Japan Glaucoma Society

Guidelines for Glaucoma
Table of Contents

Preface ........................................................................................................................................................................... 1

Introduction .................................................................................................................................................................... 3

Flow-charts
I . Examinations for glaucoma diagnosis .......................................................................................................................... 4
II . Classification of primary open-angle glaucoma (broad definition) ............................................................................. 5
III . Classification of primary angle-closure glaucoma ........................................................................................................ 5
IV . Automated static perimetry ........................................................................................................................................... 6
V . Treatment of primary open-angle glaucoma (broad definition): General principles .................................................. 7
VI . Treatment of primary open-angle glaucoma (broad definition): Target intraocular pressure .................................. 7
VII . Treatment of primary open-angle glaucoma (broad definition): Medical treatment ................................................ 8
VIII . Treatment of primary angle-closure glaucoma .......................................................................................................... 8
IX . Treatment of acute primary angle-closure glaucoma ................................................................................................... 9

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

Section 2. Classification of Glaucoma
I . Primary glaucoma ........................................................................................................................................................... 13
1. Primary open-angle glaucoma (broad definition) ........................................................................................................... 13
2. Primary angle-closure glaucoma ..................................................................................................................................... 14
3. Mixed glaucoma ................................................................................................................................................................... 15
II . Secondary glaucoma ........................................................................................................................................................ 15
1. Open angle mechanisms in secondary glaucoma ................................................................................................................ 15
2. Angle closure mechanisms in secondary glaucoma .......................................................................................................... 16
III . Developmental glaucoma .............................................................................................................................................. 16
1. Early onset developmental glaucoma ................................................................................................................................. 16
2. Late onset developmental glaucoma ................................................................................................................................ 16
3. Developmental glaucoma with other congenital anomalies ............................................................................................ 16

Section 3. Examination of Glaucoma
I . History taking .................................................................................................................................................................. 19
II . Slit-lamp microscopy ........................................................................................................................................................ 19
III . Tonometry ........................................................................................................................................................................ 20
IV . Gonioscopy ..................................................................................................................................................................... 21
V . Ophthalmoscopy ............................................................................................................................................................... 22
VI . Perimetry ......................................................................................................................................................................... 23
Section 4. Principles of Treatment for Glaucoma

I. Principles of glaucoma therapy ......................................................................................................................... 27
II. Current status of treatment ................................................................................................................................. 27
   1. Baseline data determination ............................................................................................................................ 27
   2. Target intraocular pressure ............................................................................................................................. 27
   3. Glaucoma and QOL .......................................................................................................................................... 28
   4. Compliance with glaucoma drug treatment ..................................................................................................... 28
III. Glaucoma treatment agents ................................................................................................................................... 29
   1. Classification of glaucoma treatment agents ................................................................................................... 29
   2. Selection of drugs ............................................................................................................................................. 29
   3. Treatment trials ............................................................................................................................................... 29
   4. Guidance in administration ............................................................................................................................. 29
   5. Combined treatment ...................................................................................................................................... 30
   6. Glaucoma treatment agents ............................................................................................................................. 30
IV. Laser surgery .......................................................................................................................................................... 35
   1. Laser iridotomy ............................................................................................................................................... 35
   2. Laser trabeculoplasty ...................................................................................................................................... 36
   3. Laser gonioplasty (laser peripheral iridoplasty) ............................................................................................. 37
   4. Cyclophotocoagulation ................................................................................................................................... 37
   5. Laser suturelysis ............................................................................................................................................. 38
V. Invasive surgery ....................................................................................................................................................... 38
   1. Indications ....................................................................................................................................................... 38
   2. Surgical techniques ......................................................................................................................................... 39

Section 5. Treatment for Each Type of Glaucoma

I. Primary glaucoma ..................................................................................................................................................... 41
   1. Primary open-angle glaucoma ........................................................................................................................ 41
   2. Normal-tension glaucoma ............................................................................................................................... 42
   3. Primary angle-closure glaucoma ...................................................................................................................... 42
   4. Mixed glaucoma ............................................................................................................................................ 44
   5. Ocular hypertension ..................................................................................................................................... 44
II. Secondary glaucoma ................................................................................................................................................. 45
   1. Secondary open-angle glaucoma .................................................................................................................... 45
   2. Secondary angle-closure glaucoma ................................................................................................................... 46
III. Developmental glaucoma ...................................................................................................................................... 47
   1. Early onset developmental glaucoma ........................................................................................................... 47
   2. Developmental glaucoma with other congenital anomalies ........................................................................... 48
IV. Secondary glaucomas in childhood ....................................................................................................................... 48
Preface

Glaucoma, found in approximately 5.8% of persons aged 40 and older, is a disease that can cause 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 as 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, Japan Glaucoma Society has prepared the present guidelines as an aid to ophthalmologists in providing everyday medical care for glaucoma, including appropriate diagnosis and treatment.

In the present guidelines, we have attempted to systematically present the proper standards for current glaucoma treatment. In preparing these guidelines, however, it has not been our intent to impose limitations on physicians in diagnosing various clinical conditions. It is our hope that the present guidelines 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 these guidelines, 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 guidelines will contribute toward raising the standard of glaucoma treatment in Japan.

September 2002

Yoshiaki Kitazawa, Chairman, Japan Glaucoma Society
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
Tetsuya Yamamoto, MD, PhD

Authors and assistant author of Japan Glaucoma Society

Guidelines for Glaucoma

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

Assistant author:
Kiyoshi Yaoeda, MD, PhD

Reviewed and approved by Japan Glaucoma Society Board of Trustees September 2002
Glaucoma consistently ranks among the leading causes of blindness in Japan, and it is also an extremely serious illness from a social standpoint. According to a glaucoma survey conducted in seven areas of the country from 1988 to 1989, the prevalence of glaucoma was 3.56% of the population above 40. Furthermore, a recent epidemiological survey of glaucoma conducted from 2000 to 2002 (the Tajimi Study) showed that the prevalence of normal-tension glaucoma was 3.60% of the population above age 40, which was approximately 11 times the prevalence of primary open-angle glaucoma (0.32%). Accordingly, it was found that glaucoma is by no means a rare disease in this country, with the percentage accounted for by normal-tension glaucoma being higher than expected. Moreover, as the rate of newly-discovered cases of glaucoma in the Tajimi Study was 89%, this clearly demonstrates that there are numerous latent cases of the disease in this country that have not yet been treated.

Damage to the optic nerve and visual field caused by the two most prevalent forms of glaucoma, namely primary open-angle glaucoma and normal-tension glaucoma, is essentially progressive and irreversible. In these types of glaucoma, as damage gradually progresses unnoticed by the patient, early detection and treatment are of paramount importance in arresting or controlling the progressive 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 progression 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. From a social standpoint, moreover, it is necessary to reduce health care expenses by efficiently utilizing resources from the standpoint of globalization of health care and medical economics.

Japan Glaucoma Society has therefore prepared the guidelines for glaucoma in light of these circumstances. In the guidelines, we first present flow-charts illustrating the main points of glaucoma diagnosis and treatment, followed by explanations in five sections entitled "Definition of Glaucoma," "Classification of Glaucoma," "Examination of Glaucoma," "Principles of Treatment for Glaucoma," and "Treatment for Each Type of Glaucoma" We hope that the present guidelines 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. Japan Glaucoma Society assumes no responsibility for any legal problems arising in connection with health care provided based on the present guidelines.
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. Classification of primary open-angle glaucoma (broad definition*)

- Anterior chamber angle
  - Normal open angle
    - Optic nerve
      - Glaucomatous damage
        - No
          - IOP
            - Normal
              - Normal
            - Elevated
              - Ocular hypertension
        - Yes
          - Visual field
            - Glaucomatous damage
              - No
                - IOP
                  - Normal
                    - Normal
                  - Elevated
                    - Normal-tension glaucoma (suspect)
              - Yes
                - IOP
                  - Normal
                    - Normal-tension glaucoma
                  - Elevated
                    - Primary open-angle glaucoma

* IOP= Intraocular pressure
* See Section 2; † See Section 3.

III. Classification of primary angle-closure glaucoma

- Mechanism of angle closure
  - Relative pupillary block
    - Primary angle-closure glaucoma with relative pupillary block
      - Acute type
      - Chronic type
  - Plateau iris
    - Plateau iris syndrome
IV. 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.
V. Treatment of primary open-angle glaucoma (broad definition*): General principles

- Baseline
  - Stage of glaucoma
  - IOP without treatment
  - Other risk factors

  - Establish target IOP
  - Initiate treatment

  - Target IOP achieved
    - Yes: Continue treatment
    - No: Deterioration of optic nerve and/or visual field

  - No: Change treatment
    - Yes: Change target IOP

IOP= Intraocular pressure
*See Section 2.

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

- Higher
- Target IOP
- Lower

- Early
- Stage of glaucoma
- IOP without treatment
- Other risk factors

- High
- Low

(+) (-)

IOP= Intraocular pressure
*See Section 2.
VII. Treatment of primary open-angle glaucoma (broad definition*): Medical treatment

- Initiate monotherapy
- Target IOP achieved
  - Yes
  - No
    - Change monotherapy
  - Multi-drug therapy
  - Target IOP achieved
    - Yes
    - No
      - Change medication
        - Continue medical treatment
        - Laser treatment and/or surgery†

*IOP= Intraocular pressure
*See Section 2; †See Section 4.

VIII. Treatment of primary angle-closure glaucoma

- Mechanism of angle closure
  - Relative pupillary block
    - Laser iridotomy
      - Successful
      - Unsuccessful or not possible
        - Peripheral iridectomy
  - Plateau iris
    - Miotics
    - Laser gonioplasty
      - IOP control
        - Favorable
        - Unfavorable
          - Follow-up
          - Additional treatment to lower IOP (medical treatment and/or surgery)

*IOP= Intraocular pressure
IX. Treatment of 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 disease characterized by functional or structural anomalies of the eye in which at least one characteristic change in the optic disc or visual field is present and in which the progression of optic nerve damage can ordinarily be alleviated or halted by lowering intraocular pressure. This definition cannot necessarily be applied unconditionally to all disease types. Please refer to the individual sections in question for definitions of individual disease types. In these guidelines, please refer to the individual sections in question for the definition of different disease types.
Classification of Glaucoma

Introduction

Glaucoma can be classified according to gonioscopic findings and the presence or absence of diseases or conditions that may cause elevated intraocular pressure. The disease can be classified into primary glaucoma, in which no other cause of elevated intraocular pressure is present, secondary glaucoma, in which the elevation in intraocular pressure results from other ocular diseases, systemic diseases, or drug use, and developmental glaucoma, in which the elevation in intraocular pressure results from developmental anomalies in the anterior chamber angle. Primary glaucoma is divided into primary open-angle glaucoma (broad definition) and primary angle-closure glaucoma. The former is a disease concept that encompasses both conventional primary open-angle glaucoma and normal-tension glaucoma.

In establishing treatment for glaucoma, classification according to the mechanism of intraocular pressure 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 subtype and disease stage.

In the present guidelines, we propose 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 intraocular pressure. Moreover, there are differences in the vulnerability of the optic nerve to intraocular pressure, and because primary open-angle glaucoma and normal-tension glaucoma cannot be distinguished based on specific intraocular pressure values, the term primary open-angle glaucoma (broad definition) has been developed as a concept encompassing both disease types. Primary open-angle glaucoma (broad definition) can be conveniently subdivided in the clinical setting into an elevated intraocular pressure group (primary open-angle glaucoma) and a normal intraocular pressure group (normal-tension glaucoma). 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, i.e., thinning of the disc rim and retinal nerve fiber layer defects. In primary open-angle glaucoma (broad definition), other abnormality and congenital anomalies that may cause elevation of the intraocular pressure are absent and gonioscopy shows a normal open 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 the corresponding visual field defects.

In cases of discrepancies between optic nerve findings and perimetric 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 rule out intracranial diseases, etc. Moreover, among cases of primary open-angle glaucoma (broad definition), genetic aberrations such as TIGR/MYOC and optineurin anomalies may occur.

1) Primary open-angle glaucoma

In this subtype of primary open-angle glaucoma (broad definition), intraocular pressure exceeds the statistically determined normal range during the progression of glaucomatous optic neuropathy, and abnormally elevated intraocular pressure is strongly suspected to play a role in this optic neuropathy. As intraocular pressure is known to be subject to diurnal and seasonal fluctuations, when intraocular pressure is only measured a few times, there are many cases in which abnormal intraocular pressure values are not detected.
2) Normal-tension glaucoma, normal-pressure glaucoma
In this subtype of primary open-angle glaucoma (broad definition), intraocular pressure 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 intraocular pressure does not play a role in the development of optic neuropathy in normal-tension glaucoma. In many cases, as a possible pathogenic factor, findings indicate that factors independent of intraocular pressure such as vascular factor may also play a role. As intraocular pressure is known to be subject to diurnal and seasonal fluctuations, it is often quite difficult to establish that it is within the normal range, and repeated tonometry including 24-hr phasing is necessary in many cases.

3) Ocular hypertension
Although intraocular pressure shows similarities to primary open-angle glaucoma, this subtype lacks optic neuropathy and visual field anomalies. Some believe this subtype to be a preliminary stage of primary open-angle glaucoma, while others think it to be a type in which the resistance of the optic nerve to intraocular pressure is strong. Background factors such as family history of glaucoma, vascular factors, age, race, corneal thickness and refraction are known to be associated with the progression to glaucoma. Moreover, some researchers feel that intraocular pressure may be evaluated as falsely high because of abnormal corneal thickness, at least in some patients.

2. Primary angle-closure glaucoma
In primary angle-closure glaucoma, elevated intraocular pressure results from closure of the anterior chamber angle. Some researchers feel that only patients with elevated intraocular pressure or changes in the optic nerve can be classified as suffering from primary angle-closure glaucoma. In this disease type, however, as elevated intraocular pressure or changes in the optic nerve result from closure of the anterior chamber angle, in the present guidelines, we classify as primary angle-closure glaucoma all cases with established closure of the anterior chamber angle but without elevated intraocular pressure or optic nerve changes, including early-stage cases.

In primary angle-closure glaucoma, relative pupillary block and plateau iris mechanism 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. 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 syndrome.

1) Primary angle-closure glaucoma with relative pupillary block
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 intraocular pressure within a short period of time, resulting in the clinical symptoms typical of so-called glaucoma attacks. In the chronic type, as angle closure occurs gradually or intermittently, elevation of intraocular pressure 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 acutely elevated intraocular pressure, frequently reaching 40-80 mm Hg, decreased visual acuity, and weakened or absent light reaction. On slit-lamp biomicroscopy, findings include corneal edema, shallow anterior chamber, moderate mydriasis, conjunctival hyperemia, and ciliary injection. Gonioscopy shows extensive angle closure. Ophthalmoscopic examination may show signs such as papilledema, venous dilatation, and disc hemorrhage, but the optic disc may also be normal or show glaucomatous cupping. The fellow eye shows a narrow anterior chamber angle. Subjective symptoms include decreased visual acuity, blurred vision, iridopsia, ocular pain,
headache, nausea, and vomiting. There are also cases in which subjective symptoms are less pronounced and some of these symptoms are absent.

(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, the signs and symptoms are similar to those seen in primary open-angle glaucoma. Intraocular pressure is not necessarily elevated.

2) Plateau iris syndrome

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. Cases in which angle closure occurs purely due to the plateau iris mechanism are referred to as plateau iris syndrome, but such cases are rare. 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 the latter case, 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. Ultrasound biomicroscopy is useful in making the differential diagnosis between plateau iris syndrome and plateau iris configuration.

3. Mixed glaucoma

Combined cases of primary open-angle glaucoma and primary angle-closure glaucoma are referred to as cases of mixed glaucoma.

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

II. Secondary glaucoma

Secondary glaucoma is glaucoma in which elevated intraocular pressure is caused by other ocular diseases, systemic diseases, or drug use. Secondary glaucoma can be classified from several standpoints, including etiology, mechanism of intraocular pressure elevation, and means of treatment. However, each of these classification methods has both advantages and drawbacks. For example, in classification according to etiology, it is difficult to express the concept that neovascular glaucoma begins as open-angle glaucoma and then progresses while the mechanism of intraocular pressure elevation changes, becoming angle-closure glaucoma.

In the present guidelines, we classify glaucoma according to the mechanism of intraocular pressure elevation because it is very useful as an aid in determining the etiology and optimum treatment method. Caution is required because there may be cases in which conditions having the same etiology show differing mechanisms of intraocular pressure elevation, and the mechanism of intraocular pressure elevation may change even in the same eye. In diagnosing secondary glaucoma, gonioscopic examination is essential in order to confirm the mechanism of intraocular pressure elevation.

1. Open angle mechanisms in secondary glaucoma

1) Characterized primarily by aqueous outflow resistance between the trabecular meshwork and anterior chamber

Abnormal aqueous outflow resistance occurs due to a fibrovascular membrane, the conjunctival epithelium, etc.

2) Characterized primarily by aqueous outflow resistance in the trabecular meshwork

Abnormal aqueous outflow resistance results from pseudoexfoliation material, inflammatory material, macrophages, iris pigment, 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 elevation of intraocular pressure and increased pressure in the superior vena cava.

4) Cases due to aqueous hypersecretion

2. Angle closure mechanisms in secondary glaucoma
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 intraocular tissues or mass posterior 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 intraocular tissues or mass posterior to the lens
   These cases are unrelated to anterior chamber depth, but are caused by peripheral anterior synechiae.

Ⅲ. Developmental glaucoma

Glaucoma resulting from malformation of the anterior chamber angle is treated in these guidelines not as congenital glaucoma but as developmental glaucoma. Developmental glaucoma can be easily understood when classified into early onset developmental glaucoma, in which morphological 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 the aforementioned 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.

2. Late onset developmental glaucoma
   This type of glaucoma results from congenital morphological anomalies of the anterior chamber angle, but as the extent of such morphological anomalies is slight, the age of onset is delayed until the teens or twenties.

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 neurofibromatosis.
Table 2-1. Classification of glaucoma

**I. Primary glaucoma**

1. **Primary open-angle glaucoma (broad definition)**
   A. Primary open-angle glaucoma
   B. Normal-tension glaucoma, normal-pressure glaucoma

2. **Primary angle-closure glaucoma**
   A. Primary angle-closure glaucoma
   B. Plateau iris syndrome

3. **Mixed glaucoma**

**II. Secondary glaucoma**

1. **Secondary open-angle glaucoma**
   A. Secondary open-angle glaucoma characterized primarily by aqueous outflow resistance between the trabecular meshwork and anterior chamber (pretrabecular form)
   Examples: Neovascular glaucoma, glaucoma secondary to heterochromic iridocyclitis, glaucoma secondary to epithelial ingrowth, etc.
   
   B. Secondary open-angle glaucoma characterized primarily by aqueous outflow resistance in the trabecular meshwork (trabecular form)
   Examples: Steroid glaucoma, exfoliation glaucoma, glaucoma accompanying primary amyloidosis, 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 secondary to foreign bodies in the eye, glaucoma secondary to intraocular tumors, Schwartz syndrome, pigmentary glaucoma, pigment dispersion syndrome, etc.
   
   C. Secondary open-angle glaucoma characterized primarily by aqueous outflow resistance posterior to Schlemm's canal (posttrabecular form)
   Examples: Glaucoma accompanying exophthalmos, glaucoma accompanying increased pressure in the superior vena cava, etc.
   
   D. Secondary open-angle glaucoma due to aqueous hypersecretion (hypersecretory form)

2. **Secondary angle-closure glaucoma**
   A. Secondary angle-closure glaucoma with pupillary block (posterior form with pupillary block)
   Examples: Glaucoma secondary to lens bulging, glaucoma accompanying microphthalmia, glaucoma secondary to posterior synechiae, glaucoma secondary to lens subluxation, glaucoma secondary to epithelial ingrowth, etc.
   
   B. Secondary angle-closure glaucoma due to anterior movement of intraocular tissues posterior to the lens (posterior form without pupillary block)
   Examples: Malignant glaucoma, glaucoma secondary to retinal photocoagulation, glaucoma secondary to scleral buckling surgery, glaucoma secondary to intraocular tumors, glaucoma secondary to posterior scleritis/VKH disease, glaucoma secondary to central retinal vein occlusion, glaucoma secondary to intraocular filling materials, glaucoma secondary to massive vitreous hemorrhage, etc.
C. Secondary angle-closure glaucoma due to goniosynechiae without pupillary block or movement of the lens-iris diaphragm (anterior form)
Examples: Glaucoma secondary to flat or shallow anterior chamber, glaucoma secondary to uveitis, glaucoma secondary to corneal transplantation, neovascular glaucoma, ICE syndrome, glaucoma accompanying iridodialysis, etc.

Ⅲ. Developmental glaucoma

1. Early onset developmental glaucoma
2. Late onset developmental glaucoma
3. Developmental glaucoma with other congenital anomalies
   A. Aniridia
   B. Sturge-Weber syndrome
   C. Axenfeld-Rieger syndrome
   D. Peters’ anomaly
   E. Marfan syndrome
   F. Weill-Marchesani syndrome
   G. Homocystinuria
   H. Neurofibromatosis
   I. Rubella syndrome
   J. Pierre Robin syndrome
   K. Chromosomal aberrations
   L. Persistent hyperplastic primary vitreous
   M. Congenital microcornea
   N. Lowe syndrome
   O. Rubinstein-Taybi syndrome
   P. Hallermann-Streiff syndrome
   Q. Congenital ectropion uveae
   R. Others

Ⅳ. Secondary glaucomas in childhood

Glaucoma secondary to retinopathy of prematurity, glaucoma secondary to retinoblastoma, glaucoma secondary to juvenile xan-
I. History taking

The patient's history is of fundamental importance in the diagnosis and treatment of glaucoma. In order to take into account the possibility of secondary glaucoma, in addition to taking the history of ocular trauma, inflammation, surgery, infection, etc., it is important to determine the patient's history of systemic disease and medication. It is also important to interview the patient concerning subjective symptoms, with symptoms such as blurred vision, iridopsia, ocular pain, headache, and hyperemia indicating a possible history of acute glaucoma attacks. Moreover, it is 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 the intraocular pressure, ocular fundus, or visual field, such information should be used whenever possible.

1. Ocular pain

In cases of markedly elevated intraocular pressure due to acute glaucoma attacks, etc., the patient will frequently experience sudden and severe ocular pain. In general, the patient will experience severe ocular pain when intraocular pressure rises markedly from a normal value to a high value. Ocular 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 intraocular pressure, the patient may experience headache accompanied by nausea and vomiting, as well as symptoms such as reduced visual acuity, photophobia, and iridopsia.

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 intraocular pressure.

4. Visual field defects

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

5. Congestion

Congestion 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 diagnosis and treatment of glaucoma. In this examination, the conjunctiva, anterior chamber, iris, lens, etc., are observed, but goniolenses or fundus lenses may also be used in combination in order to observe the anterior chamber angle or ocular fundus.

1. Cornea

Corneal edema is observed in cases of markedly elevated intraocular pressure, such as acute glaucoma attacks, but it is also seen in secondary glaucoma accompanying corneal endothelial dysfunction, such as iridocorneal endothelial (ICE) syndrome, even though intraocular pressure 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 developmental glaucoma, enlargement of the eye ball (buphthalmos) accompanying elevated intraocular pressure may cause breaks in the Descemet's 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 pig-
ment 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, 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 depth is largely normal, as narrow angle and angle closure are observed, assessment of anterior chamber depth by slit-lamp microscopy is not sufficient to diagnose this condition, and gonioscopy is therefore necessary.

1) 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 anterior chamber 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. Iris

Usually, 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, posterior synechiae, neovascularization, atrophy, and nodules.

4. Lens

Abnormal lens findings associated with glaucoma include abnormal size or shape of the lens (lens swelling, spherophakia, etc.), abnormal lens position (lens luxation, lens subluxation, etc.). Abnormalities of the ciliary zonule (congenital anomalies, trauma, exfoliation 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, phacolytic glaucoma may occur with outflow of lens material. Observation of the anterior surface of the lens is also important. Following laser iridotomy and peripheral iridectomy, posterior synechiae may occur. In exfoliation glaucoma, characteristic white deposits are observed on the anterior surface of the lens and the pupillary margin.

III. Tonometry

1. Intraocular pressure

Previous studies in large numbers of subjects have shown that the distribution of intraocular pressure is skewed towards higher values and does not show a normal distribution. In the normal population, the average intraocular pressure (± standard deviation) is 15.5 (± 2.6) mm Hg and the statistically determined upper limit value of intraocular pressure is approximately 21 mmHg. However, these values are based on the results of studies conducted on Western subjects. Factors associated with intraocular pressures include age, gender, refraction, race, posture, exercise, and palpebral and ocular movement. Moreover, a variety of drugs may affect intraocular pressure. There are diurnal fluctuations in intraocular pressure, with this pressure frequently being higher in the morning, but the pattern varies among individuals. Furthermore, intraocular pressure also shows seasonal variations, with pressure being higher in the winter and lower in the summer.

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 indentation tonometers such as the Schiötz tonometer, has the advantage
that measurement values are not affected by scleral rigidity. The Tono-Pen and the Perkins applanation tonometer are portable devices in which intraocular pressure 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. Intraocular pressure measurements are lower the thinner the cornea is, and this factor should be borne in mind in interpreting intraocular pressure measurement values taken following laser surgery, such as photorefractive keratectomy (PRK) and laser \textit{in situ} keratomileusis (LASIK).

\section*{4. Gonioscopy}

1. \textbf{Anterior chamber angle}

Gonioscopy is indispensable in the diagnosis and treatment of glaucoma. In eyes with angle-closure glaucoma or a narrow angle in particular, moderate pupillary dilation may induce an acute glaucoma attack, so this should be borne in mind when using drugs that affect pupil diameter. 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 body band. Angle neovascularization may occur in ischemic conditions such as proliferative diabetic retinopathy, retinal vein occlusion, and internal carotid arterial occlusion. From a physiological standpoint, blood vessels may be observed in the 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 angle, and this may also be accompanied by peripheral anterior synechiae.

1) \textbf{Schwalbe’s line}

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

2) \textbf{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 pigmented band. In diseases such as exfoliation glaucoma, pigmentary glaucoma, and pigment dispersion syndrome, a pronounced pigmentation is frequently observed on the trabecular meshwork. In exfoliation glaucoma in particular, marked wavy pigmention may be seen anterior to Schwalbe’s line, and these are referred to as Sampaolesi line.

3) \textbf{Scleral spur}

The scleral spur is observed as a white line between the ciliary body band and the trabecular meshwork. Iris processes are frequently seen on the surface thereof. Gonioscopy of the eye with developmental glaucoma reveals an anterior insertion of the iris directly into the trabecular meshwork.

4) \textbf{Ciliary body band}

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

2. \textbf{Methods}

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

3. \textbf{Indentation gonioscopy}

Indentation gonioscopy is useful to differentiate a simple narrow angle or reversible appositional angle closure from irreversible synechial angle closure (peripheral anterior synechiae). In a goniolens used for indentation gonioscopy, the area in contact with the cornea is small and flat. The anterior chamber angle is observed by lightly pressing against the center of the cornea and pressing down on the surface of the lens and iris.
In cases with a simple narrow angle or appositional angle closure, this procedure widens the anterior chamber angle. However, in cases with synechial angle closure, the angle is not widened at the closure site. Indentation gonioscopy is useful in accurately determining the pathology of angle-closure glaucoma.

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

5. Adjunctive diagnostic method
   Ultrasound biomicroscopy is a diagnostic method 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 stage of glaucoma, they are frequently detected prior to detection of visual field abnormalities. In normal-tension glaucoma in particular, the disease is frequently diagnosed when optic nerve damage is detected. Stereoscopic evaluation of the optic disc appearance is important: slit-lamp microcopy combined with a variety of auxiliary fundus lenses is convenient and useful.

   1) Cup-to-disc (C/D) ratio
      The C/D ratio is 0.7 or greater in only 1-5% of the population. In glaucomatous eyes, with progressive optic nerve damage, the size of the optic disc cup increases, and this increase occurs predominantly in the vertical direction as compared with the horizontal direction. In normal subjects, the C/D ratio is frequently equivalent in both eyes, with asymmetry of the C/D ratio being less than 0.2 and greater than 0.2 in only 1% of the population. Asymmetry between the C/D ratios in both eyes of 0.2 or more should be regarded with suspicion until glaucoma has been excluded. Since the C/D ratio is affected by the optic disc size and refraction of the eye, assessment thereof must be carried out with caution. Additional glaucomatous changes in the optic disc include saucerization (shallow saucer-shaped expansion of the optic disc cup), notching (local thinning of the neural rim) and the laminar dot sign (exposure of the lamina cribrosa).

   2) Location of retinal vessels on the optic disc
      The location of retinal vessels in relation to the optic disc cup may have some diagnostic value. Nasalization of the vessels is thought to be a sign of glaucomatous cupping.

   3) Optic disc hemorrhage
      The prevalence of optic disc hemorrhages is 0-0.21% in normal subjects and 2.2-4.1% in glaucoma patients. The prevalence of optic disc hemorrhage is high especially in normal-tension glaucoma (up to approximately 40%). Optic disc hemorrhages are usually found in the inferotemporal sector of the optic disc, and it is frequently observed prior to changes in the optic disc or retinal nerve fiber layer or progression of visual field loss. Since optic disc hemorrhage is unusual in normal subjects, it is a significant finding, particularly if it occurs repeatedly.

   4) Peripapillary chorioretinal atrophy
      The frequency and extent of peripapillary chorioretinal atrophy are greater in glaucomatous eyes than in normal eyes. Ophthalmoscopically,
the more peripheral zone alpha is characterized by irregular hypo- and hyper-pigmentation of the retinal pigment epithelium. Zone beta is located closer to the optic disc border and is characterized by visible sclera and large choroidal vessels. Zone beta has been reported to be related to the severity and progression of glaucoma.

5) Retinal nerve fiber layer defects

In addition to changes in the optic disc, the atrophy of ganglion cell axons can be observed in the peripapillary retinal nerve fiber layer in glaucomatous eyes. Glaucoma may produce localized or diffuse defects of the retinal nerve fiber layer, or a combination of both. Early localized defects are characterized by the presence of slit or wedge-shaped defects in the nerve fiber layer. Retinal nerve fiber layer abnormalities appear as darker areas, in which visibility of the normal striation pattern is reduced or lost. In general, unlike diffuse defects, localized defects are easier to detect because they are well outlined by surrounding healthy nerve bundles. Although retinal nerve fiber layer defects are also seen in other neurological disorders as well as in normal individuals, examination of the retinal nerve fiber layer is useful in detecting early glaucomatous damage.

2. Fundus photography

Fundus photography is essential for the diagnosis and follow-up of glaucoma. It allows objective recording of the optic disc and retinal nerve fiber layer findings. Stereoscopic photography is preferred. Simultaneous stereoscopic photography is particularly useful for three-dimensional observation of the optic disc.

3. Adjunctive diagnostic devices

Diagnostic devices such as the Heidelberg Retina Tomograph (HRT), GDx Nerve Fiber Analyzer (GDx), Scanning Laser Ophthalmoscope (SLO), and Optical Coherence Tomograph (OCT) allow quantitative assessment of changes in the optic disc or retinal nerve fibers, and have therefore been reported to be useful in the diagnosis of glaucoma.

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 nasally, 70-75 degrees inferiorly, and 100-110 degrees temporally. The two means for measuring the visual field are kinetic and static perimetry. Perimeters express the brightness of the target in units of apostilbs (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 O (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 kinetic perimetry using this perimeter, the technicien moves the target to plot several isopters. Experienced technicians can obtain quite accurate results using this method.

3. Automated static perimetry

In general, automated static perimetry is more sensitive in detecting visual field abnormalities in the early stages of glaucoma than kinetic perimetry using the Goldmann perimeter. The most commonly-used perimeters for this purpose are the Humphrey and Octopus perimeters. In static perimetry, sensitivity is expressed in decibels (1 decibel (dB) = 0.1 log Unit). Although 0 decibels is the brightest optical stimulus, this is not uniform among different types of devices. For example, 0 decibels on the Humphrey perimeter indicates a different luminance from 0 decibels on the Octopus perimeter, a discrepancy that must be borne in mind. Measurement results are affected by factors such as blepharoptosis, refractive error, media opacities, pupil size, and aging. Fixation loss rate, false-positive and false-negative rates, and short-term fluctuation are useful indices in evaluating the reliability of measurement results. The technician's degree of experi-
ence is also important, with first-time test results generally being less reliable than subsequent test results. Test results are expressed using threshold values, grayscale (graphic grayscale display of threshold values), total deviation (difference between the patient’s results and age-matched normals), and pattern deviation (similar to the total deviation except that it is adjusted for any generalized depression in the overall field which might be caused by other factors such as lens opacities or miosis).

1) Humphrey perimeter

The central 24-2 or central 30-2 program is ordinarily used. The background luminance is 31.5 asb, stimulus time is 0.2 seconds, and stimulus intensity is 0-50 dB, with a maximum luminance of 10,000 asb.

(1) Reliability indices

i. Fixation loss rate

Cases in which there is a response with a target displayed in the blind spot are evaluated as fixation loss. If the fixation loss rate exceeds 20%, reliability is assessed as low and XX is displayed.

ii. False-positive rate

Cases in which there is a response even though a target is not displayed are assessed as false-positive. If the false-positive rate exceeds 33%, reliability is assessed as low and XX is displayed.

iii. False-negative rate

Cases in which there is no response at sites with a confirmed response even though a high-luminance target is displayed are assessed as false-negative. If the false-negative rate exceeds 33%, reliability is assessed as low and XX is displayed.

2) Octopus perimeter

The Octopus 1-2-3, 300 Series is an automatic perimeter allowing visual field measurement within a central 30 degree-field, and it features a compact design using the direct projection system. The Octopus 101 is an automated projection perimeter that allows static and kinetic perimetry within the entire field. The standard measurement conditions are background illumination of 31.4 asb (1-2-3, 300 Series, 101: static perimetry), 4 asb (101: static perimetry), stimulus time of 0.1 seconds, stimulus intensity of 0-40 dB (1-2-3, 300 Series), 0-47 dB (101), maximum illumination of 4,000 asb (1-2-3), 4,800 asb (300 Series), and 1,000 asb (101). The programs used for glaucoma diagnosis are the G1X (1-2-3, 300 Series) and the G2 (101).

3) New techniques for visual field measurement

Recent newly-developed techniques for visual field measurement include the Octopus dynamic strategy, the TOP strategy, and the Humphrey SITA program, which permit time-efficient visual field measurements. Moreover, methods reported to be effective in the diagnosis of glaucoma at the earliest stage include blue on yellow perimetry (SWAP), frequency doubling technology, and flicker perimetry.

4. Classifications of glaucomatous visual field defects

1) Kosaki classification (based on kinetic Goldmann perimetry)\textsuperscript{4,5}

Stage I: Earliest stage without any field changes by kinetic Goldmann perimetry.

a: Normal field
b: Pathologic field detected only when a more precise method is used.

Stage II: Early stage with abnormal field for isopters I-4, I-3, I-2, and I-1, but without any abnormalities for an isopter V-4.

a: Normal for an isopter I-4, but abnormal for isopters I-3, I-2, and I-1.
b: Abnormal for all I isopters.

Stage III: Middle stage, with abnormal field for an isopter V-4, but with field loss not exceeding 1/2 of the normal field for V-4 target (V-4 field).

a: Field loss (contraction) not exceeding 1/4 of V-4 field.
b: Field loss more than 1/4 but less than 1/2 of V-4 field.

Stage IV: Late stages, with field loss exceeding 1/2 of V-4 field, but with preserved macular field.

Stage V: Very late stage.

a: Macular field only.
b: Without macular field, but with preserved field outside the macular field.
Stage VI: End stage with loss of V-4 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) Criteria for glaucomatous visual field defects (Humphrey perimetry)
Any of the following:
1. 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%);
2. The pattern standard deviation (or corrected pattern standard deviation) has a value that occurs in less than 5% of normal reliable fields (P < 5%); or
3. The glaucoma hemifield test indicates that the field is abnormal.

4) Classification of glaucomatous visual field defects (Humphrey perimetry)
An early defect meets all the following requirements:
1. The mean deviation is better than -6 dB;
2. 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;
3. Fewer than 10 points are defective at the 1% level; and
4. 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:
1. The mean deviation is worse than -12 dB;
2. More than 37 (50%) of the points depressed at the 5% level;
3. More than 20 points depressed at the 1% level;
4. A point in the central 5 degrees with 0-dB sensitivity; or
5. Points closer than 5 degrees of fixation under 15-dB sensitivity in both the upper and lower hemifields.

References
7) **Anderson DR, Patella VM**: Automated Static Perimetry. 2nd edition, 121-190, Mosby, St Louis, 1999.

-------------------
Principles of Treatment for Glaucoma

I. Principles of glaucoma therapy

1. The goal of therapy is to preserve the patient's visual function
The goal of glaucoma therapy at the present time is to maintain the patient's visual function. Visual function damage severely impairs patients' quality of life (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 implications imposed by hospital visits and/or hospitalization and the damage to QOL caused by constant worry about losing eyesight.

2. The most reliable therapy is reduction of intraocular pressure
At present, based on the evidence, the only reliable therapy for glaucoma is to lower intraocular pressure. Other therapeutic concepts are currently being attempted that might prove effective in the future. Enhancement of the optic nerve head blood flow and neuroprotective therapy of ganglion cells have attracted attention as new therapeutic methods.

3. Causal therapy must be provided for all treatable factors causing elevation of intraocular pressure
If it is possible to treat a causal factor in elevation of intraocular pressure, this factor must be treated in conjunction with therapy to lower intraocular pressure. Types of causal therapy include peripheral iridotomy in types of glaucoma in which pupillary block causes elevation of intraocular pressure, such as primary angle-closure glaucoma, antiinflammatory treatment in glaucoma with accompanying 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. Moreover, in the advanced 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, the choice of therapy must take into account factors such as QOL, treatment costs, and compliance.

6. Selecting among drugs, laser treatment, and surgery
As the therapeutic options in glaucoma include drug treatment, laser treatment, and surgical treatment, an appropriate therapeutic modality must be selected based on the individual patient and the disease stage and type. Concomitant use of multiple drugs may increase adverse effects and reduce compliance. Generally speaking, when three or more drugs are required to control intraocular pressure, other therapeutic options such as laser treatment or invasive surgery should be considered.

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, normal-tension glaucoma, primary angle-closure glaucoma following iridotomy, chronic secondary glaucoma, etc.

1. Baseline data determination
Patient status prior to treatment is important as a baseline. Unless treatment must be begun on an emergency basis, such as in late-stage cases, it is preferable to determine baseline data such as intraocular pressure, 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 irre-
versible and assessment of therapeutic effect takes long periods due to the chronic course of the illness, it is rational to treat glaucoma by setting an intraocular pressure at which it is believed that the progression of optic nerve damage can be prevented (target intraocular pressure) (see flow charts V-Ⅵ).

1) Setting of target intraocular pressure

Although it is difficult to accurately determine in advance the intraocular pressure that can prevent further optic nerve damage, this target pressure can be set for each individual case taking into account the factors listed in Table 4-1 (see flow chart ᶜ).

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

- Baseline intraocular pressure level before treatment
- Stage of glaucoma
- Age/life expectancy of patient
- Status of fellow eye
- Family history
- Other risk factors

As an example of target intraocular pressure 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 moderate stage, and 14 mmHg or below for the later stage. In normal-tension glaucoma, however, it has been found that progression of visual field damage is significantly decreased by lowering intraocular pressure 30% from the initial level at which disease progression is confirmed, and the approach has been considered of setting the target at 30% reduction of intraocular pressure from the baseline level.

2) Re-evaluation of target intraocular pressure

One limitation on the method of treatment according to a target intraocular pressure is the fact that the validity of the initially set value can only be assessed after a certain period of time. In other words, the target intraocular pressure can only be confirmed to be appropriate when the progression of optic nerve damage is halted. The target intraocular pressure is not an absolute value; just as there are cases that progress even when the target intraocular pressure has been achieved, there are also cases that show no progression even though this target has not been achieved. Accordingly, the target intraocular pressure must periodically be reevaluated and revised. For example, in cases where progression of visual field damage is observed, the target intraocular pressure must be revised downward. However, in reevaluating this target intraocular pressure, factors such as unfavorable compliance and diurnal fluctuations in pressure during the treatment period must be excluded. Moreover, if treatment is found to cause adverse effects or influence QOL, one must evaluate whether it is necessary to maintain the target intraocular pressure. It is important to remember that the target intraocular pressure is merely a therapeutic means rather than a therapeutic objective, and it would be a mistake to overemphasize this target pressure.

3. Glaucoma and QOL

QOL is one of the most important factors for the patient. Damage to visual function due to glaucoma has an enormous effect on QOL, but there is the possibility that being diagnosed as having a chronic and potentially blinding disease, 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, the physician should discuss the possibility of discontinuing treatment with the patient.

4. Compliance with glaucoma drug treatment

Glaucoma is a progressive disease that follows
an extremely chronic course, requiring long-term administration of eye drops and periodic observation of the patient's course, 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. Poor compliance (Table 4-2) is an important factor in the progression of glaucomatous visual field damage, and in selecting drugs for glaucoma treatment, compliance is therefore a vital consideration.

Table 4-2. Poor compliance

- Forgetting to instill eye drops
- Excessive use of eye drops (over-dosage may cause systemic adverse effects)
- Ineffective technique of self-administration
- Self-administration of non-prescribed drug
- Improper timing of eye drops (frequently a problem when multiple drugs are prescribed or immediately after the prescription is changed)

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

1) Adrenergic agonists
   (1) Nonselective
   (2) $\alpha$-selective

2) Adrenergic antagonists
   (1) $\beta$-blockers
      i. Nonselective
      ii. $\beta_1$-selective
   (2) $\alpha$-blockers
   (3) $\alpha_1$-blockers

3) Parasympathomimetics

4) Prostaglandin analogues

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

6) Hyperosmotics

#### 2. Selection of drugs

In open-angle glaucomas such as primary open-angle glaucoma and normal-tension glaucoma, $\beta$-blockers have an outstanding effect of lowering intraocular pressure and are favorably tolerated, and they have therefore been in use for many years as the drug of first choice. In recent years, moreover, because of their powerful intraocular pressure-lowering effect, prostaglandin analogues have also been used as first choice drugs. However, in patients in whom the use of $\beta$-blockers and prostaglandin analogues is unsuitable because of adverse effects, eye drop preparations such as carbonic anhydrase inhibitors, $\alpha$-blockers, nonselective adrenergic agonists, and parasympathomimetics have been used as the drugs of choice.

#### 3. Treatment trials

There are individual differences in drug effect, and intraocular pressure also varies both day-to-day and diurnally. Topical treatment should be started in one eye if possible, determining the intraocular ocular pressure lowering effect and adverse effects (one-eye trial), and then after the effect has been confirmed, we should begin administration in both eyes. In evaluating $\beta$-blockers, however, it should be borne in mind that these drugs also exert a slight intraocular pressure-lowering effect in the untreated fellow eye.

#### 4. Guidance in administration

In order to increase efficacy by improving intraocular distribution, while minimizing adverse effects by reducing systemic distribution 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 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 excess solution from eye drops that have overflowed around the eye and wash off any eye drops adhering to the hands.
- When multiple eye drop solutions are used, the administration interval should be 5 minutes or longer.

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 mechanism of lowering intraocular pressure, these combinations frequently do reduce intraocular pressure in actual use. The combined effect of such administration should be confirmed in actual trial use according to the points listed in Table 4-3.

Table 4-3. Practical points for combined drug therapy

- Drugs are to be added only when necessary.
- If the effect of a drug is insufficient or tachyphylaxis occurs, one should first try switching to a different drug rather than adding a further drug.
- Drugs having the same pharmacological action should not be used in combination. For example, a combination of two β-blockers or a combination of carbonic anhydrase inhibitors in eye drop and oral form should not be administered.
- Even if eye drops are administered more frequently than prescribed in the dosage regimen, this will not decrease intraocular pressure, but will increase adverse effects.
- In view of the intraocular pressure-lowering effect, adverse effects, and the effect on compliance, if three or more drugs are required in combination, other therapeutic measures such as laser surgery or incisional surgery should be considered as options.

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 as 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) Adrenergic agonists
(1) Nonselective

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Action</th>
<th>Dosage regimen</th>
<th>Main adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine</td>
<td>Increases aqueous outflow via Schlemm's canal</td>
<td>Dipivefrin 0.04%, 0.1%: 2 x daily Epinephrine 1.25%: 2 x daily</td>
<td>Allergic conjunctivitis/blepharitis, conjunctival hyperemia, mydriasis, ocular pain, cardiopalmus, pigment deposition (conjuncti-</td>
</tr>
</tbody>
</table>
va, cornea, nasolacrimal ducts), ocular pemphigoid, macular edema, headache, sweating, tremor

Contraindications
1. Patients with occludable angles (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. Hyperthyroidism

(2) $\alpha$-selective
Used to prevent transient elevation of intraocular pressure following laser surgery

Generic name
Apraclonidine

Action
Decreases aqueous production

Dosage regimen
Apraclonidine 1%: Instillation 1 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) Adrenergic antagonists
(1) $\beta$ -blockers

Generic name
1. Nonselective

Timolol
Carteolol
Befunolol
Levobunolol
2. $\beta_1$-selective
Betaxolol

Action
Decreases aqueous production

Dosage regimen
Timolol 0.25%, 0.5%: 2 x daily (Long-acting form: 1 x daily)
Carteolol: 1%, 2%: 2 x daily
Befunolol 0.25%, 0.5%, 1%: 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, asthma 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 $\beta$-receptor blockade)
2. Patients with uncontrolled heart failure, sinus bradycardia, ventricular block (grades $\Pi$, $\Pi\Pi$), or cardiogenic shock (these symptoms may be aggravated due to a negative chronotropic/inotropic action resulting from $\beta$ -receptor blockade)
3. Patients with a history of hypersensitivity to any ingredients of the drug

$\beta_1$ 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:
Nonselective:
1. Right heart failure due to pulmonary hypertension
2. Congestive heart failure
3. Diabetic ketoacidosis or metabolic acidosis
4. Uncontrolled diabetes

β₁ selective:
1. Sinus bradycardia, ventricular block (grades II, III), cardiogenic shock, congestive heart failure
2. Uncontrolled diabetes
3. Asthma, bronchospasms, or uncontrolled obstructive pulmonary disease

(2) α - β-blocking
Generic name
  Nipradilol
Action
  Decreases aqueous production
  Increases uveoscleral outflow
Dosage regimen
  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) α₂-blockers
Generic name
  Bunazosin
Action
  Increases uveoscleral aqueous outflow
Dosage regimen
  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 (cholinergic drugs)
Generic name
  Pilocarpine
  Carbachol
Action
  Increases aqueous outflow via Schlemm's canal
Dosage regimen
  Pilocarpine 0.5-4%: 4 x daily
  Carbachol 0.75%: 3-6 x daily
Main adverse effects
  Aphose due to miosis, deteriorated visual acuity, accommodation disorders due to ciliary muscle contraction, myopia, browache, 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, intraocular pressure 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 hyperthyroidism may occur, these drugs should be administered with caution

4) Prostaglandin analogues
Generic name
Unoprostone  
Latanoprost  
Action  
Increases uveoscleral aqueous outflow  
Dosage regimen  
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 of the 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 infection  
5. Pregnant women, women in labor, nursing mothers  

5) Carbonic anhydrase inhibitors  
(1) Eye drops  
Generic name  
Dorzolamide  
Action  
Decreases aqueous production  
Dosage regimen  
Dorzolamide 0.5%, 1.0%: 3 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  
Generic name  
Acetazolamide  
Action  
Decreases aqueous production  
Dosage regimen  
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 severe coronary sclerosis or cerebral arteriosclerosis
3. Patients with severe renal damage
4. Patients with liver disease/liver function disorders
5. Patients with severe 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

Generic name
D-mannitol

Action
Decreases vitreous volume

Dosage regimen
- 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 intraocular pressure

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

Generic name
Glycerin

Action
Decreases vitreous volume

Dosage regimen
- 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, diabetic coma (preparations with added fructose), rebound elevation of intraocular pressure

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

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

(3) Isosorbide
Generic name
Isobide
Action
Decreases vitreous volume
Dosage regimen
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

IV. Laser surgery

1. Laser iridotony
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 therapy of first choice 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 1 hour before surgery.
(2) In order to prevent transient postoperative elevation of intraocular pressure, apraclonidine is instilled 1 hour before and immediately after surgery.
(3) In the event of corneal edema, drugs such as carbonic anhydrase inhibitors or hyperosmotics are considered to make the cornea transparent prior to surgery.
(4) The operation 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 covered by 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 parenchyma of the iris.
3. In order to prevent iridial hemorrhage, the planned penetration site is pre-irradiated using an argon laser, etc.

(2) Thermocoagulation 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: 1,000 mW  
Duration: 0.02 seconds  
As the pigment rises up from the irradiation site in the form of oily smoke when perforation is achieved, further irradiation is carried out in order to expand the perforation wound so that it will be sufficiently large to relieve the pupillary block (100-200 μm).

7) Complications
- Corectopia  
- Anterior chamber hemorrhage  
- Corneal opacity  
- Bullous keratopathy  
- Postoperative iritis  
- Localized cataracts  
- Transient postoperative elevation of intraocular pressure  
- Posterior synechia  
- Reclosure of penetration wound  
- Unintended retinal irradiation

8) Postoperative management
   (1) Intraocular pressure 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 will often resolve spontaneously even without administration of adrenocortical 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, exfoliation glaucoma, pigmentary glaucoma, primary angle-closure glaucoma following laser iridotomy, mixed glaucoma, etc.

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

3) Preoperative preparation
   (1) In order to prevent transient postoperative increases in intraocular pressure, apraclonidine is given by instillation in the eye 1 hour before and immediately after surgery.  
   (2) The procedure is carried out under topical anesthesia.

4) Contact lens
   Goniolens for laser coagulation use

5) Technique/surgical site
   An argon laser, diode laser, etc., is used. Approximately 25 applications are performed per quadrant at uniform intervals along 90° to 180° of the anterior chamber angle on the trabecular pigment band.

6) Laser settings
   Spot size: 50 μm  
   Power: 400-800 mW (allows depigmentation without the occurrence of small bubbles)  
   Duration: 0.1 seconds

7) Complications
   - Posterior chamber hemorrhage  
   - Peripheral anterior synechia  
   - Postoperative iritis  
   - Postoperative elevation of intraocular pressure

8) Postoperative management
   (1) Intraocular pressure is measured 1-3 hours after surgery in order to determine whether transient elevation has occurred.  
   (2) Carbonic anhydrase inhibitors or hyperosmotics are administered as needed.  
   (3) Postoperative inflammation will often resolve spontaneously even without administration of adrenocortical steroids.

9) Other
   In order to perform less invasive trabeculoplasty, a dedicated half-wavelength (Nd-YAG) laser unit has been developed.
3. Laser gonioplasty (laser peripheral iridoplasty)

1) Purpose
   To contract the periphery of the iris by laser thermocoagulation in order to widen the anterior chamber angle.

2) Indications
   Performed in cases where laser iridotomy cannot be carried out due to corneal opacity in angle-closure due to plateau iris syndrome or pupillary block, cases of primary open-angle glaucoma with a narrow anterior chamber angle as a preliminary step to laser trabeculoplasty, or in eyes following goniosynechiolysis in order to prevent postoperative recurrence of synechia. However, this procedure is ineffective in subjects who have already developed peripheral anterior synechia. Moreover, in performing this procedure in glaucoma due to pupillary block, laser iridotomy should be performed at as early a stage as possible.

3) Preoperative preparation
   (1) In order to prevent transient postoperative elevation of intraocular pressure, apraclonidine is instilled 1 hour before and immediately after surgery.
   (2) The operation is carried out under topical anesthesia.

4) Lens
   A goniolens or contact lens for iridotomy is used.

5) Technique/surgical site
   Coagulation is carried out with a width of 1-2 rows on the periphery of the iris 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 intraocular pressure
   - Postoperative iritis
   - Correctopia

8) Postoperative management
   (1) Intraocular pressure 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 will often resolve spontaneously even without administration of adrenocortical steroids.

4. Cyclophotocoagulation

1) Purpose
   The ciliary body is destroyed with a laser in order to inhibit aqueous production and thereby reduce intraocular pressure.

2) Indications
   Indicated in subjects in whom other glaucoma surgery such as filtering surgery has been ineffective or is not feasible. As serious complications may occur, this procedure is to be considered a last resort for reducing intraocular pressure.
   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 each time over 180°-270°.

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

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

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

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

2) Indications
Cases in which it is assessed that 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 thread.
(2) Topical anesthesia is performed.

4) Lens
Lens for laser suturelysis.

5) Technique/surgical site
Thermocoagulation laser (use of a red laser is preferred in order to prevent burning of the conjunctiva). 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 burning, perforation
Excessive filtration

8) Postoperative management
Intraocular pressure and filtering bleb status are to be confirmed.

V. Invasive surgery

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

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

Table 4-4. Items to be considered in determining glaucoma surgery indication

- Glaucoma status
  Disease stage
  Disease type
  Intraocular pressure
  History of glaucoma surgery
- Nonsurgical treatment prognosis
  Intraocular pressure-lowering-effect
  Adverse effects, complications
  Compliance
  Visual function prognosis
- Prognosis for surgical therapy
  Intraocular pressure-lowering-effect
  Surgical complications
  Visual function prognosis
- Patient factors
  Social factors such as occupation and family environment
  Disease awareness
  Age
  Ophthalmic diseases other than glaucoma
  Systemic condition
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 new 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 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) Filtering 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 tissue. The most serious complication is late infection of the filtering bleb. Patients undergoing filtering surgery such as trabeculectomy should be given sufficient explanation concerning the risk of late infections.

(1) Full-thickness filtering surgery

In this surgery, rather than preparing a scleral flap, a direct aqueous outflow pathway from the anterior chamber is created underneath the conjunctiva. Compared to filtering 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 results. Moreover, the introduction of laser suturelysis has made it possible to regulate intraocular pressure after surgery, thus decreasing complications due to excess filtration such as hypotony. Although re-surgery and other treatments are required in some cases, long-term intraocular pressure 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 intraocular pressure. Long-term results of the procedure have not yet been sufficiently studied.

(4) Seton implant 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 concomitant administration of antimetabolites has been unsuccessful, patients showing severe conjunctival scarring as a result of previous surgeries, patients with little prospect of success in trabeculectomy, and patients in whom filtering surgery is difficult from a technical standpoint. The specialized implant is not approved in Japan as a medical device.

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 to 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 intraocular pressure. This procedure is more effective if carried out concurrently with cataract surgery.
(3) Goniotomy

Under observation with a goniolens, a scalpel 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 intraocular pressure 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


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 intraocular pressure (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 VI, 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 $a_2$ adrenergic agonist (apraclonidine) is effective in preventing IOP elevation following laser irradiation. However, it does not completely prevent IOP elevation, and IOP should be monitored continuously.

   3) Invasive surgery (with postoperative medication if necessary)

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

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

      (3) Seton implant surgery

The most widely used surgical procedure at present is trabeculectomy. The IOP level achieved by trabeculotomy is in the upper level.
of 10 mm Hg, 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.

In filtering surgery, the formation of filtering blebs in the inferior region is associated with an extremely high risk of postoperative infection. Therefore, Seton surgery is frequently indicated in many countries for patients whose upper optical field is unsuitable for filtering surgery. However, the Seton implant has 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 undergo 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.

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 filtrating 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 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. 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. Since this type of glaucoma is bilateral, when one eye undergoes laser iridotomy or iridectomy for acute glaucoma attack or chronic angle-closure glaucoma, the fellow eye also is given the same procedure as a preventive measure.

(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.

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

b. Oral administration

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

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

2. Surgical treatment

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 iridotomy 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. $\beta$-adrenergic blockers
c. $\alpha-\beta$-adrenergic blockers
d. $\alpha_1$-adrenergic blockers
e. Parasympathomimetics
f. Carbonic anhydrase inhibitors

B. Surgical treatment
a. Laser trabeculoplasty
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 synechia is likely to develop following irradiation.

b. Reconstruction of aqueous outflow pathways (goniosynechiolysis, trabeculotomy)
This procedure is indicated in patients with extensive peripheral anterior synechia (e.g., involving over half of the anterior chamber angle). It has been reported that when combined with cataract extraction (plus intraocular lenses implantation), this procedure produces an excellent IOP-lowering effect by preventing synechia reformation.

c. Trabeculectomy
This procedure is used when medical treatment has failed to achieve sufficient IOP control; when there is long-standing peripheral anterior synechia; 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.

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.

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.
5. Ocular hypertension

Of patients with IOP above the statistically determined normal upper limit without anomalies of the optic nerve or visual field, only 1-2% progress to primary open-angle glaucoma annually. In a multicenter trial conducted recently 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 mmHg or lower) and followed for 5 years. The occurrence of visual field damage or optic nerve damage was significantly lower in the treatment group. However, the effect of treatment in patients with IOP lower than 24 mmHg was not investigated. Accordingly, IOP slightly above the normal upper limit alone does not justify treatment. Patients with repeatedly measured IOPs in the upper 20s or with risk factors such as a family history of glaucoma (see Section 2) should be treated with acceptable eye drops.

Patients with ocular hypertension are observed without treatment at an interval of one to several months. For patients whose optic nerve and visual field are confirmed to be normal and without risk factors for progression to primary open-angle glaucoma in the follow-up examination, IOP measurement, optic nerve examination and perimetry can be conducted at 1-2 year intervals.

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 trabeculectomy or surgical reconstruction of aqueous outflow pathways (trabeculotomy) has not been confirmed. Seton 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. Seton 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
Seton 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 fraction, 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. Seton 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 intumescent, microophthalmia, posterior synechia, lens dislocation, epithelial ingrowth, etc.
Treatment must be selected based on the mechanisms causing pupillary block.
(1) Administration of topical and systemic ocular 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

Glucoma 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)

Glaucoma 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 (glaucoma 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)

Seton 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 for 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) Filtering 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) Seton 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 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.

IV. Secondary glaucomas in childhood

Retinopathy of prematurity, retinoblastoma, juvenile xanthogranuloma, etc.

With incidence, onset, and IOP elevation mechanism varying widely in pediatric secondary glaucoma, treatment methods are not uniform.