOP is found elevated, measures should be taken to lower it depending on the magnitude of elevation and status of the optic nerve and visual field.

(6) Pre- and postoperative instillation of an α2 adrenergic agonist (apraclonidine) is effective in preventing IOP elevation following laser irradiation. However, as this effect is not complete, IOP should be monitored for 1-3 hours after irradiation.

3) Incisional surgery (with postoperative medication if necessary)

(1) Filtering surgery (trabeculectomy with or without antimetabolites, nonpenetrating trabeculectomy)

(2) Reconstruction of the aqueous outflow pathway (trabeculotomy, viscocanalostomy, etc.)

(3) Drainage implant surgery

The most widely used surgical procedure at present is trabeculectomy.
The IOP level achieved by trabeculotomy is high teens with concomitant use of medical treatment and it is higher than that achieved by trabeculectomy. Nevertheless, trabeculotomy is advantageous because of fewer complications and no need of intraoperative antimetabolites.

Results of nonpenetrating trabeculectomy and viscocanalostomy have not yet been fully investigated. Results of many reports, however, indicate that the postoperative IOP of nonpenetrating trabeculectomy is higher than that obtained by trabeculectomy with antimetabolites.

In filtering surgery, the formation of filtering blebs in the inferior region is associated with an extremely high risk of postoperative infection. Therefore, drainage implant surgery is frequently indicated in many countries for patients whose upper optical field is unsuitable for filtering surgery. However, the drainage devices have not yet been approved in Japan as a medical device.

4) Cyclodestructive surgery

This procedure is rarely necessary for primary open-angle glaucoma. It greatly affects the globe structure and functions. Whether this surgery is indicated should be carefully determined.

4) Follow-up

Follow-up intervals may be shortened or extended depending on the individual patient’s IOP and status of the optic nerve and visual field, and should not be based on a standardized schedule. Even though the IOP is successfully controlled, IOP measurement and optic nerve examination should be conducted monthly or once every few months, and perimetry once or twice a year. Also, fundus photography once a year is useful for follow-up.

Patients who underwent filtering surgery should be informed of potential risks of filtering bleb infection and instructed to consult their ophthalmologist immediately in the event of any symptom that might indicate infection, such as hyperemia, ocular or orbital pain, tearing, or blurred vision.

Note) Ocular hypertension

Of patients with IOP above the statistically determined normal upper limit without abnormal findings of the optic nerve or visual field, only 1-2% progress to primary open-angle glaucoma annually. In a multicenter trial conducted in the U.S., patients with ocular hypertension of 24-32 mmHg were randomly assigned to a non-treatment group or a treatment group (treated with eye drops in order to reduce IOP to 24 mm Hg or lower) and followed for 5 years. The occurrence of visual field damage or optic nerve damage was significantly lower in the treatment group. The effect of treatment in patients with IOP lower than 24 mmHg was not investigated. Therefore, a modest increase in IOP is not sufficient reason for treatment, but treatment should be considered in patients with repeated IOPs in the upper twenties or with risk factors such as a family history of glaucoma (see Section 2). Follow-up interval varies from one to several months depending on the patient. For patients whose optic nerve and visual field are confirmed to be normal and without risk factors for progression to primary open-angle glaucoma, IOP measurement, optic nerve examination and perimetry can be conducted at 1-2 year intervals.

2. Normal-tension glaucoma

In a multicenter trial for normal-tension glaucoma (NTG) conducted in the U.S., the progression of visual field damage was significantly different between patients who were not treated and patients who were treated and achieved IOP reduction of 30% or more from baseline. Thus, lowering IOP has been shown to be effective treatment. However, it is not clear whether an IOP reduction of 30% or more is necessary. In this trial, more than half of the patients underwent filtering surgery to achieve this 30% reduction. In addition, progression of postoperative cataract impaired visual function. The IOP-lowering effect on patients whose IOP is at the normal average level (15 mm Hg) or lower has not been fully studied.

Treatment and follow-up are the same as in primary open-angle glaucoma. However, laser trabeculoplasty is less effective in NTG patients.

Improving optic nerve blood flow and protecting ganglion cells also may be effective treatment for NTG in addition to lowering IOP. Several
reports suggest that oral calcium antagonists are effective, but no large-scale multicenter trial or randomized clinical trial has been conducted to determine a clear therapeutic effect.

3. Primary angle-closure glaucoma

1) Primary angle-closure glaucoma with relative pupillary block

Whether the disease is chronic or acute, relieving pupillary block by iridotomy or iridectomy is the fundamental treatment and the first choice of treatment. Lens extraction is also effective, but lens extraction is controversial in cases with clear lens.

Hypotensive drugs are used to lower IOP that remains elevated even after relief of pupillary block (residual glaucoma), or to alleviate symptoms and signs of acute glaucoma attacks, as well as to facilitate laser iridotomy or iridectomy.

The fellow eye should receive a prophylactic iridotomy or iridectomy, if the chamber angle is narrow, since most primary angle closure glaucomas are bilateral.

(1) Acute primary angle-closure glaucoma

1. Medical treatment

A. Hyperosmotics

Hyperosmotics are the most effective drugs for alleviating severe elevation of IOP. Distributed in the extracellular fluid, hyperosmotics elevate blood osmotic pressure and cause the aqueous component of the intracellular fluid to migrate into the extracellular fluid. In the eye, vitreous fluid migrates to choroidal capillaries, causing a decrease in vitreous volume, resulting in IOP reduction. Because the volume of vitreous is decreased, the iris recedes, and the anterior chamber is deepened, which is effective during an acute attack of primary angle-closure glaucoma.

Intravenously administered hyperosmotics are the fastest-acting and most potent treatment in lowering IOP. However, a sudden systemic increase in the volume of extracellular fluid may increase the volume of circulating plasma and place a burden on the circulatory system; patients prone to heart failure or pulmonary congestion may develop pulmonary edema. Furthermore, the IOP-lowering effect of hyperosmotics is temporary, and repeated administration for achieving long-term IOP reduction will only aggravate the patient's systemic condition.

a. Intravenous administration

Mannitol: 20% mannitol solution is intravenously administered at the dose of 1.0-3.0 g/kg for 30-45 minutes. IOP reaches its lowest level after 60-90 minutes, and this effect persists for 4-6 hours. Since mannitol is excreted via the kidneys, patients with impaired renal function may develop acute renal failure because increased plasma osmolarity increases the volume of circulating plasma. Mannitol by its diuretic action may aggravate dehydration in patients already dehydrated due to vomiting during an attack of acute glaucoma.

Glyceol: Glyceol 300-500 mL is intravenously administered for 45-90 minutes. The lowest level of IOP is reached 30-135 minutes after initiation of intravenous administration. The effect persists for approximately 5 hours. Caution is required in administration to diabetic patients since Glyceol produces glucose during its metabolic process and it has energy of 637 kcal per liter.

b. Oral administration

Isosorbide: 70-140 mL of a 70% solution is administered daily in 2-3 divided doses.

Glycerin: 3 mL/kg of a 50% solution is administered once or twice daily.

B. Miosis

1% or 2% pilocarpine is instilled 2-3 times per hour.

When the pupillary sphincter is ischemic due to ocular hypertension and the light reflex is absent (sphincter paralysis), frequent administration of parasympathomimetics is ineffective. It does not make the pupil constrict. On the contrary, it displaces the ciliary body anteriorly and aggravates pupillary block. If a large volume of miotics is instilled, it can be absorbed systemically through the nose and cause systemic adverse effects. Therefore, topical administration of potent parasympathomimetics is not recommended.
C. Decrease of aqueous production
  a. Intravenous or oral administration of acetazolamide 10 mg/kg
  b. Topical β-adrenergic blockers
  c. Topical α-β-adrenergic blockers
d. Topical carbonic anhydrase inhibitors

D. Increase of aqueous outflow
  a. Topical prostaglandin analogues
  b. Topical α₁-adrenergic blockers
c. Topical α-β-adrenergic blockers

d. Topical carbonic anhydrase inhibitors

2. Surgical therapy
A. Laser iridotomy

When laser iridotomy is performed, the cornea must be sufficiently clear. Laser irradiation through an opaque cornea involves a high risk of bullous keratopathy. In patients with opaque cornea, laser irradiation should be avoided whenever possible, and surgical iridectomy should be considered as an alternative. Bullous keratopathy following laser iridectomy is common in patients with cornea guttata, diabetic patients, patients with a history of acute attack of primary angle-closure glaucoma, or patients whose corneal endothelial cell count is already decreased.

B. Surgical iridectomy

While surgical iridectomy is advantageous in patients with opaque cornea in whom laser irradiation is difficult, it is associated with the risks peculiar to intraocular surgery. In eyes with acute attacks of primary angle-closure glaucoma in particular, there is a risk of complications such as malignant glaucoma and choroidal hemorrhage, and IOP must be sufficiently lowered prior to surgery.

(2) Chronic primary angle-closure glaucoma

As is the case for acute primary angle-closure glaucoma, alleviation of pupillary block is the fundamental treatment. Persistent ocular hypertension following pupillary block alleviation (residual glaucoma) is treated by medication, laser or surgery, the same as in primary open-angle glaucoma.

A. Medical treatment

The following drugs may be used in combination as specified for primary open-angle glaucoma.

a. Prostaglandin analogues
b. β-adrenergic blockers
c. α-β-adrenergic blockers
d. α₁-adrenergic blockers
e. Parasympathomimetics
f. Carbonic anhydrase inhibitors

d. Surgical therapy

A. Laser iridotomy

This procedure can be performed in the area of the chamber angle where the peripheral anterior synechiae are absent. The IOP-lowering effect is rather weak. In eyes with narrow angle, peripheral anterior synechiae is likely to develop following irradiation.

b. Reconstruction of aqueous outflow pathways (goniosynechiolysis, trabeculotomy)

Goniosynechiolysis is indicated in cases of extensive peripheral anterior synechiae (e.g., involving over half of the anterior chamber angle). Trabeculotomy is usually performed in the area where the chamber angle is open, but can also be used as a technique to release the peripheral anterior synechiae. For both procedures, combined lens extraction (with or without intraocular lens implantation) increases the success rate of IOP control by preventing reformation of anterior synechiae through deepening the anterior chamber depth.

c. Trabeculectomy

This procedure is used when medical treatment has failed to achieve sufficient IOP control; when there is long-standing peripheral anterior synechiae; when poor visibility of the anterior chamber angle inhibits goniosynechiolysis; or when goniosynechiolysis or trabeculotomy is ineffective. Patients with narrow anterior chamber angle are likely to develop complications such as flat anterior chamber or malignant glaucoma.

Note) Primary angle closure

Because of the discrepancies in the frequency of narrow-angle eyes and primary angle-closure glaucoma, the surgical indication including laser iridotomy to eliminate the pupillary block mecha-
nism in cases with narrow-angle alone is controversial.

In primary angle-closure, i.e., in cases of narrow-angle eyes showing positive results in various types of provocative test, or eyes with peripheral anterior synchiae, surgery is indicated because the presence of the pupillary block mechanism is clear. In addition, in cases where periodic observation is impossible, cases in which the treatment cannot be immediately provided in acute attacks, subjects with a family history of primary angle-closure glaucoma, and cases of diseases of the fundus, such as diabetic retinopathy, in which frequent examination with mydriasis is needed, the surgery can be indicated. As the prophylactic treatment procedure for primary angle-closure, laser iridotomy should be selected rather than invasive surgical iridectomy. In cases with cataract, lens extraction can also be indicated as the procedure for eliminating pupillary block.

2) Plateau iris syndrome
(1) Medical treatment
Miotic drugs mechanically pull the peripheral iris toward the center, open the anterior chamber angle, and prevent the progression of angle closure. When administration of miotics alone does not lower IOP sufficiently, other drugs are used to decrease aqueous production or increase aqueous outflow, as is the case in chronic primary angle-closure glaucoma following relief of pupillary block.

(2) Surgical treatment
Laser gonioplasty (laser peripheral iridoplasty) shrinks the iris root to widen the distance between the iris root and the anterior chamber angle, although its long-term efficacy remains unclear. Iridectomy or laser iridotomy is only effective in plateau iris combined with pupillary block. In cases where cataract surgery is indicated, lens extraction may be useful to widen the anterior chamber angle.

4. Mixed glaucoma
A combination of primary open-angle glaucoma and primary angle-closure glaucoma is called mixed glaucoma. However, it is difficult to strictly distinguish mixed glaucoma from chronic primary angle-closure glaucoma or primary open-angle glaucoma occurring merely in eyes with narrow angle. In treating mixed glaucoma, relief of pupillary block is the primary consideration, as is the case for primary angle-closure glaucoma, after which treatment is given for primary open-angle glaucoma.

II. Secondary glaucoma

Treatment of secondary glaucoma is primarily directed to underlying diseases whenever possible. Since treatment of secondary glaucoma varies widely depending on the underlying condition, the mechanism of IOP elevation involved must be determined for appropriate selection of the treatment. Secondary glaucomas are roughly subdivided into open-angle glaucoma and angle-closure glaucoma. However, the distinction between the mechanisms of open-angle and angle-closure glaucoma is not always clear, depending on the underlying condition and its pathology. Gonioscopy is essential in assessing the mechanism of IOP elevation as well as in diagnosing the type of glaucoma.

The following are classifications of the principal mechanisms of IOP elevation and their underlying diseases, as well as their typical treatments.

1. Secondary open-angle glaucoma
1) Secondary open-angle glaucoma characterized primarily by aqueous outflow resistance between the trabecular meshwork and anterior chamber

Neovascular glaucoma, heterochromic iridocyclitis, epithelial ingrowth, etc.

(1) Medical treatment
Medical treatment is performed as specified for primary open-angle glaucoma. However, parasympathomimetics are often ineffective and may aggravate the condition by destroying the blood-aqueous barrier.

(2) Surgical treatment
Trabeculectomy (with or without antimetabolites) is performed. Laser trabeculoplasty is not only ineffective but harmful. The efficacy of nonpenetrating trabeculec-
tomy or surgical reconstruction of aqueous outflow pathways (trabeculotomy) has not been confirmed. Drainage implant surgery and cyclodestructive surgery are last resorts for lowering IOP. In neovascular glaucoma, retinal coagulation should be immediately performed by laser therapy or cryotherapy.

2) Secondary open-angle glaucoma characterized primarily by aqueous outflow resistance in the trabecular meshwork

Steroid glaucoma
(1) Discontinuation of steroids
(2) Topical and systemic administration of ocular hypotensives
(3) Trabeculotomy, trabeculectomy (with or without antimetabolites)
Efficacy of laser trabeculoplasty has not been confirmed. Drainage implant surgery and cyclodestructive surgery are last resorts for reducing IOP.

Exfoliation glaucoma
(1) Topical medication
(2) Laser trabeculoplasty often results in substantial IOP reduction
(3) Trabeculectomy (with or without antimetabolites), trabeculotomy
Drainage implant surgery and cyclodestructive surgery are last resorts for reducing IOP.

Inflammatory diseases (Posner-Schlossman syndrome, sarcoidosis, Behçet's disease, herpetic keratouveitis, bacterial/fungal endophthalmitis, etc.)
(1) Anti-inflammatory therapy
(2) Topical medication
(3) Trabeculectomy (with or without antimetabolites)

Phacolytic glaucoma
(1) Topical and systemic administration of ocular hypotensives
(2) Extraction of causative lens or lens fractions, instillation of anti-inflammatory drugs, and in some cases, vitrectomy
(3) Trabeculectomy (with or without antimetabolites)

Schwartz syndrome
(1) Topical and systemic administration of ocular hypotensives
(2) Repositioning detachment surgery
(3) Trabeculectomy (with or without antimetabolites)
Laser trabeculoplasty is ineffective. Efficacy of trabeculotomy has not been confirmed. Drainage implant surgery and cyclodestructive surgery are used as last resorts.

Pigmentary glaucoma or pigment dispersion syndrome
(1) Topical medication
Mydriatics may cause pigment dispersion and aggravate aqueous outflow.
(2) Laser trabeculoplasty
Since pigment deposition on the trabecular meshwork is extensive, the laser power should be lower than usual. IOP response fluctuates greatly.
(3) Trabeculectomy (with or without antimetabolites)
(4) Laser iridotomy, lens extraction
In cases of reverse pupillary block, these procedures may reduce pigment dispersion due to contact between the iris and the lens and prevent irreversible trabecular damage.

3) Secondary open-angle glaucoma characterized primarily by aqueous outflow resistance posterior to Schlemm's canal

Exophthalmos due to thyroid ophthalmopathy, elevated venous pressure due to carotid arteriovenous fistulae, etc
(1) Treatment of underlying diseases
(2) Administration of topical and systemic ocular hypotensives
(3) Surgical treatment tailored to the individual patient

2. Secondary angle-closure glaucoma
1) Secondary angle-closure glaucoma with pupillary block

Lens intumescence, microphthalmia, posterior synechia, lens dislocation, epithelial ingrowth, etc.
Treatment must be selected based on the mechanisms causing pupillary block.
(1) Administration of topical and systemic ocu-
lar hypotensives  
(2) Laser iridotomy  
(3) Lens extraction, vitrectomy  
(4) Discontinuation of miotics in cases of miotic-induced pupillary block

2) Secondary angle-closure glaucoma due to anterior movement of intraocular tissue posterior to the lens

Glaucome due to anterior protrusion of the ciliary body or shifting of the iris/lens (vitreous body) diaphragm: malignant glaucoma, post-retinal photocoagulation, post-scleral buckling, posterior scleritis, Harada disease, central retinal vein occlusion, etc.

(1) Miotics are contraindicated, as they promote anterior protrusion of the ciliary body  
(2) Pupillary dilation and ciliary relaxation with atropine eye drops  
(3) Systemic administration of hyperosmotics, and topical and systemic administration of ocular hypotensives  
(4) Laser or surgical anterior hyaloidotomy and capsulotomy in pseudophakic or aphakic eyes  
(5) Vitrectomy combined with anterior hyaloidotomy (in phakic eyes sometimes combined with lens extraction)

Glaucome due to intraocular space-occupying lesions: intraocular tumors, cysts, intraocular tamponade (gas, silicone, etc.), intraocular hemorrhage (choroidal hemorrhage), etc.

(1) Topical and systemic administration of ocular hypotensives  
(2) Laser ablation of cyst or surgical cystectomy  
(3) Excision of intraocular tumor  
(4) Removal of tamponade materials  
(5) Removal of intraocular hemorrhage

3) Secondary angle-closure glaucoma due to goniosynechia without pupillary block or movement of the lens-iris diaphragm (glaucome due to peripheral anterior synechia)

Persistent flat or shallow anterior chamber, inflammatory disease, post-corneal transplantation, neovascular glaucoma, ICE syndrome, posterior polymorphous corneal dystrophy, iridoschisis, etc.

(1) Medical treatment  
(2) Trabeculectomy (with or without antimetabolites)  
  Drainage implant surgery and cyclodestructive surgery are last resorts to reduce IOP.
  For peripheral anterior synechia due to persistent flat or shallow anterior chamber, lens extraction and goniosynechiolysis might be effective in some cases.  
(3) For neovascular glaucoma, retinal coagulation with laser or cryotherapy should be performed whenever possible.

III. Developmental glaucoma

1. Early onset developmental glaucoma

Surgery is the first line of therapy for early-onset developmental glaucoma for the following reasons: 1) Since this type of glaucoma results from abnormal anatomical development of the anterior chamber angle, anatomical or surgical correction is recommended. 2) Our experience shows the effectiveness of surgery. 3) It is difficult to determine the effectiveness of medical therapy in infants and children because the procedure is complicated and may require anesthesia. Medical treatment is used as an auxiliary means the following types of surgery.

1) Surgical treatment

(1) Goniotomy

This procedure is indicated in patients with transparent cornea. In a single goniotomy procedure, an incision of 90-120 degrees can be made. An additive effect is frequently seen with up to three repeated surgeries. The decision as to whether to perform goniotomy or trabeculotomy is based on the experience of the surgeon.

(2) Trabeculotomy

An advantage of this procedure is that unlike goniotomy, surgery can be performed in cases with hazy cornea. However, the conjunctival flap and scleral flap made for this procedure may inhibit
filtering surgery when it is necessary in the future. In eyes with megalocornea, it may be difficult to identify Schlemm's canal in some cases and extensive surgical experience is required for performing trabeculotomy.

(3) Filtrating surgery
This procedure is indicated in eyes for which goniotomy or trabeculotomy is ineffective. In patients with early-onset developmental glaucoma, the sclera is thin which makes it difficult to prepare a scleral flap, and anatomical anomalies of the iris and ciliary body are common. The decision to perform this procedure must be made carefully because in infants and children, filtering bleb formation may be difficult despite intraoperative use of antimetabolites. Even after filtering blebs are successfully formed, the patients may be exposed to the risk of post-surgical infections for the rest of their life because of the presence of the filtering bleb.

(4) Drainage implant surgery
(5) Cyclodestructive surgery

2) Medical treatment
Drugs may be combined as specified for primary open-angle glaucoma. However, since in infants and children, the dose of the drug administered, even a topical drug, can be great in quantity with respect to body weight and body surface area, administration should begin with the lowest possible dose. Clinicians must be aware that the safety and effectiveness of any drug in infants and children have not been established.

2. Developmental glaucoma accompanying with other congenital anomalies


Glaucoma is associated with the above diseases, although the probability of its incidence has not been fully studied. Since the age of onset varies widely from birth to adulthood and mechanisms of IOP elevation differ, treatment methods are not uniform. As a rule, for infantile onset, the first-choice treatment is surgery as specified for early-onset developmental glaucoma, while for later pediatric onset, medical treatment is the first choice.
1. Glaucoma prevalence rate in Japan

<table>
<thead>
<tr>
<th>Disease type</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary open-angle glaucoma (broad definition)</td>
<td>4.1 (3.0−5.2)</td>
<td>3.7 (2.8−4.6)</td>
<td>3.9 (3.2−4.6)</td>
</tr>
<tr>
<td>Primary open-angle glaucoma</td>
<td>0.3 (0.0−0.7)</td>
<td>0.2 (0.0−0.5)</td>
<td>0.3 (0.1−0.5)</td>
</tr>
<tr>
<td>Normal-tension glaucoma</td>
<td>3.7 (2.7−4.8)</td>
<td>3.5 (2.6−4.4)</td>
<td>3.6 (2.9−4.3)</td>
</tr>
<tr>
<td>Primary angle-closure glaucoma</td>
<td>0.3 (0.0−0.7)</td>
<td>0.9 (0.5−1.3)</td>
<td>0.6 (0.4−0.9)</td>
</tr>
<tr>
<td>Secondary glaucoma</td>
<td>0.6 (0.2−1.0)</td>
<td>0.4 (0.1−0.7)</td>
<td>0.5 (0.2−0.7)</td>
</tr>
<tr>
<td>Early onset developmental glaucoma</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total glaucoma</td>
<td>5.0 (3.9−6.2)</td>
<td>5.0 (4.0−6.0)</td>
<td>5.0 (4.2−5.8)</td>
</tr>
</tbody>
</table>

Prevalence rate (95% confidence interval). Data for subjects 40 years of age or older in Tajimi study.

References


2. Van Herick method

Taking the angle between the slit light beam of the slit-lamp microscope and the observation system as 60 degrees, the slit light beam is positioned vertically with respect to the corneal limbus, and peripheral anterior chamber depth and corneal thickness are compared in order to estimate the width of the corneal angle.

Grade 1: Anterior chamber depth is less than 1/4 of corneal thickness
Grade 2: Anterior chamber depth is 1/4 of corneal thickness
Grade 3: Anterior chamber depth is 1/4-1/2 of corneal thickness
Grade 4: Anterior chamber depth is ≥ corneal thickness

3. Gonioscopic classifications

1) Shaffer classification
Grade 0: Angle closure (angle, 0º), closure present
Grade 1: Extremely narrow angle (angle, 10º), closure probable
Grade 2: Moderately narrow angle (angle, 20º), closure possible
Grade 3-4: Wide open angle (angle, 20-45º), closure impossible

2) Scheie classification
Grade 0: All structures visible
Grade I: Hard to see over iris root into recess
Grade II: Ciliary body band obscured
Grade III: Posterior trabeculum obscured
Grade IV: Only Schwalbe’s line visible

4. Criteria for glaucomatous visual field defects

1) Criteria for glaucomatous visual filed defects (Humphrey perimetry)

Any of the following:
- The pattern deviation probability plot shows a cluster of three or more nonedge points that have sensitivities occurring in fewer than 5% of the normal population ($P < 5\%$), and one of the points has a sensitivity that occurs in fewer than 1% of the population ($P < 1\%$).
- The pattern standard deviation (or corrected pattern standard deviation) has a value that occurs in less than 5% of normal reliable
fields (< 5%).

- The glaucoma hemifield test indicates that the field is abnormal.

References


5. Classifications of glaucomatous visual field defects

1) Kozaki classification

Ia: No abnormalities in any visual field test method

Ib: No abnormalities in Goldmann perimetry (GP) dynamic visual field testing, but abnormalities present in other visual field tests

IIa: GP V-4 and I-4 isopters are normal, but I-3, I-2, and I-1 isopters are abnormal

IIb: GP V-4 isopter is normal, but I-4, I-3, I-2, and I-1 isopters are abnormal

IIIa: GP V-4 visual field contraction of up to 1/4

IIIb: GP V-4 visual field contraction of 1/4 to 1/2

IV: GP V-4 visual field contraction of 1/2 or more, but macular visual field retained

Va: GP V-4 visual field retained in macular region only

Vb: GP V-4 visual field is lost in macular region, but retained in other areas

VI: No GP V-4 visual field

2) Aulhorn classification (modified by Greve et al.)

Stage 0-1: Relative small glaucomatous visual field defect (GVFD) with an intensity of 0.6 log unit up to 1.0 log unit. With special examination methods and appropriate statistical procedures, defects with an intensity of less than 0.6 log unit can be included in this group.

Stage 1: Small GVFD with an intensity of more than 1.0 log unit up to maximum luminance. The size of stages 0-1 and 1 defects should not exceed the size of the blind spot.

Stage 2: Incomplete nerve fiber bundle defect (NFBD = arcuate defect) for maximum luminance.

Stage 3: Complete (from blind spot to nasal horizontal meridian) NFBD for maximum luminance or incomplete (stage 2) NFBD with nasal breakthrough.

Stage 4: Complete NFBD for maximum luminance with nasal breakthrough involving less than one quadrant.

Stage 5: Complete NFBD for maximum luminance with nasal breakthrough involving more than one quadrant. Two stage 5 defects in the upper and lower half of the visual field form a central and temporal island.

Stage 6: Temporal island.

3) Classification of glaucomatous visual field defects (Humphrey perimetry)

An early defect meets all the following requirements:
- The mean deviation is better than -6 dB;
- Fewer than 18 of the 76 points in a 30-2 pattern (25%) are defective in the total deviation probability plot at the 5% level;
- Fewer than 10 points are defective at the 1% level; and
- No point in the central 5 degrees has a sensitivity less than 15 dB.

A moderate defect exceeds one or more of the criteria required to keep it in the early defect category but does not meet the criterion to be severe.

A severe defect has any of the following:
- The mean deviation is worse than -12 dB;
- More than 37 (50%) of the points depressed at the 5% level;
- More than 20 points depressed at the 1% level;
- A point in the central 5 degrees with 0-dB sensitivity; or
- Points closer than 5 degrees of fixation under 15-dB sensitivity in both the upper and lower hemifields.

References


6. Glaucoma treatment agents

The following is a summarized explanation of the mechanism of action, dosage, contraindications, adverse effects, etc., of various glaucoma medications.

As none of these drugs have been established to be safe for use in children, they should be administered to children only with extreme caution. These drugs should be administered to women who are pregnant or who may possibly be pregnant only if the therapeutic benefits are assessed to outweigh the possible risks. As many drugs have been reported to be excreted in breast milk, they should not be given to nursing mothers, or if such administration is absolutely necessary, nursing should be discontinued.

1) Sympathomimetics

(1) Nonselective sympathomimetics

Nonproprietary name
Dipivefrin

Action
Increases aqueous outflow via Schlemm’s canal
Decreases aqueous production

Dosage and administration
Dipivefrin 0.04%, 0.1%: 2 x daily

Main adverse effects
Allergic conjunctivitis/blepharitis, conjunctival hyperemia, mydriasis, eye pain, cardiopalms, pigment deposition (conjunctiva, cornea, nasolacrimal ducts), ocular pemphigoid, macular edema, headache, sweating, tremor

Contraindications
1. Patients with IOP-elevating factors such as narrow anterior chamber angle or shallow anterior chamber (acute angle-closure glaucoma attacks may occur)
2. Patients with a history of hypersensitivity to any ingredients of the drug

To be administered with caution in the following cases:
1. Hypertension
2. Arteriosclerosis
3. Heart disease such as coronary failure or heart failure
4. Diabetes
5. Hyperparathyroidism

(2) α-agonists

Used to prevent transient elevation of IOP following laser surgery

Nonproprietary name
Apraclonidine

Action
Decreases aqueous production

Dosage and administration
Apraclonidine 1%: Instillation one hour before and immediately after laser surgery

Main adverse effects
Conjunctival pallor, mydriasis, eyelid elevation, thirst, dry feeling of the nose, and in continuous use, allergic blepharoconjunctivitis

Contraindications
1. Patients with a history of hypersensitivity to this drug or clonidine
2. Patients under treatment with monoamine oxidase (MAO) inhibitors

To be administered with caution in the following cases:
1. Patients with severe cardiovascular disease
2. Patients with unstable hypertension
3. Patients with a history of vasovagal attacks

2) Sympatholytics

(1) β-blockers

Nonproprietary name
1. Nonselective
Timolol
Carteolol
Levobunolol
2. β₁-selective
Betaxolol

**Action**
Decreases aqueous production

**Dosage and administration**
- Timolol 0.25%, 0.5%: 2 x daily
- Long-acting form: 1 x daily
- Carteolol: 1%, 2%: 2 x daily
- Levobunolol 0.5%: 1-2 x daily
- Betaxolol 0.5%: 2 x daily

**Main adverse effects**
- Ocular irritation symptoms, corneal epithelium disorder, dry eye, allergic conjunctivitis, contact dermatitis, blepharoptosis, asthmatic attacks, bradycardia, arrhythmia, palpitations, hypotension, heart failure, abnormal lipid metabolism, headache, depression

**Contraindications**
- Nonselective:
  - 1. Patients with bronchial asthma or a history thereof, patients with bronchospasms or severe chronic obstructive pulmonary disease (may induce/aggravate asthma attacks due to bronchial smooth muscle contraction caused by β-receptor blockade)
  - 2. Patients with uncontrolled heart failure, sinus bradycardia, ventricular block (grades II, III), or cardiogenic shock (these symptoms may be aggravated due to a negative chronotropic/inotropic action resulting from β-receptor blockade)
  - 3. Patients with a history of hypersensitivity to any ingredients of the drug
- β₁-selective:
  - 1. Patients with a history of hypersensitivity to any ingredients of the drug
  - 2. Patients with uncontrolled heart failure (symptoms may be aggravated)
  - 3. Women who are pregnant or who may possibly be pregnant (increased embryonic/fetal mortality has been reported in animal studies)

To be administered with caution in the following cases:

(2) α₁-β-blockers

**Nonproprietary name**
Nipradilol

**Action**
Decreases aqueous production

**Dosage and administration**
- Nipradilol 0.25%: 2 x daily

**Main adverse effects**
- Same as β-blockers

**Contraindications**
- 1. Patients with bronchial asthma, bronchospasms, or a history thereof, patients with severe chronic obstructive pulmonary disease (may induce/aggravate asthma attacks due to bronchial smooth muscle contraction caused by β-receptor blockade)
- 2. Patients with uncontrolled heart failure, sinus bradycardia, ventricular block (grades II, III), or cardiogenic shock (these symptoms may be aggravated due to a negative chronotropic/inotropic action resulting from β-receptor blockade)
- 3. Patients with a history of hypersensitivity to any ingredients of the drug

To be administered with caution in the following cases:
- Same as β-blockers

(3) α₁-blockers

**Nonproprietary name**
Bunazosin

**Action**
Increases uveoscleral outflow
Dosage and administration
Bunazosin 0.01%: 2 x daily

Main adverse effects
Conjunctival hyperemia

Contraindications
Patients with a history of hypersensitivity to any ingredients of the drug

3) Parasympathomimetics

Nonproprietary name
Pilocarpine

Action
Increases aqueous outflow via Schlemm's canal

Dosage and administration
Pilocarpine 0.5-4%: 4 x daily

Main adverse effects
Aphose due to miosis, deteriorated visual acuity, accommodation disorders due to ciliary muscle contraction, myopia, eyebrow pain, ciliary pain, conjunctival hyperemia, blepharitis, ocular pemphigoid, retinal detachment, cataracts, diarrhea, nausea, vomiting, sweating, salivation, uterine muscle contraction

Contraindications
Patients with iritis (possibility of iridial synechia due to pupillary contraction or aggravated inflammation thereof)

To be administered with caution in the following cases:
1. Patients with bronchial asthma
2. Patients at risk for retinal detachment
3. In cases of malignant glaucoma, ciliary muscle contraction may aggravate ciliary block
4. In addition, in glaucoma due to lens subluxation or intumescent cataracts, IOP may be increased, so caution is required
5. In the case of carbachol, as aggravation of the symptoms of acute heart failure, peptic ulcers, gastrointestinal spasms, ileus, urinary tract obstruction, Parkinson's syndrome, and hyperparathyroidism may occur, these drugs should be administered with caution

4) Prostaglandin analogues

Nonproprietary name
Unoprostone
Latanoprost

Action
Increases uveoscleral outflow

Dosage and administration
Unoprostone 0.12%: 2 x daily
Latanoprost 0.005%: 1 x daily

Main adverse effects
Unoprostone: Transient eye irritation symptoms, corneal epithelium disorder, conjunctival hyperemia, and in rare cases, iridial pigment deposition
Latanoprost: Conjunctival hyperemia, symptoms of eye irritation, corneal epithelium disorder, blepharitis, iridial/palpebral pigment deposition, hypertrichosis of eyelid/eyelashes, uveitis, cystoid macular edema (in aphakic eyes or eyes with implanted intraocular lenses)

Contraindications
Unoprostone: None
Latanoprost: Patients with a history of hypersensitivity to any ingredients of the drug

To be administered with caution in the following cases:
Unoprostone: None
Latanoprost:
1. Aphakic eyes or eyes with implanted intraocular lenses
2. Bronchial asthma or a history thereof
3. Iritis, uveitis
4. Patients with a possibility of latent herpes virus
5. Pregnant women, women in labor, nursing mothers

5) Carbonic anhydrase inhibitors

(1) Eye drops

Nonproprietary name
Dorzolamide
Brinzolamide

Action
Decreases aqueous production

Dosage and administration
Dorzolamide 0.5%, 1.0%: 3 x daily
Brinzolamide 1%: 2 x daily
Main adverse effects
Ocular irritation symptoms, conjunctival hyperemia, blurred vision immediately after instillation, allergic conjunctivitis, blepharitis, keratitis

Contraindications
1. Patients with a history of hypersensitivity to any ingredients of the drug
2. Patients with severe renal damage

To be administered with caution in the following cases:
Patients with liver function disorders

(2) Oral and injection preparations
Nonproprietary name
Acetazolamide

Action
Decreases aqueous production

Dosage and administration
Acetazolamide p.o.: Oral administration of 250-1,000 mg daily
Acetazolamide injection: Intravenous or intramuscular injection of 250-1,000 mg daily

Main adverse effects
Transient myopia, numbness of the extremities, dysgeusia, metabolic acidosis, hypokalemia, hyperuricemia, anorexia, gastrointestinal disorders, nausea, vomiting, diarrhea, constipation, polyuria, urinary frequency, kidney/urinary tract stones, acute renal failure, fatigueability, systemic malaise, drowsiness, dizziness, reduced libido, depression, mental confusion, aplastic anemia, hemolytic anemia, agranulocytosis, drug eruption, mucocutaneous ocular syndrome (Stevens-Johnson syndrome), toxic epidermal necrolysis (Lyell syndrome), shock

Contraindications
1. Should not be administered to the following patients:
   A. Patients with a history of hypersensitivity to the ingredients of the drug or sulfonamide preparations
   B. Patients with anuria or acute renal failure (adverse effects may be aggravated due to delayed drug excretion)
   C. Patients with hyperchloremic acidosis, clearly decreased sodium/potassium in the body fluids, adrenal insufficiency/Addison’s disease (electrolyte abnormalities may be aggravated)
   D. Patients under treatment with terfenadine or astemizole (QT prolongation or ventricular arrhythmia may occur)
2. Should not be administered for long periods to the following patients:
   A. Patients with chronic angle-closure glaucoma (aggravation of glaucoma may be masked)

To be administered with caution in the following cases:
1. Patients with advanced liver cirrhosis
2. Patients with serious coronary sclerosis or cerebral arteriosclerosis
3. Patients with severe renal damage
4. Patients with liver disease/liver function disorders
5. Patients with serious hypercapnia requiring a respirator, etc.
6. Patients under treatment with digitalis preparations, adrenocortical hormones, or ACTH
7. Patients on a reduced-salt diet
8. Elderly patients
9. Infants

6) Hyperosmotics
(1) Mannitol
Nonproprietary name
D-mannitol

Action
Decreases vitreous volume

Dosage and administration
20% D-mannitol
15% D-mannitol + 10% fructose
15% D-mannitol + 5% D-sorbitol
The usual dose is intravenous drip infusion of 0.1-3.0 g, 5-15 mL/kg (however, daily dose of D-mannitol of up to 200 g)

Main adverse effects
Headache, dizziness, thirst, nausea, diarrhea, rigor, diuresis, urinary retention, hematuria, dehydration/electrolyte
abnormalities, renal failure, angina pectoris, congestive heart failure, pulmonary edema, diabetic coma (preparations with added fructose), rebound elevation of IOP

Contraindications
1. Patients with acute intracranial hematomas (in patients with suspected acute intracranial hematomas, if the drug is administered without ruling out the presence of an intracranial hematoma, in the event of transient hemostasis due to intracranial pressure, bleeding may resume when intracranial pressure decreases, so the drug should not be administered until the bleeding source has been treated and the risk of renewed hemorrhage has been ruled out)
2. In the case of preparations with added fructose, patients with hereditary fructose intolerance (as such patients cannot metabolize fructose normally, hypoglycemia, etc., may occur, the risk of liver failure or kidney failure)

To be administered with caution in the following cases:
1. Dehydrated patients
2. Patients with urinary retention or renal function disorders
3. Patients with congestive heart failure
4. Patients with diabetes insipidus
5. Elderly patients

(2) Glycerin
Nonproprietary name
Glycerin
Action
Decreases vitreous volume
Dosage and administration
50% glycerin p.o. solution: 3 mL/kg is given orally 1 - 2 x daily
10% glycerin + 5% fructose (glycerol): Intravenous drip infusion of 300-500 mL daily
Main adverse effects
Headache, dizziness, thirst, nausea, diarrhea, rigor, diuresis, and for the intravenous preparation, urinary retention, hematuria, dehydration/electrolyte abnormalities, renal failure, angina pectoris, congestive heart failure, pulmonary edema, hyperosmolar nonketotic hyperglycemia, lactic acidosis, rebound elevation of IOP

Contraindications
Patients with congenital abnormalities of glycerin or fructose metabolism (severe hypoglycemia may occur)

To be administered with caution in the following cases:
1. Diabetics
2. Patients with serious heart disease
3. For the intravenous preparation, patients with kidney disorders
4. For the intravenous preparation, patients with diabetes insipidus

(3) Isosorbide
Nonproprietary name
Isobide
Action
Decreases vitreous volume
Dosage and administration
70% isosorbide solution: 70-140 mL daily given in 2 - 3 divided oral administrations
Main adverse effects
Nausea, vomiting, diarrhea

Contraindications
Patients with acute intracranial hematomas (in patients with suspected acute intracranial hematomas, if the drug is administered without ruling out the presence of an intracranial hematoma, in the event of transient hemostasis due to intracranial pressure, bleeding may resume when intracranial pressure decreases, so the drug should not be administered until the bleeding source has been treated and the risk of renewed hemorrhage has been ruled out)

To be administered with caution in the following cases:
1. Dehydrated patients
2. Patients with urinary retention or renal function disorders
3. Patients with congestive heart failure
1. Methods of observing the fundus oculi

As a rule, in observation of the optic disc and the retinal nerve fiber layer, if circumstances permit, the pupil should be sufficiently dilated and observation should be conducted with sufficient light.

1) Ophthalmoscopy

In observation of the optic disc, it is necessary to sufficiently magnify the fundus image, and in this sense, observation using a direct ophthalmoscope is recommended. Except when the ocular medium is highly opaque, which makes observation with a direct ophthalmoscope difficult, indirect ophthalmoscopy using a lens with a low magnification, such as 14 or 20 D, is unsuitable for observation because the optic disc image will be too small.

2) Slit-lamp microscopy

It is important to stereoscopically observe the optic disc and the retinal nerve fiber layer. In this case, a lens for observing the fundus oculi is used in slit-lamp microscopy.

In the direct method, slit-lamp microscopy is conducted using the central part of a Goldmann 3-mirror lens, etc. Using a slit beam, the width and depth of the cup can be observed with strong magnification.

In the indirect method, a fundus lens having a power of 78 D, 90 D, etc., is used. Caution is required in this case, as the image is inverted.

3) Ophthalmoscopic photography

One effective method of observing changes in the fundus oculi and recording their course is photographic imaging. A stereoscopic camera provides optimum results.

Imaging is conducted centering on the disc, with an angle field angle of approximately 30 degrees in recording the disc region and a field angle of 45 degrees or more in recording the retinal nerve fiber layer.

4) Red-free light funduscropy

In observation of the retinal nerve fiber layer, in the fundus oculi of Japanese subjects, the methods mentioned above can be used to a sufficient degree, but ophthalmoscopic imaging using red-free light is recommended for the detection of tiny defects in the retinal nerve fiber layer. Using high-resolution black-and-white film, the fundus images are taken using red-free light. In the case of a fundus camera not having a red-free light filter, a filter having a maximum transmittance in the vicinity of 495 nm can be used.

2. Observation points for the optic disc and retinal nerve fiber layer

The four methods for observing the fundus oculi discussed above are used as appropriate in order to evaluate whether or not there are any abnormalities due to glaucoma in the optic disc and retinal nerve fiber layer. Observation methods can roughly be divided into (1) qualitative assessment and (2) quantitative assessment. The points pertaining to the various assessment criteria are given below.

1) Qualitative assessment

- Shape of optic disc
- Shape of the cup of the optic disc (referred to in the following simply as the cup)
- Shape of the neuroretinal rim (referred to in the following as the rim)
- Hemorrhaging of the optic disc (referred to in the following as disc hemorrhage)
- Peripapillary atrophy (referred to in the following as PPA)
- Defects in the retinal nerve fiber layer

(1) Shape of the optic disc

The optic disc may have a variety of shapes, but it is ordinarily somewhat oblong, with its vertical diameter being some 7-10% longer than its horizontal diameter. Generally speaking, in myopic eyes of 8 D or below, the optic disc shape shows no clear differences compared to normal eyes, but in myopic eyes exceeding -12 D, this elongation has been reported to be greater. The shape of the optic disc is unrelated to age, sex, body weight, and height.

The size of the optic disc, i.e., the area of the papillary surface, is not uniform, with individual differences being extremely pronounced. It varies widely from approximately 0.8 mm² in small cases to 6 mm² in large cases. The size of the optic disc shows no
correlation with age from the age of around 10 on. Concerning the correlation with sex, body height, body weight, and refraction defects, reports differ, and no consensus has been reached. However, disc area shows no correlation with refraction within a range of at least ± 5 D.

(2) Shape of the cup

The excavation observed in the optic disc is referred to as a cup. Enlargement of this cup is one of the major characteristics of glaucomatous abnormalities seen in the optic disc. In the normal eye, the cup is somewhat wider in a transverse direction, and it is located not at the exact center of the optic disc, but displaced superiorly to a certain extent. Cup size in the normal optic disc is proportionate to the size of the disc, with the cup being larger as the size of the disc increases. Stereoscopic observation is the optimum method for observing the extent of this cup, but in cases where this technique cannot be used, diagnoses are made based on the course of the blood vessels in the optic disc. The retinal blood vessels run along the wall of the cup, and when they reach the rim, their course changes. The areas showing a curved course of the blood vessels on planar observations are taken as the outer rim of the cup.

In glaucoma, when the cup increases in size, 2-dimensional enlargement and 3-dimensional increases in depth occur in parallel. Specifically, while the existing cup becomes deeper, new excavations appear. When the cup rapidly increases in size, the small blood vessels originally running along the inside of the rim of the cup do not follow this expansion, but remain exposed on the floor of the enlarged cup or on its slope. These are referred to as bared vessels (exposed blood vessels). If such vessels are present, this constitutes an important finding indicating progressive expansion of the cup. As a vascular change in the optic disc accompanying expansion of the cup, one can also mention displacement of the central retinal blood vessels to the nasal side of the disc. As this change is relatively pronounced, when the disc cup is observed over time using a fundus camera, it stands out as an indicator of cup enlargement. The depth of the cup can be roughly estimated based on whether or not one can see the pores of the lamina cribrosa of the sclera through the floor of the cup. If the pores can be seen, the cup can be considered to be of considerable depth (laminar dot sign). However, this finding is not specific to glaucomatous changes alone, but is also sometimes observed in the case of physiological excavations.

(3) Shape of rim

The rim is the area between the outer edge of the disc cup and the outer edge of the disc as seen on ophthalmoscopy, and it is the site in the disc area where nerve fibers are present. Generally speaking, the larger the disc, greater the total surface area is. However, this is a general tendency, and there may also be numerous differences in rim size resulting from individual differences such as the number of nerve fibers, nerve fiber density, structure of the lamina cribrosa, and number of glial cells.

In general, the normal optic disc is somewhat vertically oblong, but the optic disc cup is usually somewhat transversely elongated, so the rim shape undergoes a variety of changes depending on the shape of the disc cup. Ordinarily, the widest part of the rim is the inferior region of the disc, followed in descending order by the superior region and nasal side of the disc, with the thinnest area being the temporal disc area (the isn’t rule). Because of this, the visibility of the nerve fiber layer of temporal-inferior region to the disc is ordinarily high. If the optic disc is large, however, this trend is not very pronounced, and the rim has a relatively uniform width along its entire circumference. Moreover, in myopic eyes, the rim on the temporal side of the disc is the thinnest, with the nasal area of the disc generally being the broadest.

In optic discs that have undergone glaucomatous changes, the cup increases in size uniformly and shallowly but in many cases, the enlargement of the cup is more predominant either in the superior or inferior areas of the disc. Accompanying this, progressive
thinning of the rim takes place at the superior, inferior, or both poles of the optic disc. With further progression, the shallow cup region increases in depth, the border between the cup and the rim becomes more clearly demarcated, and localized thinning of the rim, referred to as notching, occurs. This change is a significant finding indicating the presence of optic nerve fiber defects. As the disease progresses, one sees the initially notched areas increase their width and depth, and the blood vessels in the disc rim become more strongly curved. In such cases, the course of the blood vessels shows a bayonet-like appearance referred to as bayoneting. Moreover, as this phenomenon progresses, the cup also extends in a direction opposite to the side on which notching initially occurred, forming a clearly oblong shape, with the rim no longer being visible on both temporal-superiorly and -inferiorly. At this point, visual impairment is characterized by superior and inferior arcuate scotoma. In the late stage, the cup expands throughout the optic disc, and the rim ordinarily disappears completely, except for a part on the nasal side.

(4) Disc hemorrhage

Optic disc hemorrhage occurs quite specifically in optic discs showing glaucomatous changes. It is rare in healthy persons (0-0.21%), and particularly when seen repeatedly, its pathological significance is high. Compared to the glaucomatous eyes, the frequency of disc hemorrhaging is high in eyes with normal-tension glaucoma. Moreover, it tends to occur in the same areas where notching of the rim and defects in the retinal nerve fiber layer are present, and approximately 80% of disc hemorrhaging is observed either corresponding to the area of defects in the nerve fiber layer or in the vicinity thereof. These results support a correlation between disc hemorrhaging and local disc damage, but they do not necessarily constitute characteristic findings in eyes with normal-tension glaucoma. In any case, disc hemorrhaging, at the stage when it can be observed, indicates the presence of rim notching and nerve fiber layer defects, and subjects showing disc hemorrhaging are known to show a higher rate of visual field progression than patients in whom such hemorrhaging is not observed, so this is a finding of great clinical significance.

(5) PPA

PPA, or peripapillary atrophy, is observed with a high degree of frequency in glaucomatous eyes compared to normal eyes, and the area thereof is greater. PPA is seen in approximately 80% of eyes with primary open-angle glaucoma (broad definition), and the area thereof shows a correlation with the two visual field indicators MD (mean defect) value and CPSD (corrected pattern standard deviation). It has not yet been established whether there is a direct link between the cause of occurrence of PPA and the progression of glaucoma, but the progression of glaucoma and the presence or absence of PPA show a significant connection, and the extent of PPA is known to increase with the progression of visual field damage. Furthermore, it has been suggested that there is a correlation between disc blood flow and the area of PPA, and even though this is by no means a typical change in glaucomatous optic disc damage, it is important as a finding indicating fragility associated with some blood flow impairing factor in the optic disc.

(6) Presence or absence of retinal nerve fiber layer defects

Defects of the retinal nerve fiber layer frequently occur prior to enlargement of the optic disc cup and visual field defects, which can be said to be the earliest change in the glaucomatous fundus oculi, and this finding is therefore significant. In ophthalmoscopic examination of normal eyes, the retinal nerve fiber layer shows the highest visibility in the inferior-temporal region, followed in order by the superior-temporal, superior-nasal, and inferior-nasal regions. Identification by ophthalmoscopic examination becomes difficult directly superior and inferior to the disc, on the temporal side, and on the nasal side. This visibility of the retinal nerve fiber layer decreases with age, and this is consistent with the finding that almost 1.4 million nerve fibers decrease with age (by 4-5,000 per year).
clinical setting, slit-lamp microscopy is ordinarily carried out using a 78 or 90 D fundus lens, and the best observations are made using red-free filtered light. The nerve fiber bundle is seen as a whitish/silver-colored line. When one moves away from the optic disc by a distance approximately 2 times the diameter of the disc, the optic nerve fiber layer appears thin, taking on a brushlike appearance and then gradually disappearing.

The apparent, slit-shaped thinner than the width of retinal blood vessels, fissured, or spindle-shaped changes can be seen in the retinal nerve fiber layer in normal eyes. Nevertheless, in the case of slit-shaped defects wider than the diameter of the retinal blood vessels, it is highly likely that these are glaucomatous. In such a case, the retina in the defected area appears with dark band-like changes extending from the outer edge of the optic disc. In cases in which retinal nerve fiber layer defects are detected and accompanied by glaucomatous changes in the optic disc, the presence of glaucomatous visual field damage is virtually certain. On the other hand, when the retinal nerve fiber layer is getting thinner, the optic nerve fibers above the retinal blood vessels becomes thin, and the vascular walls are more clearly visible, appearing to rise up above the nerve fibers. Such changes are also considered to be significant findings indicating a retinal nerve fiber layer defect.

Furthermore, retinal nerve fiber layer defects are frequently seen in areas showing rim atrophy, and as mentioned above, disc hemorrhaging may be seen in an area close to this, extending from the rim onto the adjacent retina.

2) Quantitative assessment

It is useful to determine the various parameters discussed below in order to gain a semiquantitative understanding of the optic disc, and the nerve fiber layer for glaucoma diagnosis and observation of the patient's course. However, the parameters mentioned here are defined according to the definition established in clinical observation, and this differs from the definition in the case of image analysis instruments developed in recent years.

- Cup-to-disc ratio (abbreviated in the following as C/D ratio)
- Rim-to-disc diameter ratio (abbreviated in the following as R/D ratio)

(1) Definition of the outer edge of the optic disc

The outer edge of the optic disc is defined as the inner side of the white scleral ring on the periphery of the disc observed by ophthalmoscopy (Elshnig's scleral ring).

There are extremely large individual differences in the size of the optic disc, with this size ranging from approximately 0.8 mm² in small cases to 6 mm² in large cases. In large optic discs, physiological concavities are also large, and there are also cases in which a small disc does not show a clear cup. Accordingly, in determining whether or not the optic disc cup is glaucomatous, it is important to conduct this evaluation bearing in mind disc size. The approximate size can even be assessed using a slit-lamp microscope or a fundus lens. In such cases, the length of the slit being set to 1 mm, the observation axis and the light axis are aligned, the slit lamp is placed over the disc, and an assessment is made as to the rough vertical diameter of the disc. On the other hand, because the distance from the center of the optic disc to the macular fovea centralis is largely uniform, by taking the ratio of the disc diameter (DD) to that from the center of the disc to the fovea centralis (DM), it is possible to determine the approximate size of the disc (DM/DD ratio). This ratio is ordinarily in the range of 2.4 - 3.0, and it is said that when it is less than this, the disc is large, and when it is greater than this, the disc is small (Fig. 1).

(2) Definition of outer edge of the optic disc cup

In stereoscopic observation, the outer edge of the cup is located in the optic disc region demarcated by the outer edge of the disc, and it is defined as the outermost area at which the cup begins. Following the course of fine blood vessels in the optic disc, the apex showing a curved course of the blood vessels
normally correspond to the outer edge of the optic disc cup. The optic disc cup is defined as the inside of the area demarcated by the outer edge of the cup. Ordinarily, the bluish-white discoloration of the disc referred to as pallor is seen on the floor of the cup, and the disc cup should not be assessed by observing this area alone.

(3) Definition of the rim
The area between the outer rim of the optic disc and the outer rim of the disc cup is referred to as the rim.

(4) Definition of C/D ratio
The ratio of the maximum vertical diameter of the optic disc cup to the maximum vertical optic disc diameter is referred to as vertical C/D ratio, and the ratio of the horizontal diameter of the cup to the horizontal optic disc diameter is referred to as the horizontal C/D ratio (Fig. 2). In assessing whether or not there are glaucomatous changes, the vertical diameter is more useful. With respect to C/D ratio, there are also methods involving assessment of disc diameter and cup diameter along the same line, but in the present Guideline, we have selected the assessment method of Gloster et al.1

In healthy eyes, this distribution is not a normal distribution, but in many cases, the C/D ratio is from 0 to 0.3, and cases in which it exceeds 0.7 account for 1 - 2% of the total. However, in stereoscopic evaluation, the C/D ratio is in normal distribution and has been reported to average 0.4, with values of 0.7 or above accounting for 5%. Furthermore, in normal persons, the cups are symmetrical in the right and left eyes, and cases in which the difference between the left and right sides in horizontal C/D ratio exceed 0.2 account for no more than 3% of normal subjects in both adults and children.

(5) Definition of R/D ratio
The ratio of the width of the rim area and the corresponding disc axis passing through the center of the disc (Fig. 3) is defined as the R/D ratio. R/D ratios can be calculated for all regions of the disc in a radial direction. The closer the ratio is to 0, the thinner the rim.

(6) Glaucoma diagnostic criteria according to quantitative assessment of the optic disc
In the following, based on evaluation results for vertical C/D ratio and R/D ratio, we show glaucoma diagnostic criteria prepared based on the diagnostic criteria proposed by Foster et al.3 However, the final diagnosis should be made based on an overall assessment combining qualitative and quantitative findings.

1. Evaluation criteria in cases where reliable visual field test results show visual field anomalies corresponding to optic disc config-
uration and retinal nerve fiber layer defects:

Cases in which the vertical C/D ratio is 0.7 or above, the superior pole (11:00-1:00) or inferior pole (5:00-7:00) rim width shows an R/D ratio of 0.1 or less, the difference in the vertical C/D ratios between the two eyes is 0.2 or above, or retinal nerve fiber layer defects are present.

2. Assessment criteria in cases that can be diagnosed as glaucoma based on optic disc findings (however, this does not apply to cases in which reliable visual field tests show a visual field within the normal range or the presence of glaucomatous visual field impairment is clearly ruled out):

The vertical C/D ratio is 0.9 or above, the superior pole (11:00-1:00) or inferior pole (5:00-7:00) rim width shows an R/D ratio of 0.05 or below, or the difference between the vertical C/D ratio in the two eyes is 0.3 or greater.

3. Criteria in cases of suspected glaucoma:

Cases where one or more of the following findings are present: (1) the vertical C/D ratio ranges from 0.7 to 0.9, (2) the superior pole (11:00-1:00) or the inferior pole (5:00-7:00) rim width shows a R/D ratio of less than 0.1 but greater than 0.05, (3) the difference in the vertical C/D ratios between the two eyes ranges from 0.2 to 0.3, (4) or retinal nerve fiber layer defects are present, the reliability of visual field tests is poor, and the visual field results therefore cannot be taken as a reference, or cases in which there are no indications of visual field defects corresponding to optic disc configuration or retinal nerve fiber layer defects.

3. Significance of glaucoma diagnosis using computerized image analysis techniques

When persons who are experienced in the use of the methods described so far examine the fundus oculi, they are highly effective in diagnosing glaucoma, but as there are individual differences in evaluations of the fundus oculi made by various personnel, there is a need to establish a standardized method for evaluating and assessing glaucomatous changes in the fundus oculi. To this end, the use of computerized image analysis techniques that are easy to operate and show high measurement accuracy and favorable measurement reproducibility is a promising method of solving these problems. Examples of computerized image analysis instruments currently in clinical application include the Heidelberg Retina Tomograph, the GDx Nerve Fiber Analyser, the Scanning Laser Ophthalmoscope, and the Optical Coherence Tomograph. Using these diagnostic devices, one can carry out quantitative evaluations of the optic disc or retinal nerve fiber layer thickness, and they have been reported to be useful in glaucoma diagnosis. However, there are individual differences in optic disc configuration and nerve fiber thickness, and because of the overlap in measured numerical values seen between glaucomatous and normal eyes and limitations on the measuring accuracy of analysis instruments, we have not yet succeeded in fully differentiating glaucomatous and normal eyes. In image analysis instruments in which automatic diagnostic programs have been installed, it has been reported that the specificity and sensitivity of glaucoma diagnosis is on the order of 80%, therefore final assessment by specialized ophthalmological personnel having a wealth of experience in diagnosing glaucoma is required. At the present time, such instruments can only be used on an auxiliary basis.

References

Explanation of attached figures
Fig. 1: Schematic diagram of DM/DD ratio
This ratio is ordinarily considered to be in the range of 2.4-3.3.

Fig. 2: Example (a) and schematic diagram (b) of measurement of horizontal/vertical C/D ratios
Regardless of the inclination of the optic disc and cup, the diameter in a horizontal or vertical direction is determined and taken as the ratio.

Fig. 3: Example (a) and schematic diagram (b) of measurement of R/D ratio