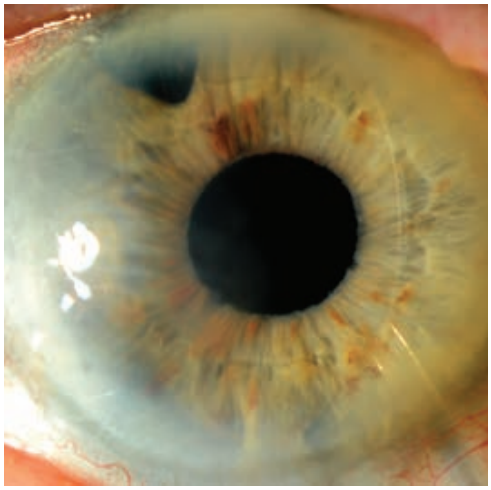
EUPO

European University Professors of Ophthalmology

Training future ophthalmologists : including you

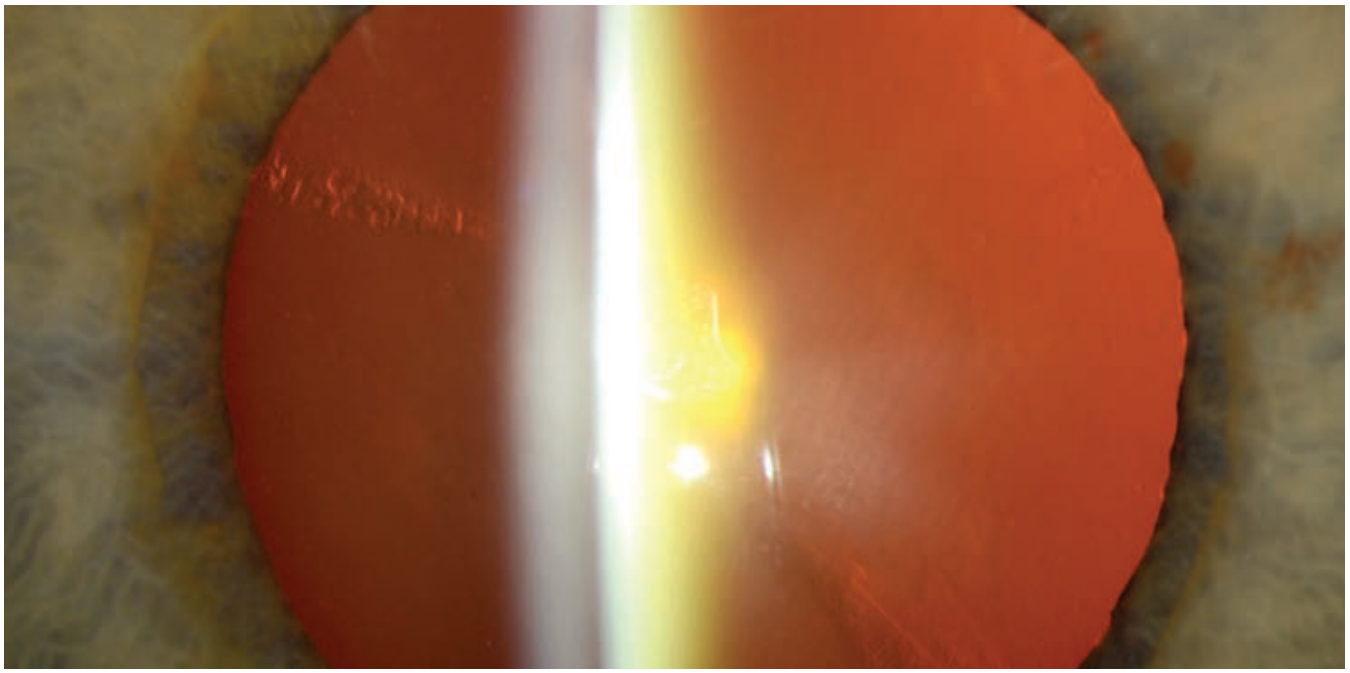
June 15-16, 2019 in NICE, France

Glaucoma & Cataract



Course Directors:

- Glaucoma: Prof. Carlo E. Traverso, University of Genova, Italy
- Cataract: Prof. Marie-José Tassignon, University of Antwerp, Belgium



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The Sequence of the EUPO Courses

2019	Nice (SOE)	Glaucoma & Cataract
2018	Nice (EVER)	Retina, Intraocular Inflammation & Uveitis
2017	Barcelona (SOE)	Cornea, Conjunctiva & Refractive Surgery
2016	Nice (EVER)	Neuro-ophthalmology & Strabismus
2015	Vienna (SOE)	Uveitis & Glaucoma
2014	Nice (EVER)	Retina
2013	Copenhagen (SOE)	Cornea, Conjunctiva & Refractive Surgery
2012	Leuven	Neuro-ophthalmology & Strabismus
2011	Geneva (SOE)	Uveitis & Glaucoma
2010	Athens	Retina
2009	Amsterdam (SOE)	Cornea, Conjunctiva & Refractive Surgery
2008	Geneva	Neuro-ophthalmology & Strabismus
2007	Vienna (SOE)	Glaucoma & Uveitis
2006	Ghent	Retina
2005	Berlin (SOE)	Cornea
2004	Nijmegen	Neuro-ophthalmology & Strabismus
2003	Madrid (SOE)	Glaucoma & Uveitis
2002	Erlangen	Retina
2001	Istanbul (SOE)	Cornea
2000	Leuven	Neuro-ophthalmology & Strabismus
1999	Stockholm (SOE)	Glaucoma & Uveitis
1998	Amsterdam (ICO)	Chorioretina
1997	Budapest (SOE)	Cornea, Conjunctiva, Lids & Orbit
1996	Athens	Neuro-ophthalmology & Strabismus
1995	Milano (SOE)	Uveitis, Lens & Glaucoma
1994	Montpellier	Retina
1993	Santiago de Compostella	The External Eye
1992	Brussels (SOE)	Neuro-ophthalmology & Strabismus
1991	Torino	Uveitis, Lens & Glaucoma
1990	Bonn	Chorioretina
1989	Leuven	The External Eye & Orbit
1988	Nijmegen	The First EUPO Course

Word from the EUPO President

Bienvenue à Nice !

Whether you are a resident looking forward to eventually passing your final examination or a specialist looking toward an update on glaucoma and cataract, we – your EUPO Course Faculty, representing the European University Professors of Ophthalmology – are most delighted to have you here with us. This course is for you.

The EUPO course is a tradition established three decades ago, in 1988. It provides annual structured subspecialty instruction in four fields of ophthalmology, rotating on a yearly basis. Key points of the ophthalmology curriculum are covered so as to provide a full and broad update on most relevant and latest knowledge for delegates who partake in all four courses.

The course is an excellent concept, yet every endeavour benefits from continuous feedback and assessment. Upon returning home, please, make use of the opportunity to provide comments and suggestions to the Faculty and contribute to the future of the EUPO Course. We will much appreciate your opinion!

We have redesigned the EUPO Course Cycle for years 2018 to 2021 by aligning it more precisely with the four viva voces of the European Board of Ophthalmology (EBO) Diploma Examination in which about 650 residents and specialists sit annually. The topic this year is thus "Glaucoma & Cataract" and in the next two years the topics are "Strabismus, Paediatric ophthalmology and Neuro-ophthalmology" and "Cornea, External Diseases, Orbit and Ocular Adnexa". We definitely hope to see you again.

The structure of the Course likewise was thoroughly revised in 2018 by then Course Directors Prof. Catherine Creuzot-Garcher and Prof. Bahram Bodaghi. Short lectures are amended with case-based round tables that resemble the EBO viva voces and, hopefully, further help residents prepare for that part of the Diploma Examination. Moreover, the course even more than before focuses on what is new since the previous EUPO course on the same topic.

We have kept the EUPO Course Book with its key point summaries of most talks that you are presently reading. At the end of most summaries, you will find a brief list of recommended reading that directs you to recent literature on each topic; papers that often include important new information not yet incorporated in your textbooks. We recommend that you familiarise yourself with these references e.g. when you prepare for your final examinations.

The Faculty is at your disposal for the next two days. Make use of this opportunity and bombard it with questions and comments!

Thank you to the SOE Board for its collaboration in organising the EUPO Course.

Tero Kivelä, MD, FEBO
President, EUPO

available on www.eupo.eu

EUPO 2019
Glaucoma & Cataract

EUPO 2018
Retina, Intraocular
Inflammation & Uveitis

EUPO 2017
Cornea, Conjunctiva
& Refractive Surgery

EUPO 2016
Neuro-ophthalmology
& Strabismus

EUPO 2015
Uveitis & Glaucoma

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& Strabismus

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EUPO 2010
Retina

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Cornea, Conjunctiva
& Refractive Surgery

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Neuro-Ophthalmology
& Strabismus

EUPO 2007
Uveitis

EUPO 2006
Retina

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Programme EUPO 2019
Saturday, June 15

Course directors: Carlo E. TRAVERSO, Marie-José TASSIGNON

• Introduction to the EUPO Course — 08:00 - 08:15

Introduction EUPO by President Tero KIVELÄ

Introduction EUPO 2019 course by Course Director Marie-José TASSIGNON

• Glaucoma 1: Physiology and Examination Techniques — 08:15 - 09:35

Moderators: Karl MERCIECA, Luis PINTO

		Course	Page
• 08:15	Pathophysiology *MERCIECA K (UK)*	01	12
• 08:35	Tonometry and pachymetry *CUTOLO CA (Italy)*	02	20
• 08:55	Gonioscopy and anterior segment OCT *PINTO L (Portugal)*	03	25
• 09:15	Disc and RNFL exam *IESTER M (Italy)*	04	30

• Break — 09:35 - 10:00

Programme EUPO 2019
Saturday, June 15

Course directors: Carlo E. TRAVERSO, Marie-José TASSIGNON

- **Cataract 1: Pathophysiology and Surgical Techniques** **10:00 - 11:45**

  Moderators: Sorcha NI DHUBHGHAILL, Ewa MRUKWA KOMINEK

• 10:00	Optical characteristics of the cataractous lens *SÖDERBERG P (Sweden)*	05	34
• 10:15	IOL calculation: How precise are we? *HIRNSCHALL N (Austria)*	06	42
• 10:30	IOL optics *TASSIGNON MJ (Belgium)*	07	44
• 10:45	Ideal wound shape and wound size *NI DHUBHGHAILL S (Belgium)*	08	49
• 11:00	What OVD to choose? *NI DHUBHGHAILL S (Belgium)*	09	55

- **Round table: How Do You Diagnose These Cases?** **11:15 - 11:45**

  Moderator: Marie-José TASSIGNON 61

  Panel: Faculty members

- **Lunch break** **11:45 - 13:15**

Programme EUPO 2019
Saturday, June 15

Course directors: Carlo E. TRAVERSO, Marie-José TASSIGNON

• SOE: Theodor Axenfeld Lecture **13:15 - 14:00**

A 20-year Journey Towards Gaining Insight into Glaucoma. The Thessaloniki Eye Study
TOPOUZIS F (Greece)

• Glaucoma 2: Visual Fields and Intraocular Pressure **14:15 - 14:45**

Moderators: Ingrida JANULIEVICIENE, Luciano QUARANTA

• 14:15	Perimetry *GONI F (Spain)*	10	66
• 14:35	Glaucoma classification/differential diagnosis *QUARANTA L (Italy)*	11	70
• 14:55	Treatment principles and Target IOP *JANULIEVICIENE I (Lithuania)*	12	76
• 15:15	IOP-lowering medications *THYGESEN J (Denmark)*	13	81
• 15:35	How do you diagnose this... *Audience*		92

• Break **15:45 - 16:15**

Programme EUPO 2019
Saturday, June 15

Course directors: Carlo E. TRAVERSO, Marie-José TASSIGNON

• Cataract 2: Tips and Tricks of the Trade **16:15 - 17:45**

Moderators: Rafael BARRAQUER, Nino HIRNSCHALL

• 16:15	Anterior capsulorhexis: how to excel *BLANCKAERT J (Belgium)*	14	93
• 16:30	Lens extraction techniques *REUS N (The Netherlands)*	15	102
• 16:45	Paediatric cataract surgery *BILLOTTE C (France)*	16	107
• 17:00	Toric IOLs, corneal marking *HIRNSCHALL N (Austria)*	17	111
• 17:15	Myth and reality about accommodative/EDOF IOLs *BARRAQUER R (Spain)*	18	113
• 17:30	How do I treat this patient... *Audience*		115

Programme EUPO 2019
Sunday, June 16

Course directors: Carlo E. TRAVERSO, Marie-José TASSIGNON

• Glaucoma 3: Is Medication Not Enough? **08:00 - 09:30**

Moderators: Carlo TRAVERSO, Gordana SUNARIC-MEGEVAND

• 08:00	Laser treatment *HOMMER A (Austria)*	19	116
• 08:20	Filtration surgery *CVENKEL B (Slovenia)*	20	120
• 08:40	Alternative IOP lowering surgery *SUNARIC MEGEVAND G (Switzerland)*	21	128
• 09:00	Phacoemulsification in glaucoma *TRAVERSO C (Italy)*	22	137
• 09:20	How do I treat this patient... *Audience*		139

• Break **09:30 - 10:00**

Programme EUPO 2019
Sunday, June 16

Course directors: Carlo E. TRAVERSO, Marie-José TASSIGNON

• Cataract 3: The Going Gets Tough — 10:00 - 11:30

Moderators: Christian BILLOTTE, Tillmann ECKERT

• 10:00	When to call the vitreoretinal surgeon? *SPIELBERG L (Belgium)*	23	142
• 10:15	Postoperative retinal detachment *TILLMANN E (Germany)*	24	144
• 10:30	Pseudophakic macular oedema *WIELDERS L (The Netherlands)*	25	154
• 10:45	Pre- and postoperative prevention of endophthalmitis *MRUKWA KOMINEK E (Poland)*	26	160
• 11:00	Cataract and uveitis *VAN OS L (Belgium)*	27	167
• 11:15	Discussion *Audience*		

• Break — 11:30 - 11:45

• Round table: My Job is Difficult! — 11:45 - 12:15

Moderators: Carlo E. TRAVERSO 175

Panel: Faculty members

• Closing & Farewell — 12:15 - 12:30

Moderator: Course director, Carlo E. TRAVERSO

01

Pathophysiology

Karl MERCIECA - UK

MCQs

1. **In glaucoma:**
   a. Lowering IOP by 20–40% reduces the rate of progressive visual field loss by 50%
   b. Non-IOP-dependent risk factors appear to play an important role in approximately 10% of patients
   c. Retinal ganglion cell (RGC) loss occurs late in the glaucoma disease process
   d. IOP is only one of several known modifiable risk factors

2. **With regard to glutamate excitotoxicity in glaucoma:**
   a. In glaucoma, the initial insult to RGCs leads to reduced levels of extracellular glutamate
   b. Glutamate exerts a neuro-protective effect in glaucoma
   c. *N*-methyl-D-asparate (NMDA) receptors are overstimulated in glaucoma, resulting in a large influx of calcium into neurons with resulting RGC death
   d. Memantine, an NMDA-receptor antagonist, has been shown to slow down glaucoma progression in large phase III clinical trials

3. **With regard to oxidative stress and nitric oxide (NO) in glaucoma:**
   a. Oxidative stress has not been shown to promote RGC death in glaucoma
   b. Vitamin E (α -tocopherol) but not Gingko biloba has been shown to ameliorate RGC death via its antioxidant effects.
   c. Nitrous oxide is a free radical known to induce apoptosis in glaucoma by destroying mitochondrial but not DNA function.
   d. Inhibition of NO synthase-2 by administration of its specific blockers may be an effective neuroprotective approach for glaucoma treatment

4. **With regard to microglia overactivation and apoptosis inhibition in glaucoma:**
   a. Microglia are glial cells that act as macrophages in the peripheral nervous system
   b. Overactivation of microglia leads to excessive production of toxic materials surrounding RGCs, including tumour necrosis factor alpha (TNF-α), NO, and reactive oxygen species
   c. Apoptosis, the process of programmed cell death, is initiated intrinsically but not extrinsically
   d. Apoptotic pathway initiation leads to deactivation of downstream effector caspases

GLAUCOMA is characterised by progressive retinal ganglion cell (RGC) loss and optic nerve head damage. Elevated intraocular pressure (IOP) is still considered to be the main risk factor, and lowering of IOP remains the mainstay of treatment to slow disease progression. Lowering IOP by 20–40% has been shown to reduce the rate of progressive visual field loss by half. However, a significant proportion of patients with glaucoma experience vision loss despite successful IOP reduction. Non-IOP-dependent risk factors appear to play an important role in approximately 30–70% of glaucoma patients. Therefore, despite the fact that IOP-lowering interventions reduce the risk of progression and delay the onset of glaucoma, the pathogenesis of glaucoma remains controversial and is not fully understood.

Understanding of the underlying pathological mechanisms has increased considerably within the past decade. In glaucoma, toxic substances such as glutamate, reactive oxygen species, and nitric oxide (NO) are released, microglia are overactivated, mitochondrial function decreases, and the transcription of survival- or death-related genes is modulated. Common final signalling pathways are activated, with subsequent neuronal apoptosis in RGCs. Elevated IOP, among other mechanisms, seems to trigger a self-perpetuating process of RGC degeneration. Neuroprotection could play a substantial role in the deceleration of pathological processes associated with vision loss, and may help to reduce vision loss in these patients by protecting RGCs and the optic nerve.Because of underlying pathogenetic findings, the following current targeted approaches prevail: (1) excitotoxicity, (2) oxidative stress, (3) NO blockage, (4) prevention of microglia overactivation, and (5) inhibition of apoptosis.

1. Glutamate excitotoxicity

Under physiological conditions, glutamate is the principal excitatory neurotransmitter in the retina, playing an essential role in retinal visual transduction. Glutamine synthetase, secreted by Müller cells, eliminates glutamate. Excessive glutamate levels are neurotoxic. However, it has been seen that dying cells release intracellular glutamate reservoirs. In glaucoma, the initial insult to RGCs leads to elevated levels of extracellular glutamate. Patiemnts with glaucoma show a chronic elevation of glutamate concentrations in the eye. Because of the increase in extracellular glutamate levels, the clearance mechanism by Müller cells through glutamine synthetase is overpowered, resulting in excessive, neurotoxic glutamate levels. As a consequence, ionotropic receptors, mainly the N-methyl-D-asparate (NMDA) receptors, are overstimulated, resulting in a massive influx of calcium into neurons, leading to glutamate-mediated RGC death. Extensive evidence has demonstrated this glutamate-induced RGC death in experimental animal models of glaucoma both in vitro and in vivo. During glaucoma progression, dying cells release more glutamate, perpetuating a vicious circle. Strategies to modify glutamate-induced neurotoxicity, either by blocking NMDA-receptors or by promoting clearance of glutamate by Müller cells, have been widely studied for their neuroprotective effects.

Memantine, an NMDA-receptor antagonist was shown to be neuroprotective in animal models of both acute and chronic RGC death. However, no significant benefit was found in the memantine-treated group compared with the placebo group in a large prospective controlled clinical trial. The two large phase III clinical trials of oral memantine failed to reach their primary endpoint of slowing glaucoma progression compared with placebo (evaluated using achromatic visual field loss), although progression was significantly slower in the higher than in the lower dose group.

2. Oxidative stress

Oxidative stress reflects an imbalance between the production and the clearance of reactive oxygen species. Several studies have shown that oxidative stress promotes RGC death in glaucoma. As such, the concept of antioxidants as a neuroprotective treatment strategy is widely accepted.

Among the most-studied antioxidants, vitamin E (α -tocopherol) and Gingko biloba have been shown to ameliorate RGC death; vitamin E acts as a scavenger for peroxyl radicals. Although some studies have suggested a decreased rate of glaucomatous progression in patients receiving vitamin E, long-term results are still needed. To further elucidate the role of vitamin E in glaucoma treatment, current studies suggest that vitamin E released from special contact lenses may be used in preventing reactive oxygen species-induced glaucomatous damage. Gingko biloba increases blood flow, has a free radical scavenger property, interferes with glutamate signalling, and preserves mitochondrial metabolism. The precise mechanism of Gingko biloba is still not understood; however, the available literature favours a possible beneficial effect on RGC survival.

3. Nitric oxide

Nitric oxide (NO), which is synthesised by NO synthase-1 and 2, is a free radical known to induce apoptosis and to inhibit both mitochondrial function and destroy DNA. Additionally, NO reacts with superoxides to form toxic perioxynitrate. NO is considered to be an important mediator of RGC death. Increased levels of NO synthase-2 were observed in the optic nerve head in glaucoma patients, indicating a high exposure of the optic nerve head to NO. Accordingly, NO synthase-2 and extensive RGC loss were found in the inner retinal cells in experimental animal models of glaucoma. Since NO neurotoxicity may contribute to progressive optic neuropathy in glaucoma, treatments aimed at decreasing NO levels are considered to be neuroprotective.

Both oral and topical administration of aminoguanidine, a specific inhibitor of NO synthase-2, significantly enhanced RGC survival in experimental rat models of glaucoma. SC-51, another NO synthase-2 inhibitor, had similar protective effects on RGCs in an animal model of glaucoma. Therefore, inhibition of NO synthase-2 by administration of its specific blockers seems to be an effective neuroprotective approach for treatment in experimental animal models of glaucoma. However, clinical trials are yet to be performed in this area.

4.Microglia overactivation

Microglia are glial cells that act as macrophages in the central nervous system. Under physiological conditions, microglial activation facilitates injured nerve rehabilitation by clearance of toxic components. Overactivation of microglia leads to excessive production of toxic materials surrounding RGCs, including tumour necrosis factor alpha (TNF-α), NO, and reactive oxygen species – all of which promote RGC death. Overactivated microglia are present in the optic nerve head and lamina cribrosa in glaucomatous human eyes. Interventions decreasing microglia overactivation might be useful for enhancing survival of RGCs in glaucoma.

One agent that inhibits microglia activation is minocycline, a second-generation tetracycline. Minocycline was effective in maintaining RGC survival in rat and mouse models of experimental glaucoma. While research on the neuroprotective effects of minocycline in primates and humans is still pending, the safety of minocycline has been proven in clinical practice. This molecule can penetrate the blood–brain barrier, and could become a promising neuroprotective agent in prospective glaucoma trials.

5. Apoptosis inhibition

Apoptosis is the process of programmed cell death, initiated either intrinsically or extrinsically. The extrinsic pathway is mediated by *Fas* receptors, known as apoptosis antigen-1 or tumour necrosis factor receptors (TNFR). The intrinsic pathway is initiated by efflux of cytochrome c from mitochondria. Both the extrinsic and the intrinsic apoptotic pathway initiation leads to activation of downstream effectors caspases 3, 6, and 7. These caspases degrade a number of intracellular proteins involved in the cell death process. Based on these findings, antiapoptotic agents may preserve RGC death in glaucoma.

Because the extrinsic apoptotic pathway is mediated by activation of TNFR, the TNF-α inhibitor etanercept was applied intraperitoneally in a rat model of glaucoma. Axonal degeneration and RGC loss were effectively suppressed. Oral administration of calcineurin inhibitor FK506 to rats with acutely increased IOP significantly decreased the release of cytochrome c from mitochondria and decreased apoptosis of RGCs. Alternatively, the anti-apoptotic Bcl2 proteins (including Bcl2 and Bcl-xL) act by directly inhibiting mitochondrial apoptosis-induced channel formation. Medications that enhance the endogenous antiapoptotic pathways may also have neuroprotective effects on optic nerves. Brimonidine, an ocular hypotensive that activates 2 adrenergic receptors to decrease aqueous humour production, elevates intracellular levels of antiapoptotic proteins Bcl2 and Bcl-xL in RGCs in vivo.

6. Conclusion

It is widely accepted that glaucoma is a multifactorial ocular disease the complex pathophysiology of which is not yet fully understood. A variety of treatments other than conventional IOP-lowering therapies have been studied in an effort to delay progressive glaucomatous optic neuropathy. However, the mechanisms leading to RGC apoptosis in glaucoma are complex and multifactorial, making therapeutic targets vague and making it difficult to find an agent that inhibits all these processes. Many agents have shown neuroprotective activity in animal models of glaucoma but failed to show clinical usefulness. One reason for this is that currently a robust animal model for glaucoma is lacking: most neuroprotective agents were tested in animal models of optic nerve crush that induces acute RGC apoptosis, but is far from the chronic damage related to glaucoma. Several newly developed medications have been tested in patients with glaucoma (neurotrophic growth factor, orally administered calcium channel blocker nilvadipine, and topical betaxolol or brimonidine), but the number of subjects enrolled has not yet been sufficient to find significant clinical differences. Further clinical trials are necessary to confirm safety and efficacy.

Acknowledgments: Dr. Verena Prokosch-Willing, MD, for providing all research background and references underlying this summary

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Answers to MCQs on page 12

1. a. *True*
   b. *False*
   c. *False*
   d. *False*

2. a. *False*
   b. *False*
   c. *True*
   d. *False*

3. a. *False*
   b. *False*
   c. *False*
   d. *True*

4. a. *False*
   b. *True*
   c. *False*
   d. *False*

02

Tonometry and pachymetry

Carlo Alberto CUTOLO - Italy

MCQs

1. **Regarding central corneal thickness (CCT);**
   a. It increases over the lifetime
   b. Diabetes is associated with a thicker CCT
   c. Air puff tonometry is not influenced by CCT
   d. It is not associated with progression of ocular hypertension to glaucoma
   e. Measurement of CCT is recommended in the management of glaucoma

2. **Regarding tonometry:**
   a. Different tonometers can be used interchangeably in clinical practice
   b. Goldmann applanation tonometer measures the true IOP
   c. Valsalva's maneuver influences IOP measurements
   d. Corneal refractive surgeries influence IOP measurements
   e. Rebound tonometry is not influenced by CCT

3. **Regarding corneal hysteresis:**
   a. It can be measured noninvasively
   b. Emerging evidence suggests an association between lower corneal hysteresis and glaucoma progression
   c. It does not correlate with pachymetry
   d. It can be measured with Goldmann applanation tonometer
   e. It can be influenced by corneal pathology

4. **Regarding intraocular pressure (IOP):**
   a. Diurnal IOP fluctuation is generally larger in untreated glaucoma patients than in healthy subjects
   b. 24 h IOP curves are impractical in the clinical setting
   c. Multiple diurnal measurements of IOP are recommended only for selected patients
   d. It can change with physical exercise
   e. It is the only modifiable major risk factor for glaucoma

TONOMETRY is an essential part of a comprehensive ocular examination. Because the intraocular pressure (IOP) is consistently associated with the development and progression of glaucoma, measuring it is of vital importance in glaucoma management and treatment. For now, IOP is the only modifiable risk factor for glaucoma. IOP can fluctuate during the day, and IOP diurnal fluctuations are larger in glaucoma patients than in healthy individuals. In fact, one limitation of tonometry is probably the scarcity of measurements that are obtained in clinical practice; multiple diurnal measurements of IOP have usually been recommended only for selected patients. Currently, insufficient evidence supports 24 h IOP fluctuation as a risk factor for glaucoma onset or progression. Pachymetry is well recognised in the setting of glaucoma diagnosis and management. Substantial variation in central corneal thickness (CCT) can produce a clinically significant discrepancy between measured IOP and true IOP. Corneal thickness has been highlighted as a risk factor for the development of glaucoma, but its association with severity and progression of glaucoma is still controversial.

1. Types of tonometry

Goldmann applanation tonometer (GAT) is the most frequently used instrument and the current reference standard. Although the evidence is limited, GAT is considered more precise than other tonometers. GAT measures the force necessary to flatten a fixed circular area at the central cornea. Based on empirical experimentation, the flattening force is converted to IOP (mmHg). Accuracy can be influenced by CCT, previous corneal surgeries, excessive or insufficient amount fluorescein in the tear film, astigmatism, tight collar or tie, breath holding, Valsalva's maneuver, and inadvertent pressure from the finger on the eyelid while taking the measurement. In case of higher astigmatism, the red mark of the Goldmann biprism should be aligned with the axis of the minus cylinder. Alternatively, the mean IOP measured with the biprism first in the vertical and then in the horisontal positioncan be used.

The Pascal® Dynamic Contour Tonometer contains a sensor embedded in the tip of the tonometer that is applied to the eye much like the Goldmann biprism to measure the dynamic pulsatile fluctuations in IOP. This technique is less influenced by CCT than GAT. This tonometer provides the IOP and the ocular pulse amplitude that corresponds to the variation of IOP during the cardiac cycle.

Air puff tonometer uses the applanating force of a rapid air pulse to flatten the cornea. IOP is determined from the air jet pressure required to applanate the cornea. Advantages include speed, minimal training needed, no topical anaesthesia and no contact with the eye. The evidence to replace GAT with air puff tonometry is insufficient.

Ocular Response Analyzer® uses air puff technology to record two applanation measurements: the force required to flatten the cornea as the air pressure rises and the force at which the cornea becomes flat again as the air pressure falls. The average of the two measurements is the Goldmann-correlated IOP. The difference between the two measurements is the corneal hysteresis. Corneal compensated intraocular pressure and

corneal resistance factor can also be calculated. In patients with glaucoma, a lower corneal hysteresis was associated with risk of glaucoma progression.

***Corneal Visualization Scheimpflug Technology tonometer* uses** Scheimpflug high-speed camera technology to record the corneal deformation produced by an air pulse. Analysis of the dynamic corneal reaction permits calculation of the IOP and several other biomechanical properties of the cornea. CCT is also measured.

Rebound tonometry (Icare®) uses a platic coated metal rod probe that is propelled towards the cornea. As the probe impacts the cornea, it decelerates and then rebounds from corneal surface; rebound speed increases as the IOP increases. The speed of deceleration is measured and is converted by the device into IOP. Rebound tonometry does not require topical anaesthesia.

2. How CCT affects IOP

The relationship between CCT and IOP as measured by GAT (and most other tonometers) is complex and non-linear. No agreement exists on an algorithm to correct IOP based on corneal pachymetry. The clinical use of any IOP correction formula is discouraged because it could add further error rather than reduce them. In general, higher CCT results in an overestimated IOP. However, a large amount of corneal oedema is supposed to produce an underestimate of IOP. Corneal refractive surgeries unpredictably result in some amount of IOP underestimation by GAT (and most other tonometers) because they alter the thickness, curvature, and mechanical properties of corneal tissue.

3. CCT as a risk factor for progression of ocular hypertension to glaucoma

The Ocular Hypertension Treatment Study (OHTS) and the European Glaucoma Prevention Study (EGPS) found a thinner CCT to be an independent risk factor for progression from ocular hypertension to glaucoma. A validated prediction model has been built based on OHTS results and validated on the EGPS placebo group. The pooled OHTS-EGPS predictive model has demonstrated good predictive accuracy. The result that CCT is a *statistically* independent risk factor does not necessarily indicate that CCT is a *completely* independent risk factor. It is not possible, in the OHTS or EGPS analyses, to fully separate the effect of IOP and CCT. This is because IOP was measured by applanation tonometry that is affected by CCT. However, CCT is a helpful clinical measurement to consider in risk stratification of ocular hypertension.

RECOMMENDED READING

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Answers to MCQs on page 20

1. a. *False*
   b. *True*
   c. *False*
   d. *False*
   e. *True*

2. a. *False*
   b. *False*
   c. *True*
   d. *True*
   e. *False*

3. a. *True*
   b. *True*
   c. *False*
   d. *False*
   e. *True*

4. a. *True*
   b. *True*
   c. *True*
   d. *True*
   e. *True*

03

Gonioscopy and anterior segment OCT

Luis PINTO - Portugal

MCQs

1. **Which of these features can be determined by gonioscopy but not with standard anterior-segment OCT?**
   a. Pigment in the trabecular meshwork
   b. Exfoliative material
   c. Neovessels over the trabecular meshwork
   d. Circumferential vessels over the iris root ("sea serpent vessels")
   e. Iris cleft

2. **Concerning gonioscopy technique:**
   a. Three-mirror lens can be used for indentation gonioscopy
   b. The majority of gonio lenses provide direct angle visualization
   c. It should be done in photopic conditions
   d. Gonio-related interventions (such as SLT) should be done with indentation lenses
   e. It has a significant learning curve

3. **Concerning the differences between anterior-segment OCT (AS-OCT) and UBM,**
   a. AS-OCT can be used to detect ciliary body rotation
   b. UBM requires a skilled observer
   c. UBM can be used for angle-closure screening programmes
   d. AS-OCT involves direct contact and local anesthestic application
   e. Iridocorneal angle opening are usually overestimated with AS-OCT compared to UBM

4. **Which of these are features that can be provided by AS-OCT:**
   a. Iris volume
   b. Iris thickness
   c. Central corneal thickness
   d. Scleral spur
   e. Filtration bleb volume of glaucoma drainage device

THE MAJORITY of glaucoma patients have a primary form of the disease, with an otherwise open iridocorneal angle. However, this fact should not preclude the need to assess this anatomical region. Not only because angle-closure type is usually a more aggressive form of the disease, accounting for nearly half of those who are blinded, but also because a number of features can help in the diagnosis of both open-angle and angle-closure secondary glaucomas. Level of pigmentation, exfoliaton material, presence of synechia, vessels, and even structural abnormalities, such as dialysis or clefts, are of extreme importance in diagnosing and defining treatment strategies for each individual patient. As the vast majority of these features is not clearly visible at a slit-lamp observation, several techniques and devices have been described to overcome this physical limitation.

1. Gonioscopy

Gonioscopy is the gold-standard method for assessing the anterior chamber angle (ACA). As total internal reflection prevents direct observation, an interface with a lens is needed in order for the angle structures to be observed. Of the several types of lens available on the market, the vast majority are meant to provide indirect visualisation through slit lamp observation. If indentation is required to differentiate between appositional and synechial iridocorneal contact, a lens with a smaller diameter than the cornea is required. Whilst potentially more difficult to maneuver because of the dynamic nature of the exam, these have the advantage of not requiring a contact fluid other than the anaesthetic and they are thus quicker and more comfortable for the patient.

Furthermore, the variability of this technique is large and overall requires a non-negligible learning curve. It is, however, a crucial technique because the ophthalmologist must be aware of what normal ACA anatomy is like in order to perform a number of daily procedures, ranging from selective laser trabeculoplasty (SLT) or to screening patients suitable for the increasingly popular minimally invasive glaucoma surgery (MIGS) devices.

Whilst other devices than gonioscopes have evolved to make a quantitative assessment of the opening of the angle (such as anterior segment optical coherence tomography [AS-OCT] and ultrasound biomicroscopy [UBM]), limitations exist concerning these technologies. As they provide gray scale images based on reflectivity, they cannot provide colour. Thus, features such as pigmentation or the presence of exfoliation material are not adequately visible without gonioscopy. Furthermore, AS-OCT cannot differentiate whether or neovascular vessels exist in the synechiae covering the trabecular meshwork. Accordingly, a diagnosis such as pigmentary or neovascular glaucoma cannot be confirmed based only on AS-OCT images.

To minimize the level of variability in the technique of gonioscopy and to allow detailed *post hoc* image analysis, several devices have emerged for goniophotography. Similar to the concept of making a funduscopic image to allow proper optic disc description, these novel images can try to maximize image interpretation and thus aim to allow for proper diagnosis and patient management.

2. Anterior segment OCT

OCT is a modality that uses low coherence interferometry to enable non-contact, *in vivo* imaging of ocular structures. Specific modifications to the technology have allowed structures in the anterior segment of the eye to be imaged in previously unobserved resolution. Furthermore, image processing software now allows combination of multiple scans, 3D reconstruction and accurate measurements. Although AS-OCT is not able to acquire images behind the iris tissue like UBM can, it can visualise angle-to-angle with one scan, resulting in good visualization of the angle recesses. AS-OCT can be performed easily, with relatively good repeatability and reproducibility. In addition, AS-OCT can acquire images under dim conditions and is performed in a non-contact fashion. All of these characteristics make AS-OCT a popular method for anterior chamber assessment. It has applications in several fields, from cornea and ocular surface to oculoplastic characterization, but it is especially widely used in glaucoma for iridocorneal characterization.

Qualitative and quantitative assessment of ACA, anterior chamber, iris, and lens are accomplished with AS-OCT. Angle closure is defined as any contact between the iris and the angle wall anterior to the scleral spur whereas by gonioscopy, the quadrant would still be considered open unless the apposition reached the posterior trabecular meshwork. The scleral spur is an important landmark to be assessed, although Schwalbe's line (SL) has been proposed as another possible landmark because it has better identification in OCT devices. However, current commercially available Fourier domain OCT devices are inconsistent in determining the scleral spur and have poor visibility of angle recess in many subjects. Nevertheless, the high definition provided by these devices provided some insights into the location of Schlemm's canal (SC) and its relationship to other anterior segment structures. Recent studies have been able to quantify the volume and area of structures such as trabecular meshwork and SC, allowing exploratory analysis of its relevance to clinical parameters such as intraocular pressure. Finally, its ability to quantitatively make the anterior segment measurements with very low variability, makes this technology widely used in assessing the success of interventions such as iridotomy, iridoplasty, and even cataract surgery as regards anterior segment morphology. Furthermore, as it less dependent on the interpretation skills of the ophthalmologist, it can be become one option for future mass-screening of angle-closure suspects once specificity and sensitivity parameters have been validated.

3. Limitations

Although AS-OCT has become popular for ACA evaluation, the images from most devices are limited to the cross-sections of the anterior chamber that are selected (usually horizontal) and the remainder of the angle circumference is not assessed at all. Furthermore, it provides limited visualisation of the ciliary sulcus and posterior border of the ciliary body in most cases because the iris pigment epithelium is not transparent to infrared light. In addition, poor definition of the scleral spur was also reported in approximately 25% of AS-OCT images. Owing to the influence of the eyelids, AS-OCT is less likely to obtain a good image at the superior and inferior angles. Such restriction may impede the accuracy of the measurement of iris

volume and anterior chamber volume. Indeed, AS-OCT tends to return smaller measurements of angle and slightly higher measurements of the anterior-chamber depth/central corneal thickness ratio as compared to UBM.

RECOMMENDED READING

Recent

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Classic

5. Friedman DS, He M. Anterior chamber angle assessment techniques. Surv Ophthalmol. 2008;53(3):250-73.

Answers to MCQs on page 25

1. a. *True*
   b. *True*
   c. *True*
   d. *True*
   e. *False*

2. a. *False*
   b. *False*
   c. *False*
   d. *False*
   e. *True*

3. a. *False*
   b. *True*
   c. *True*
   d. *False*
   e. *True*

4. a. *True*
   b. *True*
   c. *True*
   d. *True*
   e. *False*

04

Disc and RNFL exam

Michele IESTER - Italy

MCQs

1. **The RNFL trajectories provide crucial information for connecting local retinal sensitivity to local optic nerve head anatomy, EXCEPT FOR:**
   a. the area close to the fovea where the intraretinal pathway runs radially (Henle's layer) and the RGCs are located further away from the fovea than the corresponding photoreceptor cells
   b. the area far from the fovea where the intraretinal pathway runs radially (Henle's layer) and the RGCs are located further away from the fovea than the corresponding photoreceptor cells
   c. the area close to the fovea where the intraretinal pathway runs radially (Henle's layer) and the RGCs are located closer to the fovea than the corresponding photoreceptor cells
   d. the area far from the fovea where the intraretinal pathway runs radially (Henle's layer) and the RGCs are located closer to the fovea than the corresponding photoreceptor cells

2. **In clinical ophthalmoscopy, the disc margin (usually termed the 'ring of Elschnig') is defined as the following peripheral boundary:**
   a. the innermost white reflective ring within the termination of RPE and has been assumed to represent the histological border tissue of Elschnig, a connective tissue 'cuff' limiting the choriocapillaris at the boundary of the ONH
   b. the innermost white reflective ring within the termination of RPE and has been assumed to represent the histological border tissue of Elschnig, a connective tissue 'cuff' within the peripheral choriocapillaris
   c. the innermost white reflective ring within the peripapillary beta atrophy
   d. The ring of Elschnig is located within alpha atrophy

3. **With the advent of spectal domain (SD) OCT, it was hoped that the anatomical basis for the clinician-defined disc margin could be identified.**
   Initial studies undertaken in normal monkey eyes identified that the clinician-defined disc margin was:
   a. either the termination of Bruch's membrane (i.e., Bruch's membrane opening [BMO]) or the termination of the border tissue of Elschnig.
   b. the termination of Bruch's membrane (Bruch's membrane opening [BMO]).
   c. the termination of the border tissue of Elschnig.
   d. neither the termination of Bruch's membrane (Bruch's membrane opening [BMO]) nor the termination of the border tissue of Elschnig.

4. **The presence of focal pits, or disinsertions, of the lamina cribrosa, detected by enhanced depth imaging (EDI) SD OCT has been found to be strongly associated with:**
   a. glaucomatous visual field progression
   b. an increase of IOP
   c. an increase of beta atrophy
   d. a change in Bruch's membrane opening

BECAUSE glaucoma is a characteristic optic neuropathy, the ability to capture structural changes in the 3D structure of the optic nerve head (ONH) is of great value both in the diagnosis and in the monitoring of patients with, or at risk of, glaucoma. To diagnose glaucoma we have to discover glaucomatous ONH changes, but this is not easy because of the different ONH appearances. Clinical approach is always fundamental to diagnose diagnosis. Glaucoma changes the surface contour of the ONH in a typical way that helps in diagnosis. Contour changes can best be appreciated with a stereoscopic view. Therefore, the initial examination and the follow-up examinations to detect a contour change should be made through a dilated pupil, whereas follow-up examinations for detecting qualitative features such as disc haemorrhages, can be performed through an undilated pupil. The EGS guidelines suggest for stereoscopic examination of the posterior pole the use of:

- *An indirect non-contact fundus lens* with enough magnification at the slit-lamp
- *A direct contact fundus lens* (e.g. the central part of a Goldmann 3-mirror or a Zeiss 4-mirror lens) at the slit-lamp.

Today the direct ophthalmoscope is used infrequently, but for ONH and retinal nerve fibre layer (RNFL) examination it can still be good enough and it can give additional information such as show RNFL defects and disc haemorrhages. Also, three-dimensional information using parallax movements is possible. The biomicroscopic clinical evaluation of the ONH and retinal nerve fibre layer (RNFL) should assess the following features: disc area and shape, rim area and shape, cup, RNFL, disc haemorrages, and peripapillary atrophy.

Four emerging anatomic relationships of interest as regards ONH phenotyping in glaucoma are increasingly appeciated. First, the axis between the fovea and the centre of Bruch's membrane opening (BMO) – the FoBMO axis; second, the composition and behaviour of the neuroretinal rim compared to the peripapillary RNFL; third, ONH torsion and tilt; and fourth, the position of the temporal raphe relative to the FoBMO axis.

Despite the usefulness of this new knowledge and these data from the scientific point of view, the ophthalmoscopic way to observe the ONH is still the same. The data are, however, useful if an optical coherence tomography (OCT) analysis is performed or a structure-function correlation has been done.

Another important issue to consider in the examination of the disc and RNFL is the effect of age on the imaging parameters such as those of OCT and the Heidelberg Retina Tomograph (HRT). Chauhan *et al.* described longitudinal rates of change of neuroretinal parameters in patients with glaucoma and in healthy controls, and evaluated the influence of covariates. Subjects were followed for a median of 4 (range, 2 to 6) years. The proportion of controls who had significant decrease of neuroretinal parameters was 35% for Bruch's membrane opening-minimum rim width (BMO-MRW), 31% for RNFL thickness, and 11% for disc margin-based neuroretinal rim area (DMRA) whereas in the glaucoma group these percentages (42%, 31%, and 14%, respectively) were not statistically different from those of controls.

Currently no clinical or commercial applications are available for measurement of lamina cribrosa with OCT. A key issue is the variable visualisation of this structure, which makes reliable automated segmentation very difficult.

Answers to MCQs on page 30

1. a. *True*
   b. *False*
   c. *False*
   d. *False*

2. a. *True*
   b. *False*
   c. *False*
   d. *False*
   e. *False*

3. a. *True*
   b. *False*
   c. *False*
   d. *False*
   e. *False*

4. a. *True*
   b. *False*
   c. *False*
   d. *False*
   e. *False*

05

Optical characteristics of the cataractous lens

Per SÖDERBERG - Sweden

MCQs

1. **Absorption in the lens:**
   a. causes a more yellow appearance in the slit lamp microscope
   b. impacts contrast sensitivity
   c. changes color sensitivity
   d. causes reduction of visual acuity

2. **Regarding scattering in the lens:**
   a. Mie scattering describes scattering in a volume of deviating refractive index with a diameter smaller than the wavelength of light
   b. Small particle scattering in the lens may cause a slight bluish appearance in the slit lamp microscope
   c. Reflection at the interface between the crystalline lens and the surrounding media causes light scattering
   d. Volumes much larger than the wavelength of the light cause isotropic light scattering distribution

3. **Regarding the pupil and visual acuity:**
   a. A small pupil size (<< 2 mm) improves the visual acuity
   b. A pupil size of approximately 2 mm may functionally improve the visual acuity in an eye with cataract
   c. A large pupil size improves the visual acuity if the optical surfaces are perfect
   d. The pupil may shield scattering in the lens

4. **Regarding the optical system of the eye:**
   a. The point spread function describes the intensity distribution in the image point for a reciprocal infinitely small luminous object point on dark background
   b. Contrast on the retina determines visual acuity
   c. Stray light is a measure of how light at an angle outside the object point is imaged on the reciprocal image point
   d. Rayleigh scattering makes the point spread function on the retina wider

THE CRYSTALLINE lens contributes to collecting light incident to the eye from a point in the object plane and to refocusing it to a point in the image plane on the retina. Short wavelength light energy may selectively be absorbed in a cataractous lens. In the slit lamp microscope, the lens then appears yellow to brown in colour. The reduced transmission of blue light through the lens reduces sensitivity to blue light and may cause decreased perception of blue light. Redirection of light in a cataractous lens appears in the slit lamp as general haziness or structured sources of back scattering, and causes reduced contrast sensitivity in the visual system. At ophthalmoscopy, the retinal image is seen with reduced contrast.

1. Properties of light

To understand light transmission in a cataractous lens it is necessary to consider both the model of light as units of energy, ***photons***, and the model of light as sinusoidal variations of electric and magnetic fields perpendicular to each other and perpendicular against the direction of propagation of ***electromagnetic radiation***.

In vacuum without objects, light propagates with a finite phase velocity in the same direction infinitely without losing energy.

Two sinusoidal variations of electromagnetic field with different directions are said to be *correlated* (associated) over a defined time if the amplitude and phase of one of them can be predicted based on the other, knowing the time that has elapsed. If two correlated electromagnetic fields merge in space (***interfere)***, the resulting electromagnetic field is the electric field in the point of interference from one superimposed on the other.

Light propagation in matter

The outer electrons in a matter may, depending on their configuration, can be considered as oscillators with an inherent frequency. If the frequency of the incident beam corresponds to the inherent frequency of the matter (resonance), the incident energy may be transferred to the electrons of the matter, thus attaining a higher state of energy, while the incident electromagnetic energy is absorbed (*resonance absorbance)*.

In addition, the electric field of the incident electromagnetic wave interacts instantly with charges of low mass such as electrons. A fraction of the incident electromagnetic field is *scattered*, as secondary electromagnetic waves isotropically are distributed in space but with a phase shift and a reduced amplitude. Both the amplitude and the phase shift depends on the compliance between the frequency of the incident electromagnetic field and the resonance frequency of the matter.

Light propagation in homogenous optical medium containing correlated scattering sources

In dense media, the secondary scattered waves are correlated and thus will interfere. Interference will cancel out scattering in all directions but forward, resulting in a forward-propagating secondary wave. The optical medium then appears transparent (e.g., glass).

Interference of the primary wave and the forward propagating secondary wave results in a wave with a slower phase velocity in the medium (longer wavelength but retained frequency).

Refraction and absolute refractive index

At the interface between two clear optical media, light changes direction around the normal to the surface so that the fraction of the sine of the angle of incidence, $sin(\alpha_i)$, and the sine of the angle of excitance, $sin(\alpha_e)$, equals the fraction between the velocity of light in the medium of incidence, v_i and the velocity of light in the medium of excitance, v_e (Eq. 1).

$$\frac{Sin(\alpha_i)}{Sin(\alpha_e)} = \frac{v_i}{v_e} \qquad \text{Eq. 1}$$

For practical purposes, the ***absolute refractive*** index for a specific medium, n_s, is expressed as phase velocity in the medium, v_s, normalized to the velocity of light in vacuum, v_c. (Eq. 2).

$$n_s = \frac{v_c}{v_s} \qquad \text{Eq. 2}$$

Using absolute refractive index for medium of incidence, n_i, and for medium of excitance, n_e, in Eq. 1 results in the law of refraction (Eq. 3).

$$n_i\, Sin(\alpha_i) = n_e\, Sin(\alpha_e) \quad \text{Eq. 3}$$

Reflection

Light incident at an angle to the normal of the surface between to optically homogenous media is reflected out of the surface at a similar angle to the normal of the surface (***law of reflection)***. The intensity of reflected light increases with the angle of incidence and the refractive index shift over the surface.

External reflection refers to incident light reflected at a transition from low to high refractive index. ***Internal reflection*** refers to incident light reflected at a transition from high refractive index to low. It is realized from Eq. 3 that light incident with a high enough angle of incidence, α_i, at a transition from high to low refractive index, results in an angle of excitance, α_e, ≥ 90 deg. Then, all the light will be internally reflected (*total internal reflection)*.

Light propagation through a homogenous medium containing a subvolume with a deviating refractive index

The diameter of the subvolume is much smaller than the wavelength of light: If the diameter of the volume with deviating refractive index is considerably smaller than the wavelength (d << λ, e.g, molecule in water), light will be scattered isotropically around the refractive index deviation. If the concentration of volumes of deviating refractive index is low, the scattering events at single points of matter are uncorrelated. Then, the intensity of the scattered light is isotropically distributed around the volume and inversely proportional to the 4^{th} power of the wavelength (***Rayleigh scattering)***.

The diameter of the subvolume is approximately equal to the wavelength of light: If the diameter of the volume with deviating refractive index is approximately equal to the wavelength of light (d ≈ λ, e.g., organelle in a cell), the distribution of the electrical field in the volume has to be considered. A solution for spherical particles was derived by Mie (***Mie scattering)***. The light scattering from the volume then becomes independent of wavelength with smaller scattering angle (angle to incident beam), the larger the diameter of the scattering volume (e.g. white cloud).

The diameter of the subvolume is larger than the wavlenght of light: If the diameter of the volume of deviating refractive index is much larger than the wavelength of the light (d >> λ), the volume behaves as a homogenous densely packed optical medium resulting in refraction and reflection.

2. Optics of the non-cataractous lens

Refraction in the crystalline lens

The crystalline lens can be simplified to a bag of protein in aqueous solution. However, the concentration of protein decreases smoothly from the center to the periphery of the lens, both towards the anterior and the posterior pole and towards the equator of the lens. The refractive index in an aqueous solution of protein, n_p, has empirically been found to be directly proportional to the protein concentration [P] depending on an intercept, k_0, and an inclination coefficient, k_1 (Eq. 4).

$$n_p = k_0 + k_1 [P] \qquad \text{Eq. 4}$$

Considering the protein concentration gradient in the crystalline lens, the clear crystalline lens is to be considered a gradient index lens with a smooth transition of refractive index from the center to the periphery. The propagation of light through the crystalline lens, therefore, has to be calculated as the result of an infinite amount of consecutive refractive surfaces surrounding consecutive optically homogenous media.

Loss of power during refraction in the crystalline lens

Light that is incident on an optical medium, e.g. the crystalline lens, may be *directly transmitted*, *scattered* to another direction, or *absorbed*. ***Transmittance*** simply expresses the power out in relation to the power in, potentially considering also the collection angle when power out is measured.

3. Optical consequences of erroneous light conduction in the crystalline lens

Light from a point of an object incident on the crystalline lens may be lost for detection because of resonance absorption or scattering.

Resonance absorption in the lens

During lifetime, tryptophan residues in lens proteins are excited by ultraviolet radiation to *N*-formylkynurenine that is metabolised in the lens to yellow pigments that absorbe an increasing proportion of blue light with increasing age. This primarily occurs in the center of the lens where the lens proteins are densely packed. The optical consequence for the patient is reduction of blue photons on the retina, implying less sensitivity of the visual system

for incident blue light. Incident white light is perceived as more yellow and color sensitivity testing will demonstrate a relative loss of blue light sensitivity. When the anterior segment is illuminated with white light, the backscattered light observed in the slit lamp microscope similarly is lacking in blue light so that the lens appears yellow to brown.

Scattering in the lens

Undesirable scattering in the lens occurs if there are volumes within the lens of deviating refractive index within the physiological gradient index distribution. The optical impact of these optical impurities depends on the refractive index of the impurity, the radius of the volume of impurity in relation to the wavelength, and the position along the optical axis. In ophthalmoscopy, scattering in the lens causes less contrast in the image of the retina.

Spatially small deviations of refractive index

Local spatially small (diameter<<wavelength of light) deviations of refractive index may develop because of crosslinking of lens proteins. Such deviations will cause light scattering that strongly depends on wavelength and that is isotropic around the scatterer (*Rayleigh scattering)*. In the backscattered light, the image is overlaid with haze, and local scatterers may form structures.

Spatially intermediate deviations of refractive index

Local spatially intermediate (diameter≈wavelength of light) deviations of refractive index may develop because of swelling of cell organelles. Such deviations will cause light scattering that is wavelength independent and behavs similar to ***Mie scattering that*** causes forward scattering.

Spatially large deviations of refractive index

Because of the low refractive index in the superficial layers of the lens, essentially no shift of refractive index takes place between the aqueous humour and at the anterior superficial layer of the crystalline lens, or between Berger's space behind the lens and the posterior superficial layer of the crystalline lens. These interfaces, therefore, cause negligible reflection.

Large volumes in the lens may alter the gross refractive index gradient and cause deviation from perfect refraction in the lens (***aberrations)***.

If large volumes in the lens (diameter>>wavelength of the light) accumulate water, the refractive index in the volume decreases (Eq. 4). Then, both local reflection and refraction within the lens matter may develop, deviating light from a point in the object space away from the reciprocal point in the image space.

Pupil size dependence

A smaller pupil potentially shields light from an image point that is deviated, thereby increasing the contrast at the retina. Higher contrast at the retina makes it easier for adjacent photoreceptors to detect differences in irradiance. The visual acuity functionally increases.

However, if the pupil becomes small enough (typically <2 mm) deviation of light due to ***diffraction*** increases and contrast decreases.

Location of the scatterers in relation to the retina

The closer the scattering event in the lens is to the retina, the higher the intensity of scattered light on the retina (e.g., posterior subcapsular cataract) implying lower contrast at the retina.

The point spread function in a non-scattering optical system

If an infinitely small light source at infinite distance (e.g., a star) is imaged in the optics of the eye, the intensity distribution at the retina centered around the reciprocal point in the image will be a spread-out becasue of diffraction in the pupil. The intensity distribution on the retina is referred to as the point spread function. It is realised that if two adjacent stars are imaged, the intensity distributions have to be narrow enough for 3 photoreceptors to distinguish differences in illuminance (contrast for the stars to be resolved).

Changes to the point spread function from scattering in the optical system

Surface deviation from perfect refraction (*aberrations*) typically give rise to increased light scattering within 1 degree. Rayleigh scattering, Mie scattering, and local reflection/refraction, increase the light scattering outside 1 degree.

If light is scattered in the refractive media, some of the light in a point in the object space will be lost in the reciprocal point in the image space and it will illuminate outside the point in the image space. Concurrently, light outside a point in the object space may fall on the point in the image space (*stray light)*. This leads to less contrast in the image space between the point in the image space and its surrounding than in the object space. In a luminous visual field, the patient then perceives a general haze of luminosity overlaying the perceived image. In a dark visual field (e.g., driving in darkness) lights appear with halos.

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Answers to MCQs on page 34

1. a. *True*
   b. *False*
   c. *True*
   d. *False*

2. a. *False*
   b. *True*
   c. *False*
   d. *False*

3. a. *False*
   b. *True*
   c. *True*
   d. *True*

4. a. *True*
   b. *False*
   c. *True*
   d. *True*

06

IOL calculation: how precise are we?

Nino HIRNSCHALL - Austria

MCQs not available

06 IOL calculation: how precise are we? - HIRNSCHALL N - Austria

Abstract not available

07

IOL optics

Marie-José TASSIGNON - Belgium

MCQs

1. **Regarding optical properties of IOLs:**
   a. The lower the refractive index the thinner the monofocal IOL will be
   b. Light transmission is higher in diffractive IOLs
   c. Spherical aberrations in a well-aligned monofocal IOL increase depth of focus
   d. The amount of spherical aberrations of a monofocal IOL increases with the IOL power
   e. Chromatic aberrations are higher in low power monofocal IOLs

THE OPTICAL CHARACTERISTICS of the intraocular lenses (IOL) currently available on the market have experienced remarkable changes after they became available in 1949.

The inventor of the modern implant technology is Sir Harold Ridley, appointed consultant surgeon at both Moorfields Hospital and Saint Thomas Hospitals, London, in 1939.

The number of IOL designs and shapes have boomed to such degree that it is impossible for a single ophthalmic surgeon to have used them all. Selection is thus crucial. The best is to select an IOL based on the current knowledge of the optical characteristics of the IOLs instead of letting the surgeon be guided by the selling arguments of different companies.

1. Three very distinct aspects regarding the IOL properties to be addressed

- Geometry: thickness will depend on the following parameters:
  - Refractive index
  - Power
  - Shape (defined by the radii of curvature of both surfaces)
- Optical quality: can be defined by the following parameters:
  - Wavefront characteristics
  - Transmission of light of the biomaterial
- Biomaterial:
  - Foldability/memory of the biomaterial

2. Monofocal IOLs

The monofocal IOL remains the most used design even in 2019. Its shape is typically equiconvex. It is defined by the anterior and posterior radius of curvature that are similar in equiconvex IOLs.
The refractive index varies from 1.41 to 1.55, which is much higher than that of the crystalline lens that is around 1.386. The thickness of the IOL will depend on this refractive index.

Keep the following rule in mind regarding monofocal IOLs:
The higher the refractive index the thinner the IOL will be for the same power.

3. IOL surface profiles

Many different profiles have been proposed during the last 15 years. Multifocal IOLs take benefit of the fact that transmission of light is largely increased postoperatively compared to the transmission of light of the natural crystalline lens. This benefit of light transmission will be influenced by the following parameters:

- Parameters of the IOL environment (e.g., posterior capsule opacification)
- Parameters of the IOL profile (e.g, diffractive pattern of the IOL)
- Chromophores used to absorb light in a particular part of the spectrum of the visible light
  (e.g., yellow or orange chromophores)

Keep the following rules in mind regarding IOL transmission of light :

- Reduced transmission of light means reduced contrast sensitivity.
- Yellow chromophores reduce the transmission of light in the blue spectrum.
- Multifocal IOLs split the transmission of light at different foci and reduce contrast sensitivity at each focus according to the manufacturere algorithm.

4. The optical quality of the IOL

Each shape of the IOL will define its proper wavefront aberrations. An equiconvex IOL will present the lowest coma and spherical aberrations. Its manufacturing process is also easier. The natural crystalline lens presents stronger high-order aberrations (coma and spherical aberrations) than a monofocal IOL.

Keep the following rules in mind regarding high order aberrations of the IOL:

- The drawback from low IOL high-order aberrations is decreased depth of focus.
- When targeting emmetropia, the patient will typically complain of blurred vision at intermediate and near distance.
- The patient will thus be dependent on spectacles for about all distances.
- The solution will then be IOL exchange by replacing it with an IOL with a lower refractive index in order to increase the IOL thickness.

Keep the following in mind regarding spherical aberrations:

- Spherical aberrations of the IOL depend on its thickness which in its turn depends on
  - IOL refractive index
  - IOL power

Aspherical IOLs have been introduced to correct for the spherical aberrations of the high power IOLs. Low spherical aberrations reduces depth of focus. However, high power IOLs will be more sensitive regarding centration. Tilt of high power IOLs will induce coma aberrations.

Keep the following in mind regarding the chromatic aberrations:

- The higher the IOL power the higher the chromatic aberrations
- The more irregular the anterior face of the IOL the higher the chromatic aberrations

5. Environmental factors influencing IOL behavior

Two very important factors influence the effect of the **implanted** IOL:

- **Capsular bag variations in response to the contact of the IOL with lens epithelial cells.**
- **Alignment of the IOL within the eye as decided by the surgeon.**

Untill now, only one IOL design controls both factors: the IOLs suspended by the capsular bag in contrast to the very widely used IOL inserted in the capsular bag. This opens new challenges of the bag-in-the-lens compared to the lens-in-the-bag surgical techniques.

Answers to MCQs on page 44

1. a. *False*
   b. *False*
   c. *True*
   d. *True*
   e. *False*

08

Ideal wound shape and wound size

Sorcha NI DHUBHGHAILL - Belgium

MCQs

1. **Regarding cataract incisions:**
   a. Scleral tunnel incisions induce more astigmatism than clear corneal incisions of the same length
   b. Scleral tunnel incisions are preferred when a larger incision is required
   c. Clear corneal incisions are better when using polymethylmetacrylate (PMMA) lenses
   d. Incisions placed temporally have a greater influence on surgically induced astigmatism than superiorly placed incisions
   e. Short incisions cause a risk for iris prolapse

2. **Regarding cataract incisions:**
   a. Corneal wound burns should always be sutured
   b. Corneal incision sutures increase the corneal curvature (higher K values) along the axis of the suture
   c. Absorbable sutures (e.g., Vicryl) are contraindicated in cataract surgery
   d. Children under 1 year of age should always have their cataract incisions sutured
   e. The longer the tunnel, the less the influence it has on the surgically induced astigmatism

3. **Regarding cataract incisions:**
   a. The scleral tunnel technique should be used in cases of radial keratotomies
   b. Scleral tunnels are contraindicated in cases of severe scleralmalacia
   c. The self-sealing properties of the clear corneal incisions are better in younger people than with older people
   d. Clear corneal incision cause more conjunctival ballooning than scleral tunnels
   e. Stromal hydration can improve the sealing properties of a leaking wound

4. **Cataract incisions:**
   a. Incisions in the nasal and inferior direction are uncomfortable for the surgeon
   b. Femtosecond laser surgery is most commonly used to perform scleral tunnel incisions
   c. An irregular third step of a clear corneal incision can predispose to detachment of Descemet's membrane
   d. A deep first step of a scleral tunnel incision can predispose to scleral perforation
   e. A leaking clear corneal incision is a risk factor for endophthalmitis

08 Ideal wound shape and wound size - NI DHUBHGHAILL S - Belgium

MASTERING cataract incisions is often the first opportunity for the surgical trainees to show their competency to their trainers. We will focus on two types of wounds most commonly used in modern cataract surgery:

- Scleral tunnel incisions
- Clear corneal incisions

In the past decade, the clear corneal incision has risen to prominence and is the preferred surgical approach for over 90% of cataract surgeons. There are still some situations (e.g., in the presence of radial keratotomies or where large incisions are needed) where a scleral incision is preferred. The latter is a versatile approach and useful to learn in parallel with the clear corneal approach.

1. Scleral tunnel incisions

Whilst a scleral tunnel can theoretically be placed anywhere, most surgeons chose the superior or superotemporal area. The incision starts with a conjunctival peritomy using conjunctival scissors, followed by dissection through Tenon's capsule. The peritomy should be slightly larger than the planned incision. Cautery may be needed to achieve haemostasis before starting the incision.

The first step is to fixate the eye by holding it with a toothed forceps, creating 1–2 mm posterior to the limbus an incision that is approximately half the thickness of the sclera. The knife (keratome) is then turned to have the blade flush with the sclera. The blade is slowly advanced towards the cornea. Once you reach the limbus, you should angle the blade slightly upward to avoid entering the anterior chamber prematurely. Making side-to-side movements allows you to control the speed of the blade as it enters the eye. When the tip of the blade becomes visible in the cornea you can start the third part of the incision. The blade is now tilted downward and advanced into the anterior chamber. Make sure to advance the blade so that the shoulder of the knife enters the eye, thus making sure that the internal width of the wound is adequate.

Advantages:
- Safer for larger incision (e.g., when implanting/explanting a large non-foldable lens)
- Easier if you need to convert to extracapsular cataract extraction (ECCE)
- Covered with conjunctiva so that the rate of endophthalmitis may be lower
- May cause less endothelial damage (larger vertical distance from the cornea)
- Less surgically induced astigmatism

Disadvantages:
- Can be difficult to perform (deep-set eye, prominent brow, or sunken eye)
- If the incision is too deep in the sclera, damage or disinsertion of the ciliary body can occur, and can cause globe perforation or iris prolapse
- A scleral incision that is too thin can cause a tear or buttonhole
- Cannot be performed if history is positive for scleritis or scleromalacia, or in an eye with a trabeculectomy
- Blood along the tunnel into the anterior chamber can cause a hyphema

2. Clear corneal incisions

For a clear corneal incision, you may wish to create a paracentesis and fill the anterior chamber with ophthalmic viscosurgical device (OVD). The additional anterior chamber pressure can help you to create a controlled incision and can prevent you from accidentally puncturing the anterior chamber when completing the incision.

Some surgeons choose to create the first step of a three-step incision by using the knife to make a partial thickness incision in the limbus. Other surgeons skip this entirely and make a two-step or a one-step incision. The blade of the knife is then pressed to be flush with the sclera and advanced 2 mm into the cornea. Once you have reached the required tunnel length, you change the angle of the blade slightly to point the tip downward to enter the anterior chamber. Finally ease the blade into the eye and, once you enter the eye, change your angle of approach and tilt upwards to avoid puncturing the lens capsule (unless you want to do so).

Advantages:
- Easier and faster, no conjunctival dissection or cautery needed
- Femtosecond laser can alternatively be used to make the incision
- Better immediate cosmetic result
- Leaves a pristine conjunctiva for a future trabeculectomy
- The corneal curvature flattening effect can be used to reduce an astigmatism "operating on the steep"

Disadvantages:
- Theoretically increases the risk for endophthalmit
- Increased risk for postoperative wound leak
- If too posterior, can cause conjunctival ballooning
- More likely to cause a detachment of Descemet's membrane

3. Wound location

Astigmatism: The closer the incision is to the optical center, the greater the degree of astigmatism induced. Given the elliptical shape of the normal cornea, temporal incisions induce less astigmatism than superior ones. This is true for both corneal and scleral incisions. You may wish to "operate on the steep" and adapt your wound location to the keratometry readings of the eye.

Ergonomics: Surgeon comfort is also important in planning your wound location. Right or left handed surgeons may decenter the wound toward the side most comfortable for them. Typically, the 12 o'clock position is more comfortable because you can rest your hands on the forehead for stability. In the temporal position, it can be difficult for taller surgeons to position their knees under the head of the patient.

4. Wound architecture

Size: As cataract surgical techniques and lens biomaterials that can be compressed but still retain their shape have improved, incisions have become much shorter. Microincision cataract surgery (MICS) can be performed with incisions 1.5 mm to 2.0 mm in width. The width is not only determined by the keratome, but is also determined by the injector of the IOL. If the wound is too small, the pressure of the injector can stretch the wound. This can reduce the self-sealing properties of the wound.

Shape: Although the trend toward smaller, more astigmatism-neutral incisions is making the shape of the wound less relevant, the shape can still play a role. The four shapes described for scleral incisions are: arcuate, straight, frown, and chevron. The arcuate incision has a most significant impact on astigmatism, whereas the frown incision induces the least astigmatism.

Length: Tunnel length depends on its width, but 2 mm is usually preferable. Shorter tunnels can lead to more leakage, poorer control of the anterior chamber, and iris prolapse. Longer tunnels can cause corneal striae and reduced visibility, and limit your ability to pivot instruments during surgery.

5. Wound closure

When created correctly, both scleral and corneal incisions should be self-sealing with a valve-like tunnel design. It is extremely important to ensure that the wound is water-tight at the end of the surgery, prior to injecting the intracameral antibiotic. If the wound closure is inadequate there are strategies to improve the closure:

Stromal hydration is performed routinely by many surgeons. This involves forceful injection of balanced salt solution (BSS) into the wound. This causes the stroma to expand and improves wound apposition though there is some evidence that once the oedema resolves, the wound can leak later.

Sutures can be used to provide additional support. Absorbable 10-0 sutures like Vicryl can be used at the end of the surgery to secure the main wound. Babies and children under two always need sutures as their wounds do not tend to self-seal, even with stromal hydration. The suture provides more wound stability, but it will induce a short term steepening effect.

6. Take home messages

- The two most common types of incisions are scleral tunnel and clear corneal
- Both have distinct advantages and disadvantages
- Learning both techniques is valuable so that you can adapt your approach to the patient
- Choice of wound location depends on astigmatism and surgeon comfort
- Incision characteristics (width, shape, length, presence of endothelial cell loss) influence the wound

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Answers to MCQs on page 49

1. a. *False*
   b. *True*
   c. *False*
   d. *False*
   e. *True*

2. a. *True*
   b. *True*
   c. *False*
   d. *True*
   e. *True*

3. a. *True*
   b. *True*
   c. *False*
   d. *True*
   e. *True*

4. a. *True*
   b. *False*
   c. *True*
   d. *True*
   e. *True*

09

What OVD to choose?

Sorcha NI DHUBHGHAILL, Belgium

MCQs

1. **Cohesive ophthalmic viscosurgical devices (OVDs):**
   a. Are the most popular OVDs
   b. Sodium hyaluronate was the first OVD
   c. Have very good endothelium coating properties
   d. Have very good elasticity properties
   e. Are more likely to be retained in the eye at the end of surgery

2. **Dispersive OVDs:**
   a. Display better coatability properties than cohesive OVDs
   b. Have a higher molecular weight than cohesive OVDs
   c. Display good pseudoplastic properties
   d. Hydroxypropylmethylcellulose (HPMC) used in many OVDs is derived from plant fibres
   e. Are more likely to lead to a phaco burn than cohesive OVDs

3. **OVDs in general:**
   a. Viscoadaptive OVDs are made of sodium hyaluronate
   b. Sodium hyaluronate was originally derived from rooster combs but is now produced synthetically
   c. The Arshinoff triple soft shell technique requires three OVDs
   d. The best OVD for patients with Fuchs' endothelial dystrophy is Healon®
   e. Viscoat® is easier to remove from the capsular bag than Healon 5®

4. **OVDs in general:**
   a. Dispersive OVDs coat intraocular lenses and capsular tension rings better than cohesive OVDs
   b. HPMC was the first OVD developed
   c. Cohesive OVDs are contraindicated in paediatric cataract surgeries
   d. Dispersive OVDs are more effective tamponades of the vitreous than cohesive OVDs
   e. Chondroitin sulfate is derived from animal cartilage such as cow trachea and shark fin

OPHTHALMIC VISCOSURGICAL DEVICES (OVDs) are an essential tool in cataract surgery. They deepen and stabilise the anterior chamber, protect the endothelium, and provide space for surgical manipulation. The can also be used to widen small pupils, tamponade the vitreous, lubricate intraocular lens (IOL) injection, and break posterior synechiae. The first OVD, Healon®, was introduced in 1979 and has been followed by a myriad of OVDs with varying properties.

1. Rheology and OVDs

Rheology is the study of deformation and flow of matter, particularly the non-Newtonian flow of liquids and plastics. Newtonian fluids have a single coefficient of viscosity for a given temperature. The viscosity of non-Newtonian fluids changes with strain rate (flow). The rheological properties of OVDs are very important because they help to describe characteristics of the OCD.

Viscosity: Resistance to flow, which is predominantly determined by the molecular weight and concentration. The higher the molecular weight and concentration, the higher the viscosity. Substances with a higher viscosity are more difficult to displace from the anterior chamber than those with a low viscosity.

Pseudoplasticity: The change in viscosity with an increase in sheer rate. Sheer refers to the friction that occurs when a plate is made to move in relation to another plate. Substances made of chondroitin sulfate do not display pseudoplasticity, whereas sodium hyaluronate and methylcellulose do. With the latter OVDs, the faster the sheer rate, the lower the viscosity. This is useful as it allows an OVD to pass easily through a cannula. Note that chondroitin sulphate OVDs require an extra safety guard whereas sodium hyaluronate does not.

Viscoelasticity: Elasticity is the ability of a body to resist a distorting influence and return to its original shape once the force is removed. The elastic properties of the OVD allows it to maintain anterior chamber volume as instruments move through it. It dampens the high frequency mechanical effects of phacoemulsification. Viscoelasticity is dependent on viscosity, molecular length, and molecular configuration.

Coatability: The coatability of an OVD refers to its ability to cover a surface and is determined by surface tension and contact angle. Surface tension is the tendency of fluid surfaces to shrink to the minimum surface area possible. The contact angle quantifies the wettability of a liquid. Chondroitin sulfate displays better coatability than sodium hyaluronate.

2. Cohesive and dispersive OVDs

Surgeons generally divide OVDs into three categories: cohesive, dispersive, and viscoadaptive.

Cohesive OVDs:
- Higher molecular weights
- High viscosity
- Good space maintainers
- Minimal movement in the anterior chamber
- Easily removed from the anterior chamber, but also easily extruded

Dispersive OVDs:

- Lower molecular weights
- Spreads out and disperses in the anterior chamber
- Coats the endothelium very well
- Less likely to extrude
- More difficult to remove with a higher risk of postoperative pressure spike

Viscoadaptive OVDs:

- High molecular weight and high concentration
- Combined behaviour of cohesive and dispersive OVDs
- Remains in the anterior chamber more effectively than classical cohesive OVDs
- Coats the endothelium well
- Good pseudoplasticity
- Easier to remove from the anterior chamber than dispersive but can still give postoperative pressure spikes

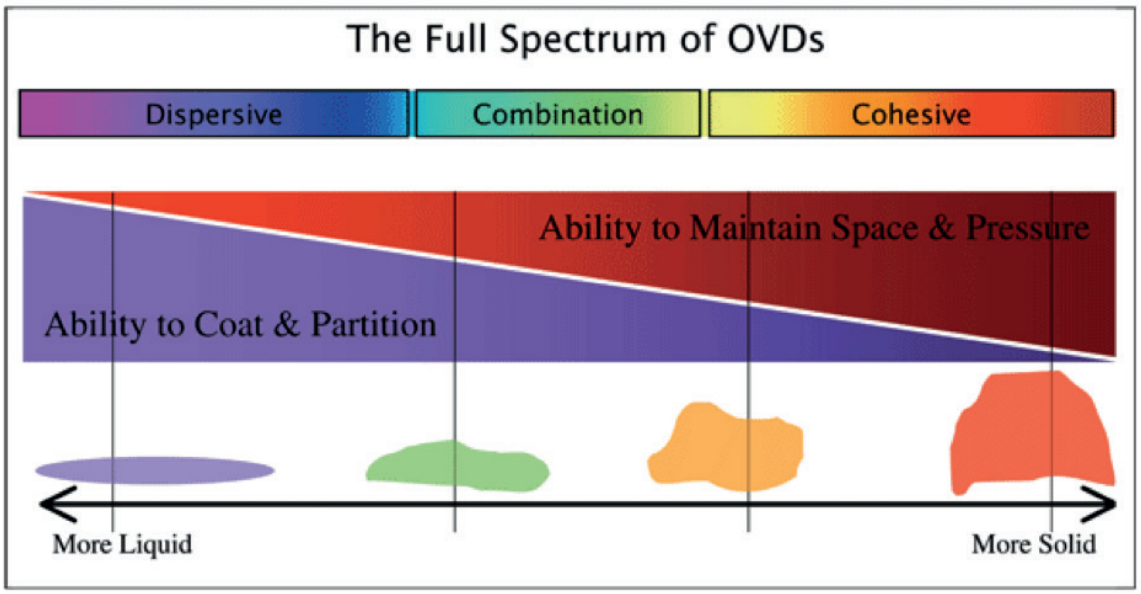

Figure 1. Ophthalmic viscosurgical devices can be described according to the consistency spectrum, from dispersive to cohesive. Dispersive OVDs have a better ability to coat and partition, while cohesive OVDs have a better ability to maintain space and pressurize. Combination products aim to address both ends of the spectrum.

(Source – Review of Ophthalmology)

3. Choosing an OVD

In general, cohesive OVDs are the most popular, but surgeons can adapt their OVDs based on the patient need (e.g., a floppy iris eye may benefit from the better retention properties of a dispersive OVD, whereas filling the capsular bag may be better done by a cohesive OVD as it will be easier to remove at the end of the surgery). The capsulorhexis and disassembly is easier to perform under a cohesive OVD. A combined approach like the Arshinoff Triple Soft Shell technique uses both types of OVDs and it can combine the best of both worlds to provide better protection for the endothelium in cases of Fuchs' endothelial dystrophy.

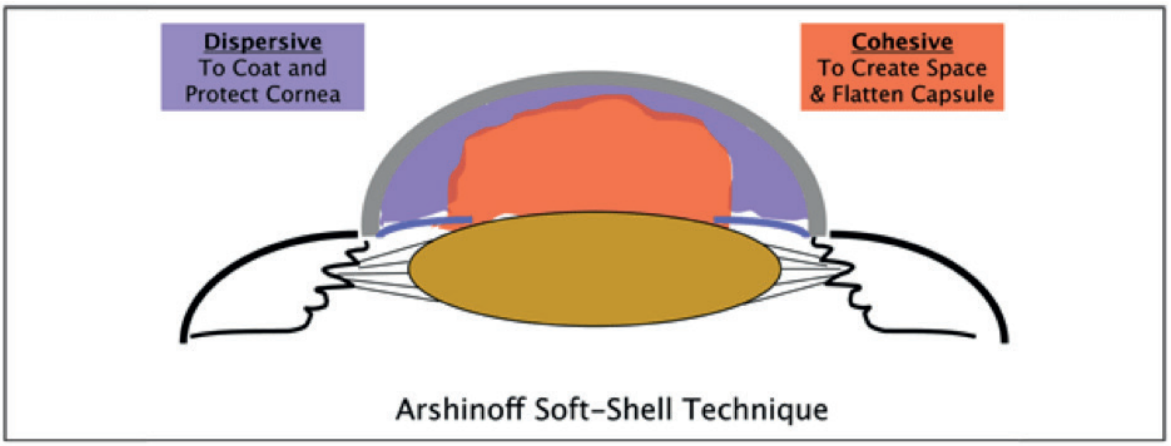

Figure 2. The Arshinoff soft-shell technique is useful to provide the endothelial protection of a dispersive viscoelastic while giving the space creation and pressurizing effects of a cohesive viscoelastic.

(Source – Review of Ophthalmology)

4. Take home messages

- Three types of OVDs; cohesive, dispersive and viscoadaptive
- Cohesive and viscoadaptive OVDs have higher molecular weights
- Dispersive OVDs have lower molecular weights
- Dispersive OVDs protect the endothelium better
- Cohesive OVDs make capsulorhexis and nucleus removal easier

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Answers to MCQs on page 55

1. a. *True*
   b. *True*
   c. *False*
   d. *True*
   e. *False*

2. a. *True*
   b. *False*
   c. *False*
   d. *True*
   e. *True*

3. a. *True*
   b. *True*
   c. *False*
   d. *False*
   e. *False*

4. a. *True*
   b. *False*
   c. *False*
   d. *True*
   e. *True*

RT

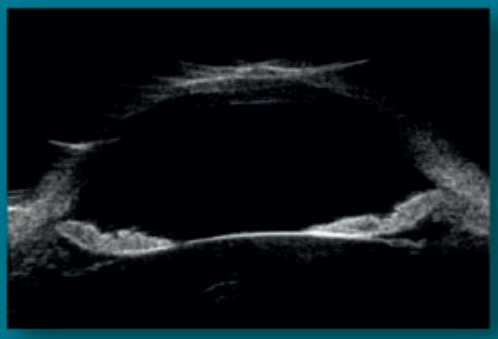
Round Table: How do you diagnose these cases?
Case - Karl MERCIECA

A 30-year-old male was referred with diagnosis of ocular hypertension (OHT). Best corrected visual acuity (BCVA) was 1.0 (20/20) on a Snellen chart with –2.50 myopic prescription in both eyes. Intraocular pressure (IOP) was 24 mmHg, OD, and 26 mmHg, OS. Central corneal thickness (CCT) was 550 µm in both eyes. Latanoprost had been started a year earlier.

- **Describe the finding in the photo**
- **What is the likely diagnosis**
- **What other signs could be found in this condition?**
- **Which typical elements may be found in the history ?**

RT

Round Table: How do you diagnose these cases?
Case continues - Karl MERCIECA

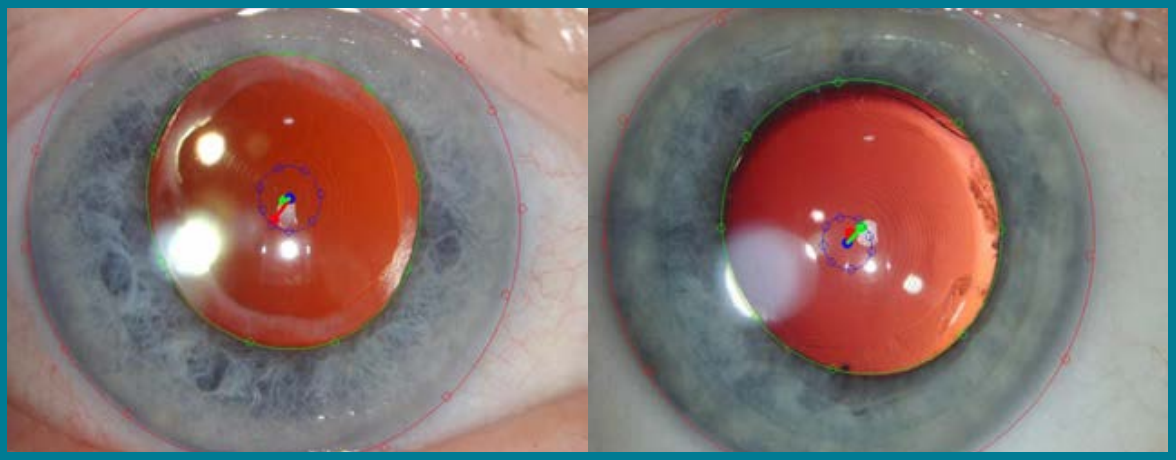


Name the above investigations and describe the findings shown related to the case on the previous page.

- **What investigations would confirm glaucoma secondary to this condition?**
- **What are the treatment options?**

RT

Round Table: How do you diagnose these cases?
Case - Marie-José TASSIGNON

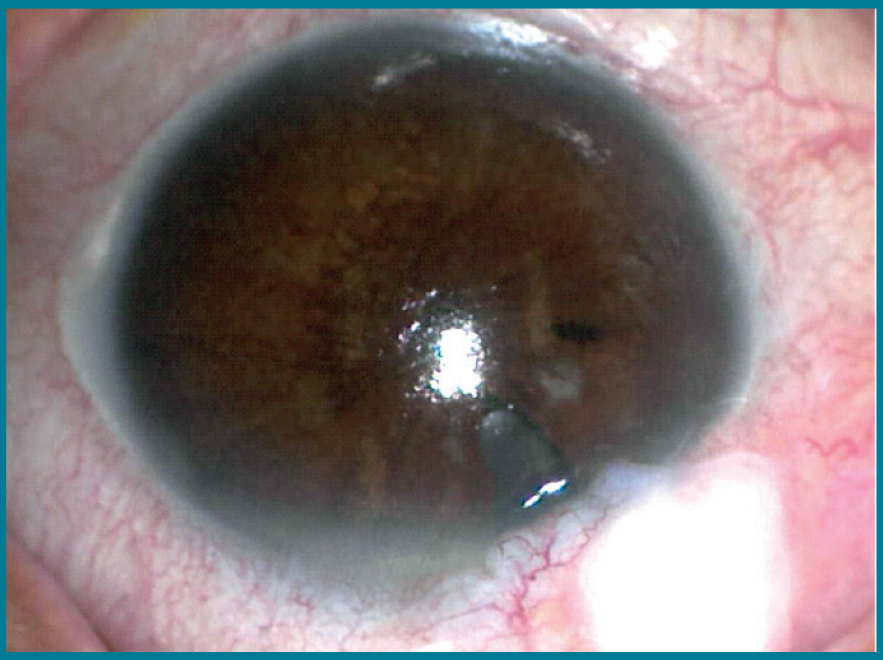


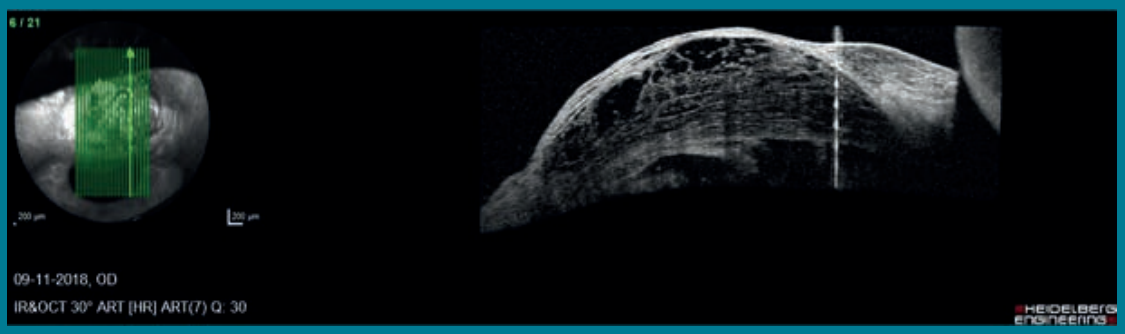
Both eyes of a 52 year-old male were implanted with a diffractive IOL. Simultaneous subsequent surgery both eyes. Two months after surgery his quality of images decreased dramatically. Early Nd:YAG laser capsulotomy was performed, OS. Quality of the image improved a little but not to the degree of satisfaction as experienced by the patient.

- What do you suggest?

RT

Round Table: How do you diagnose these cases?
Case - Luis PINTO



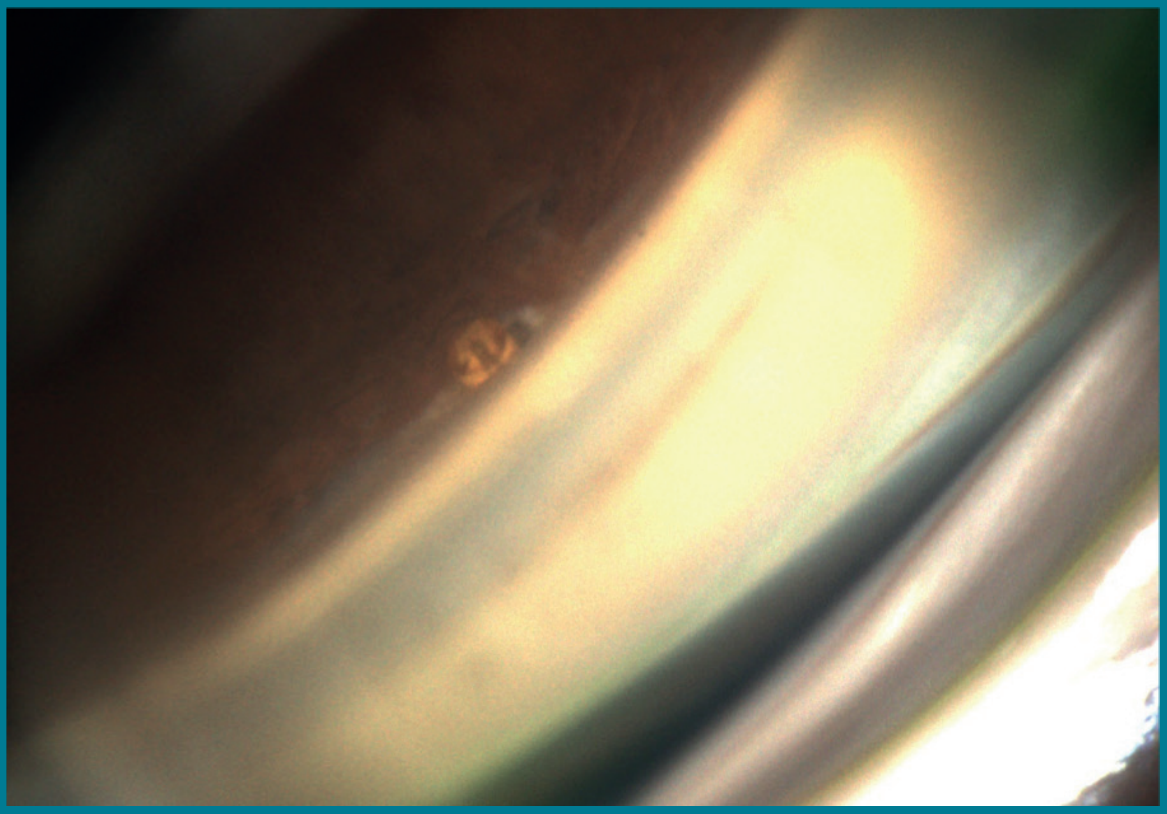


A 82-year-old lady with a diagnosis of primary open-angle glaucoma (POAG) in 2005. Past surgery XEN in 2017, OD. In 2019, visual acuity is 0.3 (20/70). Visual field: mean defect (MD) 12.0 dB. IOP 23mmHg. Cup/Disc ratio 0.6. Current medication: bimatoprost and timolol/dorzolamide combination.

- Why has XEN failed?

RT

Round table: How do you diagnose these cases?
Case continues - Luis PINTO



- Why has XEN failed?

10

Perimetry

Francisco GONI - Spain

MCQs

1. **About the quality of results of visual field testing:**
   a. The reliability of a single visual field examination is estimated using catch trials
   b. Unreliable visual field results frequent as demonstrated by the Ocular Hypertension Treatment Study
   c. The reliability of a visual field series trend depends mainly on the location of the visual field losses
   d. Variability influences the quality of a visual field series and can be estimated by the amount of dispersion associated with the trend

2. **Regarding different criteria used to define functionally manifest glaucoma:**
   a. They are employed as binary classifiers (i.e., disease is present or absent).
   b. Mean defect/deviation is less sensitive than pattern standard deviation/loss variance
   c. Glaucoma hemifield test outside normal limits maximizes specificity rather than sensitivity
   d. Combining two or more criteria helps to increase specificity

3. **Regarding the rate of functional progression:**
   a. It is usually represented as the amount of global visual field loss per year
   b. Average values of 1 dB/year have been observed in several glaucoma studies
   c. It can slow down after a strong hypotensive intervention
   d. A ratio of visual field index (VFI) / mean defect of 3:1 is frequently observed in progressing patients

4. **In patients with severe glaycomatous damage:**
   a. VFI measurements can show artifactual changes when MD crosses the 20 dB loss boundary
   b. Variability is significantly higher than in moderate damage
   c. Trend analysis is less sensitive than event analysis to detect progression
   d. Size V stimulus helps to expand the dynamic range to continue detecting progression

GLAUCOMA is a chronic progressive optic neuropathy measured and evaluated by specific indicators of disease, namely biomarkers. Standard automated perimetry (SAP) is the most frequently used method to obtain functional biomarkers, which remain the main clinical outcome measure not only to diagnose and follow up glaucoma, but also to stage, predict and/or monitor the clinical response to an intervention.

1. Glaucoma diagnosis using perimetry

Diagnosis of manifest glaucoma is based on a significant and reproducible functional loss determined with examinations of good quality. Different diagnostic criteria are available in the literature for SAP, but no definite consensus exists as to the best criterion. In clinical practice, objective criteria like the glaucoma hemifield test (HFT) or pattern standard deviation/loss variance are preferred when few visual field tests are available. Functional loss must always be analysed in the context of structural and clinical findings to rule out artefacts and other sources of false positive diagnosis. The observation of a structure-function correlation strongly suggests glaucoma diagnosis. After obtaining five or more good quality visual fields glaucoma diagnosis can be confirmed by measuring progression.

In severe cases functional loss can be barely measured with SAP and non-standard perimetry using stimulus size V can be recommended to expand the dynamic range of visual field testing.

2. Glaucoma progression using perimetry

Progressive functional loss can be measured after obtaining at least five examinations over time, using event and/or trend analyses. Event analysis is more sensitive but less specific than trend analysis, mainly in early glaucoma. In clinical practice it is recommended to use both methods, as they are complementary. In moderate and advanced glaucoma, trend analysis is more useful than event analysis.

The clinical value of any amount of visual field progression is related to the time for this loss to have taken place, thus it can be characterised as speed, or rate of progression (RoP). RoP can be established locally (in specific regions represented by clusters of points) or for the entire visual field, using global indicators like mean defect/deviation (MD) or the visual field index (VFI) Linearity, variability, quality, and number or tests are all important factors that must be considered when calculating ROPs. Very fast ROPs can be estimated with sufficient statistical power with just six visual fields taken over two years. The longer the follow-up, the more accurate is the prediction. It is the most important outcome measure in glaucoma management, as it has prognostic implications.

In severe cases stimulus size V can also be used to measure progression, calculating the remaining mean sensitivity of each visual field test.

3. Frequency of perimetric examinations

During the first two years after glaucoma diagnosis it is recommended to obtain six visual fields to rule out catastrophic progression. In the case that this specific recommendation cannot be followed, it is still encouraged to continue performing periodic visual field testing to detect fast progression as early as possible, because these patients are at the highest risk of visual disability. When early functional progression is seen, intraocular pressure (IOP) is not appropriately controlled, or significant structural progression is documented, it is recommended to maintain a high frequency of examinations. In case of slow progression and good IOP control, the frequency of tests can be lower.

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Answers to MCQs on page 66

1. a. *True*
   b. *False*
   c. *False*
   d. *True*

2. a. *True*
   b. *True*
   c. *False*
   d. *False*

3. a. *True*
   b. *False*
   c. *True*
   d. *True*

4. a. *True*
   b. *False*
   c. *False*
   d. *True*

11

Glaucoma classification/differential diagnosis

Luciano QUARANTA - Italy

MCQs

1. **Regarding primary angle-closure glaucoma (PACG):**
   a. Angle closure is defined as either appositional or synechial.
   b. Pupillary block is a more common angle-closure mechanism than plateau iris.
   c. Most angle-closures are asymptomatic.
   d. Medical treatment of PACG does not differ much from treatment of primary open-angle glaucoma.

2. **Regarding paediatric glaucoma:**
   a. Childhood glaucoma is as good as always a primary glaucoma.
   b. In juvenile glaucoma, high intraocular pressure distends the eyeball.
   c. Phakomatoses are one cause of childhood glaucoma.
   d. Glaucoma may develop in up to 50% of children who undergo cataract surgery before the age of 9 months.

THE TERM "glaucoma" refers to a complex group of diseases, primarily classified according to irido-corneal angle findings and the presence or absence of other pathologic conditions, responsible for intraocular pressure (IOP) increase.

Glaucoma is first classified into *primary glaucoma*, when no evident cause of optic nerve damage other than glaucoma is present; *secondary glaucoma*, when the typical optic neuropathy is a consequence of IOP increase that results from ocular or systemic disorders, or from external causes (e.g., drugs); and *childhood glaucoma*, when the disease affects children and follows congenital anomalies of the anterior chamber angle (i.e., primary congenital glaucoma, PCG) or secondary alterations in ocular and systemic disorders.

Glaucomatous optic neuropathy is the functional and structural hallmark of glaucoma, on which all the classifications from international glaucoma societies typically relies. IOP, even if it is the main risk factor for glaucoma development and progression, is not always included in classifications. Indeed, we know from the Ocular Hypertension Treatment Study (OHTS) and the Early Glaucoma Prevention Study (EGPS) that only a small proportion of hypertensive patients, according to their risk profile, develops manifest glaucoma in long term. Nevertheless, normal tension glaucoma (NTG) is a well-known entity, in which glaucomatous neuropathy develops while IOP values are within normal limits. High IOP values remain mandatory in some types of glaucoma, such as childhood glaucoma, where the *primum movens* is a developmental anomaly of the anterior chamber that increases outflow resistance and, consequently, the IOP.

1. Primary glaucoma

Primary glaucoma includes *primary open-angle glaucoma* (POAG) and *primary angle-closure glaucoma (PACG)*. The former includes both conventional POAG and NTG. As individual differences in the vulnerability of optic nerve to IOP are probably present, the term "primary open-angle glaucoma" is a concept encompassing both these diseases. It may be convenient, however, to differentiate an ocular hypertensive form (POAG) and a normotensive form (NTG) in routine medical practice. Both POAG and NTG are chronic progressive optic neuropathies that result in characteristic morphological changes in the optic nerve head and retinal nerve fiber layer (RNFL). Visual field loss is merely the consequence of ganglion cell degeneration. Obviously, anterior chamber angle should be evaluable at gonioscopic examination, because "open-angle" is a critical part of the definition of the disease.

PACG is an optic neuropathy caused by increased IOP (acute or chronic), resulting from anterior chamber angle closure. No universally accepted definition of "angle closure" actually has been elaborated, and scientific publications on PACG lack uniform diagnostic criteria. Angle closure is generally defined as the presence of iridotrabecular contact, both appositional or synechial at gonioscopy. Relative pupillary block and iris plateau are the two main mechanisms that determine angle-closure, the latter being much less frequent than the first, especially in Western countries. It should be noted, however, that a mixed mechanism of pupillary block and plateau iris may be present. The term primary angle closure (PAC) indicates the presence of a narrow angle, and signs that angle occlusion by peripheral iris apposition has previously occurred. Interestingly, most angle-closures are asymptomatic, although symptoms of pain, redness, blurred vision, and haloes may be present, especially

in cases referred to as "acute". Angle closure is generally classified in three (potentially) evolutionary steps:

- Primary angle-closure suspect (PACS): two or more quadrants of iridotrabecular contact, normal IOP, no synechiae, and no evidence of glaucomatous optic neuropathy.
- Primary angle-closure (PAC): Iridotrabecular contact that results in synechiae, raised IOP. or both, with no evidence of glaucomatous optic neuropathy.
- Primary angle-closure glaucoma (PACG): iridotrabecular contact causes glaucomatous optic neuropathy and synechiae; of note, IOP may not be high at the time of first examination, due to an intermittent mechanism.

According to the mode of presentation, PAC has been further divided in five subtypes, even if it is actually unknown whether this classification may be useful in determining the prognosis and management of the disease. This classification includes: PACS, acute angle-closure, intermittent angle-closure, chronic angle-closure, and post-acute angle-closure attack.

2. PACG vs. POAG

Evaluation of the anterior chamber angle is essential to differentiate PACG from POAG, and it should always be performed in patients with glaucoma, especially at first diagnosis. Treatment algorithms for PACG and POAG are different, and treating a PACG patient as a POAG patient is a serious error. Despite new instruments that have recently surfaced for the evaluation of the anterior chamber angle, gonioscopy remains the mainstay of angle evaluation, and an indispensable instrument for the clinician who wants to manage glaucoma. Although anterior segment optical coherence tomography (AS-OCT) has recently acquired the ability to give information about anatomical structures involved in angle closure mechanism (such as the iris, lens, and anterior chamber depth), no single parameter or a combination thereof have been demonstrated to be superior to gonioscopy for a clinical decision. Very recently, a 360° degree automatic gonioscope has been developed (GS1-Gonioscope®, Nidek, Gamagori, Japan), capable of rapid angle image acquisition. However, recent studies have showed poor agreement between automated gonioscopy, performed with a GS1 prototype, and manual gonioscopy in detecting eyes with angle closure.

3. Secondary glaucoma

Secondary glaucoma refers to conditions where optic neuropathy follows an IOP increase determined by other ocular or systemic conditions, or medication use. Secondary glaucoma may be classified from several standpoints, including aetiology, mechanisms of IOP elevation, and means of treatment. The most used classification takes into account anterior chamber angle, distinguishing *secondary open-angle glaucoma and secondary closed-angle glaucoma*. However, it may be difficult to encompass all the complexity of secondary glaucoma by taking into account only this classification. For example, neovascular glaucoma, one of the commonest types of secondary glaucoma, begins as an open-angle disease, but later develops angle-closure because of neovascular membrane contraction. On the other hand, though an optic neuropathy is mandatory for the definition of glaucoma, it may be difficult to assess morphological and functional changes in secondary glaucoma because of the presence of the underlining disease. For these reasons, conditions with secondary

increase of IOP are often treated as secondary glaucoma, independently of the anatomical and functional damage.

Secondary open-angle glaucoma is classified, according to its mechanism, into:

- Pretrabecular forms from increased outflow resistance between the trabecular meshwork and the anterior chamber (e.g., neovascular glaucoma, glaucoma secondary to epithelial ingrowth).
- Trabecular forms from increased outflow resistance at the trabecular meshwork level (e.g., steroid glaucoma, exfoliation glaucoma, pigmentary glaucoma, uveitic glaucoma, traumatic glaucoma, glaucoma secondary to vitreous surgery).
- Posttrabecular forms from increased outflow resistance posterior to Schlemm's canal (e.g., glaucoma in exophthalmos, glaucoma from increased venous pressure).

Secondary angle-closure glaucoma is typically classified into:

- Posterior forms with pupillary block (e.g., glaucoma due to lens swelling, microphthalmos, lens sub-luxation).
- Posterior forms without pupillary block from anterior movement of tissue posterior to the lens (e.g., malignant glaucoma, glaucoma secondary to scleral buckling, glaucoma due to intraocular tumours).
- Anterior forms where angle-closure is due to goniosynechiae without pupillary block or movement of the iris-lens diaphragm (e.g., neovascular glaucoma, irido-corneo-endothelial [ICE] syndrome, glaucoma secondary to uveitis).

4. Childhood glaucoma

Childhood glaucoma comprises *primary congenital glaucoma (PCG)*, deriving from isolated developmental anomalies of the anterior chamber angle, and *secondary congenital glaucoma*, associated with ocular or systemic anomalies. The onset of PCG is typically at birth or before 2 years of age, even if instances of late diagnosis may be found. The IOP increases because of anterior chamber angle dysgenesis, characterized by incomplete development of the trabecular meshwork at birth.

Primary childhood glaucoma comprises a subtype named juvenile glaucoma, occurring from 2 years to puberty. Juvenile glaucoma is typically characterized by elevated IOP, glaucomatous optic neuropathy, and consistent visual field defects without ocular enlargement or congenital ocular anomalies or syndromes. For these reasons, it is often misdiagnosed as POAG, even if the young age of onset may easily help in the diagnosis.

Secondary childhood glaucoma results from a variety of pathogenetic mechanisms, comprising non-acquired ocular anomalies (e.g., Axenfield-Rieger anomaly/syndrome, Peters' anomaly, aniridia, ectopia lentis, etc.), non-acquired systemic diseases (e.g., chromosomal disorders, connective tissue disorders, metabolic disorders, phacomatoses), and acquired conditions (e.g., uveitis, trauma, tumours, etc.). *Glaucoma following congenital cataract extraction* is

a frequent type of childhood glaucoma, with an incidence that may be as high as 50% if cataract surgery is performed before the 9th month of life.

5. Conclusion

Classification of glaucoma remains a very challenging task, both for the ophthalmologist in training and the experienced clinician. Careful evaluation of patients is essential to make a correct diagnosis and to avoid errors that unequivocally have effects on the therapeutic approach and on the outcome of our interventions.

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5. Teixeira F, Sousa DC, Leal I, et al. Automated gonioscopy photography for iridocorneal angle grading. Eur J Ophthalmol. Oct 2018. doi: 10.1177/1120672118806436.

Answers to MCQs on page 70

1. a. *True*
   b. *True*
   c. *True*
   d. *False*

2. a. *False*
   b. *False*
   c. *True*
   d. *True*

12

Treatment principles and target IOP

Ingrida JANULIEVICIENE - Lithuania

MCQs

1. **Large randomized clinical trials showed that:**
   a. IOP reduction reduces incidence of glaucoma in ocular hypertension
   b. IOP reduction increases rate of progression in glaucoma
   c. IOP reduction reduces rate of progression in manifest glaucoma
   d. IOP reduction by 20% reduces the risk of progression by 90%

2. **The principle of combination therapy is to:**
   a. use multiple separate instillations of drugs
   b. use more than 2 separate bottles
   c. combine drugs of the same pharmacological group
   d. increase dosing schedule

3. **Individual glaucoma patient management includes:**
   a. monitoring the rate of progression
   b. starting with monotherapy
   c. the highest amount of medication required to achieve the therapeutic response
   d. evaluation of patient-related outcomes

4. **Preservatives in ophthalmic medications are used for:**
   a. reducing risk of ocular surface disease and Meibomian gland dysfunction
   b. decreasing patient's quality of life
   c. keeping the bottles sterile
   d. stabilization of the active agents in solution

12 Treatment principles and target IOP - JANULIEVICIENE I - Lithuania

GLAUCOMA is a progressive optic neuropathy and current medical therapy for this potentially blinding condition focuses on lowering and maintaining a target intraocular pressure (IOP) that is the primary identified risk factor for disease progression.

According to the European Glaucoma Society (EGS) guidelines, the goal of glaucoma treatment is to maintain visual function and quality-of-life, at a sustainable cost. There are several factors to be considered when setting the target IOP:

- Glaucomatous damage at the time of diagnosis – ther greater the damage, the lower the target IOP.
- Life expectancy – younger age implies longer life expectancy and lower target IOP.
- Untreated IOP level – the lower the initial IOP at baseline, the lower target IOP should be.
- Additional risk factors (e.g., exfoliation syndrome).
- Rate of progression during follow-up – the faster the progression, the lower the target IOP.

The target IOP is defined as the upper limit of the IOP estimated to be compatible with a rate of progression that is slow enough to maintain vision-related quality-of-life for the expected lifetime of the patient. Target IOP needs to be estimated for every individual patient and every eye, and it must be re-evaluated regularly. The evidence is insufficient to support any particular algorithm to determine a threshold IOP, percentage of IOP reduction, or calculated IOP. Ocular Hypertension Treatment Study (OHTS) demonstrated that 20% IOP reduction as a target lowered the 5-year risk of glaucoma from 9.5% to 4.4%. Some individuals still developed glaucoma with treatment, whereas a significant number of non-treated individuals did not. In the Collaborative Initial Glaucoma Treatment Study (CIGTS) patients with newly diagnosed glaucoma were randomised to medical treatment or trabeculectomy with individualised target IOP. The mean IOP in the medically treated group was 17–18 mmHg (>35% reduction) and 14–15 mmHg (>40% reduction) in the surgical group. However, glaucoma progression rates were not different.

Topical antiglaucoma drugs are available today in a wide variety of types – prostaglandin analogs, beta-receptor blockers, carbonic anhydrase inhibitors, adrenergic agonists, and parasympathomimetics. In routine clinical practice, individualized glaucoma management is based on the least amount of medication required to achieve the desired therapeutic response. It is recommended to initiate treatment with monotherapy. If IOP reduction is effective, comparable to the average range of the particular drug class and well tolerated, the treatment should be continued. During follow-up it is important to check the IOP, optic discs, visual fields, and also quality-of-life.

If the initial therapy is not effective it is recommended to switch to another monotherapy. If IOP reduction is comparable to the average range of the particular drug class but the target IOP is not reached, the second drug should be added and efficacy with tolerability evaluated again. Fixed combination treatment should be preferred over two separate bottles. If combination therapy fails to stop glaucoma progression, a third medication can be added, or laser or incisional surgery should be considered.

Major challenges with long-term medical glaucoma therapy are patient non-compliance and non-adherence, problematic treatment schedules, difficulties in application, and wash-out of medication by tears. Various adverse effects may have a negative impact on doctor–patient relationship and patient's quality-of-life. Topical glaucoma medications have been associated with ocular surface disease such as dry eye, Meibomian gland dysfunction, and allergy. This interaction can involve the active agent itself or the preservative used to keep the bottles sterile, to stabilize the active agents in solution, or both. Most preservatives act like detergents and might also influence corneal penetration of topical drugs. Ocular surface disease is more common with age just like glaucoma. Elderly patients with long-term and especially multiple topical medications ultimately have a risk for ocular surface disease that might contribute to poor patient compliance and, thus, disease progression.

Preservative-free medications might be used in patients who do not tolerate eye drops with preservatives. New implantable drug delivery devices that address patient non-compliance and fluctuation of IOP issues also have clear limitations. An invasive surgical procedure is needed and it is not possible to change – increase, decrease, or stop drug delivery once it has been introduced into the eye.

Generic medications must contain the same active ingredients as the original formulation and to be identical to a brand name drug in dosage, strength, route of administration, performance characteristics, and intended use. Generic medications are produced and distributed without patent protection. Genericisation reduces medication prices by increasing competition between manufacturers and saves a lot of money for the healthcare system and consumers. Generic drugs are sold at substantially lower prices than brand name drugs because the latter require substantially greater time and investor money for clinical development. Statistics illustrate how significant a role the generic drug market plays in present healthcare systems. However, concerns regarding generic medications exist because of the lower regulatory standards required by the FDA in USA or EMEA in EU for ophthalmic formulations. Generics are not required to have same excipients (i.e., substances formulated alongside the active ingredient of a medication) as branded medications. Different size of drug particles and pH can change the pharmacokinetics and distribution in tissues. Different inactive ingredients such as preservatives, pH adjusters, antioxidants, thickening agents, buffers, and tonicity adjusters can vary considerably between generic and brand medications. This may influence penetration, absorbtion, retention time on the eye, bioavailabilty, induce changew in viscosity, osmolality and pH tolerability, and impact safety and efficacy of medication. Bottle design often influences drop size, and researchers have found that drop sizes can range from about 25 µl to 70 µl. If a patient receives a different amount of drug than intended, efficacy may be affected or adverse effects may result.

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6. Chen J, Stephen A Runyan SA, Robinson MR. Novel ocular antihypertensives in clinical trials.Clinical Ophthalmology 2011:5 667–677.
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Answers to MCQs on page 76

1. a. *True*
   b. *False*
   c. *True*
   d. *False*

2. a. *False*
   b. *False*
   c. *False*
   d. *False*

3. a. *True*
   b. *True*
   c. *False*
   d. *True*

4. a. *False*
   b. *False*
   c. *True*
   d. *True*

13

IOP-lowering medications

John THYGESEN - Denmark

MCQs

1. **Regarding adrenergic receptors:**
   a. Beta-1 receptors are found in the ciliary, retinal and choroidal blood vessels but not in the cardiac muscle
   b. Alpha-1 receptors, when stimulated, increase aqueous formation
   c. Alpha-2 receptors, when stimulated, increase aqueous formation
   d. Beta-2 receptors, when stimulated, enable increased airflow within pulmonary bronchioles

2. **Which of the following is considered to be a side-effect of using beta blockers?**
   a. Depression
   b. Fatigue
   c. Tachycardia
   d. Bronchoconstriction

3. **Which of the following medications is most likely to cause side-effects, including allergic conjunctivitis?**
   a. Bimatoprost
   b. Timolol
   c. Brimonidine
   d. Brinzolamide

4. **The following drug(s) is contraindicated for patients with cardiac or pulmonary disease:**
   a. Latanoprost
   b. Dorzolamide
   c. Timolol
   d. Brimonidine

SEVERAL prospective randomized multicentre controlled clinical studies have clearly established the benefits of IOP reduction in managing primary open-angle glaucoma (POAG) at various stages of the disease, whether of the 'high pressure' or 'normal pressure' variety, as well as in reducing the conversion of ocular hypertension (OHT) to POAG.

Most forms of open-angle glaucoma and many types of chronic angle-closure glaucoma are initially treated with topical and occasionally with orally administrated agents that reduce aqueous humour production, enhance aqueous outflow or on both. Although acute angle closure with or without glaucoma needs rapid laser or incisional surgery, medical treatment usually will be initiated as a first step in most cases.

Laser treatment may be a suitable first option for patients with known intolerance or allergy to topical medications or suspected poor compliance.

When initially selecting medical therapy it is important to consider some relevant patient characteristics as well as features related to the drug.

1. An overview of IOP-lowering medications

The currently available glaucoma eye drops all seek to decrease the IOP. They can be grouped into therapeutic agents that decrease the production of aqueous humor, increase the drainage through the trabecular meshwork (TM), increase uveoscleral outflow, or have a combined effect (Fig. 1). Various drugs differ in their effectiveness, side effect profile, dosing schedule, and cost.

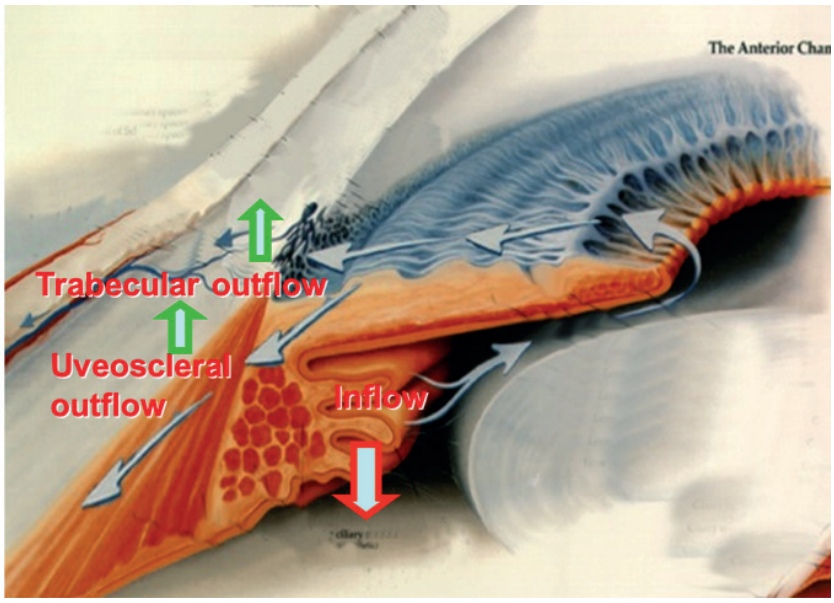


Fig. 1 Mechanisms of IOP lowering medications

2. Receptors in the eye

Most drugs used in the medical management of glaucoma work by modifying the activity of the autonomic nervous system. Some of them mimic the effects of naturally occurring neurotransmitters (agonists) whereas others compete with naturally occurring neurotransmitters, thus reducing their effect (antagonists).

Postganglionic parasympathetic nerve fibres innervate the ciliary muscle and iris sphincter muscle via the short ciliary nerves. Stimulation of these parasympathetic cholinergic (muscarinic) receptors has the effect of increasing aqueous outflow.

There are four types of receptors in the postganglionic sympathetic nerve fibres that innervate the eye:

1. Alpha 1 receptors are found in the iris dilator muscle, ciliary, retinal and choroidal blood vessel walls. When stimulated, the effect on aqueous dynamics is to reduce aqueous formation.
2. Alpha 2 receptors are distributed throughout the nonpigmented ciliary epithelium, and their stimulation also reduces aqueous formation.
3. Beta 1 receptors are distributed in the ciliary, retinal, and choroidal blood vessels whereby stimulation causes increased aqueous formation. Very importantly, these receptors are also found in cardiac muscle, increasing heart rate on stimulation (tachycardia).
4. Beta 2 receptors are distributed throughout the nonpigmented ciliary epithelium as well as in the ciliary, retinal and choroidal blood vessels. Stimulation effects increased aqueous formation. As well as being in the heart muscle, beta 2-receptors are also located within the tracheal and bronchial musculature, producing relaxation and, therefore, increased air inflow.

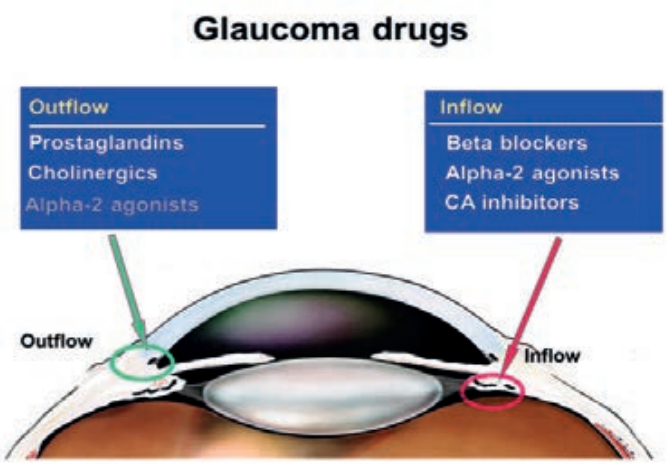


Fig. 2. Mechanisms of IOP lowering medications

3. Current medical IOP lowering treatments available for glaucoma:

1. Prostaglandin analogs
2. Beta blockers
3. Carbonic anhydrase inhibitors
4. Sympathomimetic drugs
    A. Alpha-2 selective adrenergic receptor agonists
    B. Alpha and beta adrenergic agonists
5. Parasympathomimetic drugs (cholinergics)
6. Hypertonic or osmotic agents

Prostaglandin analogs

Prostaglandins are the most potent IOP-lowering drugs, lowering the IOP by 28–33 mmHg at peak. The primary mechanism of action of prostaglandins is to increase uveoscleral outflow, reducing IOP by 25–35%. Reduction of IOP starts approximately 2–4 h after the first administration, with the peak effect within approximately 8–12 h. Thus, IOP measurements taken in the morning represent the peak effect of the prostaglandin analogue for patients administering the drug in the evening. Clinical trials that measured 24 h IOP suggested that evening administration is generally preferable because it gave a better circadian IOP profile. Maximal IOP lowering effect is often achieved 3–5 weeks from beginning the treatment. Differences among drugs within this class in the capability of reducing IOP did not exceed 1 mmHg.

The most common adverse effects are conjunctival hyperaemia or irritation, a change in eye colour (mostly in hazel or green eyes) and an increase in thickness and length of eyelashes. The prostaglandin analogs may also cause periocular skin pigmentation, iritis, and cystoid macular edema. Latanoprost requires refrigeration. In addition, prostaglandin administration has been reported to enhance recurrence of corneal epithelial *Herpes simplex*, and it should, therefore, be used with caution in susceptible patients.

No significant systemic adverse reactions have been associated with the use of prostaglandin analogs. Today, prostaglandin analogs are the most frequently used first choice/first line anti-glaucoma medications and available in many different generic options. Since their development in the 1990s, prostaglandin derivatives (i.e., latanoprost, travoprost, bimatoprost, tafluprost; Fig. 3) have progressively replaced beta blockers as first-choice/first line therapy. This is because they are the most effective IOP-lowering agents, lack relevant systemic side effects ,and require just once-daily administration. Recently, a number of latanoprost generics as well as preservative-free and benzalkonium chloride (BAK)-free prostaglandin formulations have entered the market.

Beta-receptor antagonists (beta blockers)

These drugs reduce the production of aqueous humour by blocking beta-receptors in the ciliary body. They have been used since 1978 (Fig. 3). The non-selective beta blockers lower the IOP by 4–6 mm Hg (20–25%), and the selective beta-1-blocker betaxolol lowers it by 3–4 mm Hg (15-25%). All beta blockers are less effective in eyes with dark irides.

Ocular adverse reactions include conjunctival allergies, conjunctival injection, and corneal epithelial disorders. Corneal sensitivity may be reduced. One major challenge for the use of beta blockers is their frequent systemic adverse effects because of their interaction with both beta-1- and beta-2-receptors. In this matter, adverse effects on the respiratory system of beta-2-blockers include worsening of bronchial asthma attacks and chronic obstructive pulmonary disease.

The most critical adverse effects of ß1-blockage are reduced heart rate and reduced cardiac contractility. Hence, ß-blockers should be used with caution in patients with slow or irregular heartbeat or congestive heart failure. Finally, adverse effects from the use of ß-blockers include depression, impotence, and drowsiness. Two drops of 0.5% timolol equates to a 10 mg oral dose. This is not enough to cause symptoms in many patients, but unfortunately glaucoma and airways disease frequently coexist. ß-blockers have for many years been the most frequently used first line and first choice anti-glaucoma medication, but now in many countries replaced by the prostaglandins.

Carbonic anhydrase inhibitors

Carbonic anhydrase inhibitors (CAIs) reduce IOP by inhibiting the enzyme in ciliary epithelium and thus by controlling aqueous formation. Acetazolamide and methazolamide are able to reduce IOP when taken orally. An IOP reduction of 30–40% can be expected. Systemic CAIs have been used since 1956. Methazolamide is given two times daily and acetazolamide 3–4 times daily. Acetazolamide is available in a slow-release formulation, which can be dosed twice a day.

Systemic CAIs can cause several side effects, including paraesthesia of the lips, fingertips and toes, fatigue, depression, kidney stones, anorexia, weight reduction, nausea and diarrhea, metabolic acidosis, agranulocytosis, aplastic anemia, and Stevens–Johnsons syndrome.

Since 1994, topical CAIs have been available (Fig. 3). An IOP reduction of 20% can be expected. Although the adverse effects are much less as compared to systemically administered CAIs, topical CAIs have some ocular adverse reactions such as conjunctival allergy and hyperaemia. Carbonic anhydrase naturally exists in corneal endothelial cells, and CAIs should be used with caution in patients with corneal endothelial disorders.

Sympathomimetic drugs

Alpha-2 selective agonists, more specifically the autoreceptors of alpha-2 neurons, are used in the treatment of glaucoma to decrease the production of aqueous fluid by the ciliary body and also by increasing uveoscleral outflow. Sympathomimetic drugs like brimonidine and apraclonidine act on alpha-2-receptors and activate G protein-coupled receptors, thereby reducing cAMP. In this way, the production of aqueous humour is reduced and the uveoscleral outflow increased. Brimonidine is able to reduce the IOP by approximately 18–25% and apraclonidine by 25–35%. Approximately 45% of patients treated with apraclonidine show tachyphylaxis by 6 months. The recommended dosing frequency is three times per day. Apraclonidine is contraindicated in infants, in whom it can cause serious systemic side effects

Allergic reactions frequently occur with this class of medication, especially with apraclonidine. An allergy rate of 15–30% has been observed. Side effects may further include irregular heart rate, elevated blood pressure, headaches, blurred vision, fatigue, dry mouth, and redness in or around the eye. A randomized trial of the alpha-2-receptor agonist brimonidine versus the beta blocker timolol, found a less likely visual field progression in patients treated with brimonidine compared to timolol, but a potential neuroprotective role of alpha-2 agonists is still under debate.

Non-selective adrenergic agonists such as epinephrine and the prodrug dipivefrin decrease aqueous humour production and may increase uveoscleral outflow. These drugs lower IOP by 15–20% on average. Non-selective adrenergic agonists are infrequently used today for the treatment of glaucoma or ocular hypertension, and have been replaced by the alpha-2-selective agonists mentioned above.

Parasympathomimetics or cholinergic agonists (miotics)

Parasympathomimetic drugs are cholinergic agents that cause pupillary constriction, thereby increasing the rate of fluid drainage from the eye through the trabecular meshwork. Pilocarpine is the most commonly used cholinergic agonist. It is able to increase the outflow facility through conventional outflow pathways and lower IOP by 20–25%, on average. It is less effective in eyes with dark irides. Pilocarpine gel is applied once a day, but pilocarpine drops have to be given four times a day.

Adverse effects include miosis, induced accommodation, browache, myopic shift, further decrease of vision in patients with cataracts, visual field constriction because of pupillary constriction, and reduced vision in darkness. Increased risk of retinal detachment (especially in patients with high myopia) and iritis are seen. Overdosing miotics may cause excessive salivation and tearing, sweating, diarrhea, vomiting, and bradycardia.

Hypertonic or osmotic agents

Osmotic agents are an additional class of medications used especially to treat sudden (acute) forms of glaucoma where the eye pressure remains high despite other treatments. These medications include isosorbide (given by mouth) as well as mannitol or hypertonic saline (given intravenously). These medications must be used cautiously as they have significant side effects, including nausea, fluid accumulation intra- and extravascularly (congestive heart failure, pulmonary edema), intracerebral bleeding, and kidney problems. Their use is contraindicated in patients with uncontrolled diabetes, heart, kidney, or liver problems.

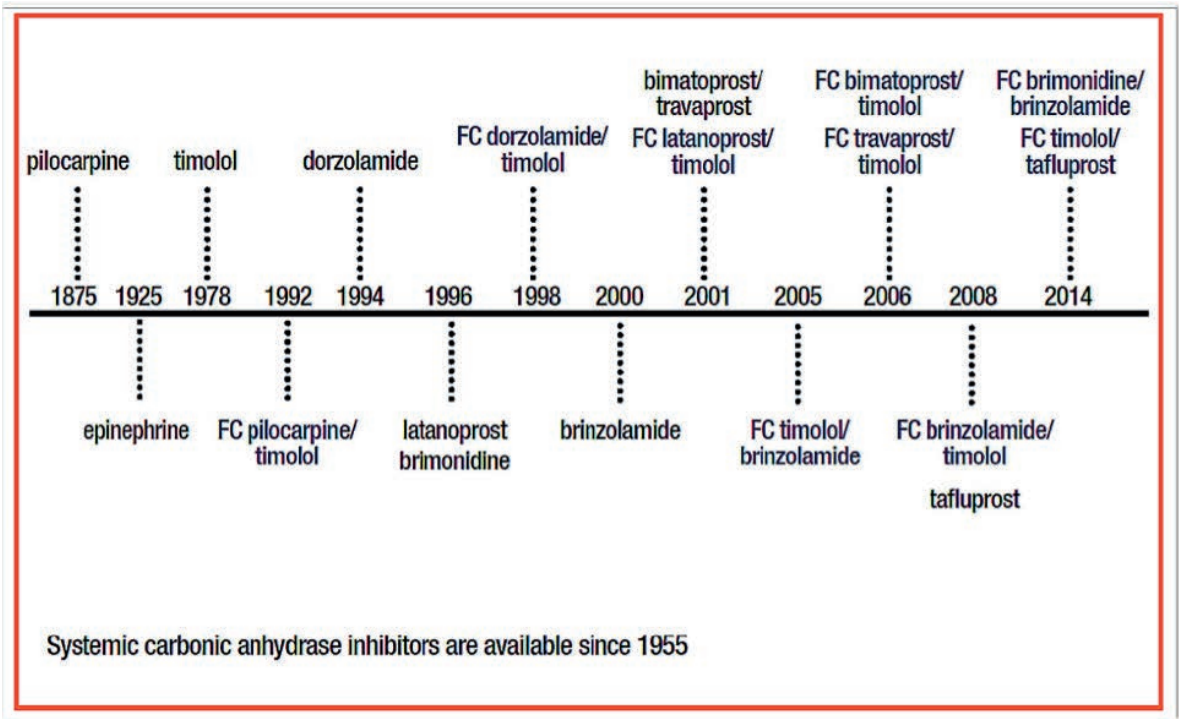


Fig. 3. From EGS Guidelines (2014)

4. The role of preservatives

Long-term topical glaucoma medications may cause or exacerbate pre-existing ocular surface disease (OSD), such as dry eye, Meibomian gland dysfunction and chronic allergy, which, in glaucoma patients, has a much higher prevalence than in the general population. OSD may follow chronic use of antiglaucoma medication with or without the preservative benzalkalonium chloride (BAK), a quaternary ammonium compound. BAK is the most frequently used preservative agent in eye drops and its ue correlates well with the signs and symptoms of OSD. Such signs and symptoms can diminish if BAK-preserved eyedrops are substituted with non-preserved drops. An unwanted effect of BAK is a reduction in the success rate of filtering surgery. *In vitro* studies suggest that alternative preservatives, like polyquad, are significantly less toxic than BAK.

Other therapeutic possibilities are use of preservative-free or BAK-free medication, decreasing the number of preserved eye drops (i.e., use of fixed combinations). Four factors have to be considered: the active compound, the specific preservative, the ability of the patient to use single-dose preparations, and the ocular surface.

The European Medicines Agency (EMEA) has suggested that the use of preservatives should be avoided in "patients who do not tolerate eye drops with preservatives" and in those on long-term treatment, or else to use "concentration at the minimum level consistent with satisfactory antimicrobial function in each individual preparation", with a specific indication to avoid mercury- containing preparations.

Not all patients are sensitive to preservatives, and not all local side effects observed with topical anti-glaucoma medications are induced by preservatives.

Particular attention should be paid to glaucoma patients with pre-existing OSD and to those developing dry eye or ocular irritation over time. This can be done by careful assessment of redness of the eyelid margin, positive corneal and conjunctival fluorescein staining, and reduced tear break-up time.

5. Generic IOP-lowering topical medications

By definition, a generic drug is identical to a brand named drug in dosage, strength, route of administration, performance characteristics, and intended use. For the purposes of drug approval, the interchangeability of a generic drug and the corresponding brand name drug is based on the criterion of "essential similarity". In ophthalmology, this concept is problematic, because it is difficult to prove "essential similarity" in clinical studies. With systemic drugs, bioequivalence studies are performed using blood samples to determine whether the plasma concentration within certain limits equals the branded drug. With topical eye drops such studies obviously cannot be performed.

No clinical studies are usually required for generic approval for ophthalmic use, and a 10% difference between the concentration of the active component between the generic and the branded product is considered acceptable. Whereas the active component is assumed to be equal, the adjuvants can vary considerably. This is a critical issue because different adjuvants may alter the viscosity, osmolarity, and pH of eye drops and, therefore, may have an impact on both tolerability and corneal penetration.

Nevertheless, anti-glaucoma generic drugs are currently prescribed at a large scale, as many drugs are becoming off-patent. For latanoprost, the generic share was more than 65% in most European countries in 2014. To which degree these generics are similar in efficacy and tolerability is not well studied. Only few clinical studies have compared the effect of generic and brand IOP lowering medications in glaucoma, with variable results depending on the type of generic drug. Other studies have shown a difference between the branded and generic preparations concerning the size and number of drops in the bottle, the structure of the bottle,

and the bottle tips. Safety issues with corneal epithelial disorders have also been described with generics, because of an additional stabiliser compound. When switching patients from branded to generic drugs, the IOP should be closely monitored.

6. General recommendations for medical glaucoma therapy

- Monotherapy is the first choice when initiating therapy.
- Baseline IOP should be considered when evaluating the efficacy of a therapy.
- Fixed combination therapy should be considered when patients fail to achieve their individualised IOP targets with monotherapy.
- The prescription of more than two bottles of IOP-lowering eye drops for simultaneous use should be avoided as it can lead to noncompliance.
- Fixed combination preparations may be preferable to the use of separate instillation of two agents.
- Fixed combination therapy is not first-line medication and they are only indicated in patients who need adjunctive therapy, when IOP is not sufficiently controlled by one single agent.
- Ocular surface should be evaluated and considered in management of glaucoma patients. In case of ocular surface disease, preservative-free formulations should be considered.
- Generic drops can differ from branded drops, and it may be necessary to monitor patients more closely after switching.
- During pregnancy, the potential risks to the fetus (and neonate) of continuing anti-glaucoma medications must be balanced against the risk of vision loss to the mother

EGS Guidelines (2014)

RECOMMENDED READING

1. van der Valk R, Webers CA, Schouten JS, et al. Intraocular pressure-lowering effects of all commonly used glaucoma drugs: a meta-analysis of randomized clinical trials. Ophthalmology 2005;112:1177-85.
2. European Glaucoma Society Terminology and Guidelines for Glaucoma, 4th Edition. Chapter 3: Treatment principles and options. Br J Ophthalmol 2017;101:130-195.
3. Boimer C, Birt CM. Preservative Exposure and Surgical Outcomes in glaucoma patients: The PESO Study. J Glaucoma 2013;22:730-5
4. Kolko M. Present and new treatment strategies in the management of glaucoma. Open Ophthalmol J. 2015;9:89-100.
5. Thygesen J. Treatment of Glaucoma with or without Medications, Lowering Intraocular Pressure: Options and Relevant General Health Issues. In: Glaucoma, Vol 8. Karger, pp. 52-75, 2016.
6. Li T, Lindsley K, Rouse B, et al. Comparative effectiveness of first-line medications for primary open angle glaucoma – a systematic review and network meta-analysis. Ophthalmology. 2016;123:129-40.

Answers to MCQs on page 81

1. a. *False*
   b. *False*
   c. *False*
   d. *True*

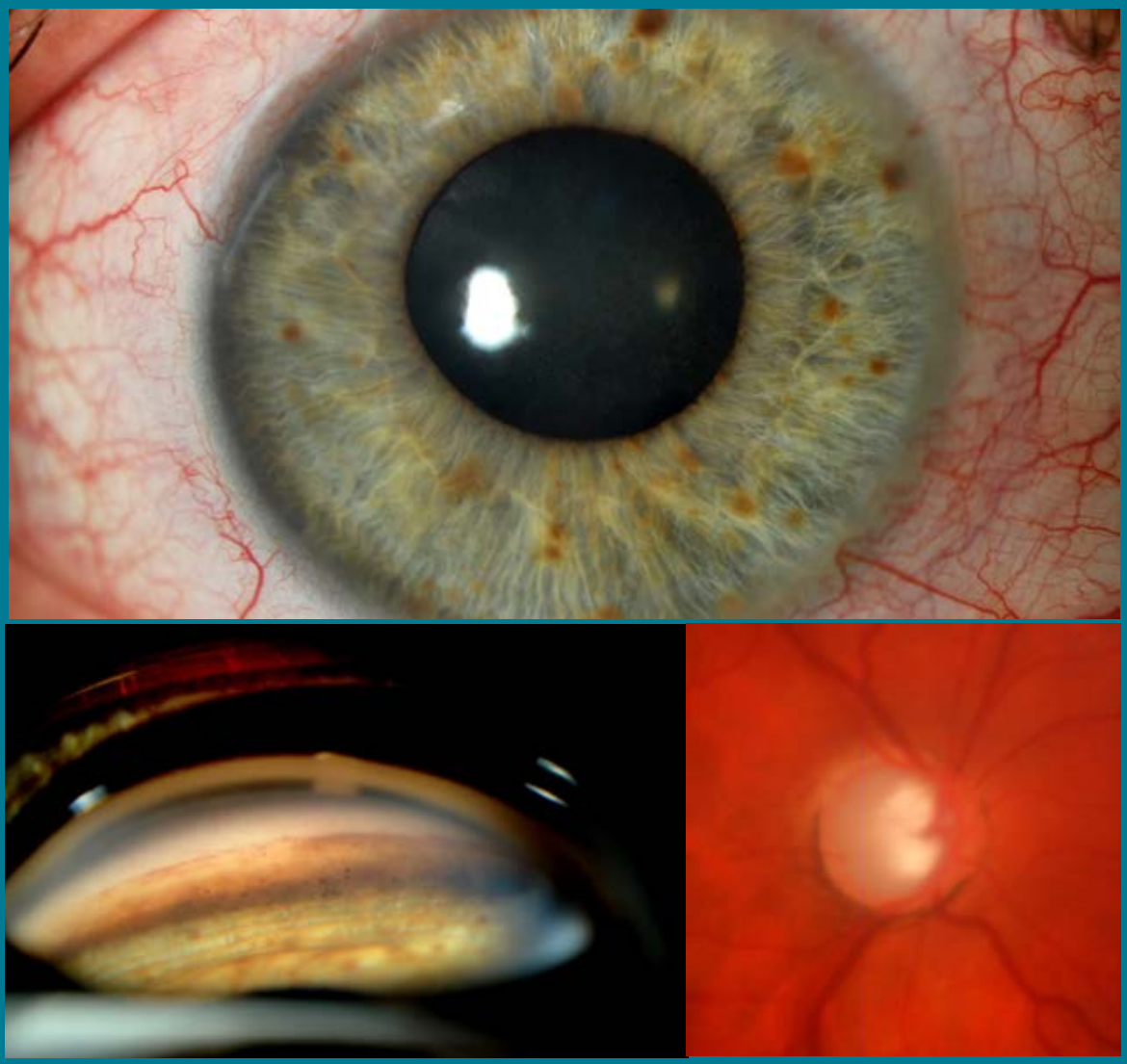
2. a. *True*
   b. *True*
   c. *False*
   d. *True*

3. a. *False*
   b. *False*
   c. *True*
   d. *False*

4. a. *False*
   b. *False*
   c. *True*
   d. *False*

C

How do you diagnose this ...?
Case - Tero KIVELÄ



A 19-year-old man experienced blurred vision without pain, OD. He had no history of ocular injury. His visual acuity was 20/400, OD, and 20/20, OS, without spectacles. The intraocular pressure was 60 mmHg and 12 mmHg, respectively. Mild conjunctival hyperemia was present. The cornea was clear with no Krukenberg spindle. The anterior chamber was deep. Mild pigment dispersion was seen on the anterior capsule. The fellow eye was unremarkable.

- What other test would you request?
- What is your differential diagnosis?
- How do you treat this eye?

14

Anterior capsulorhexis: how to excel

Johan BLANCKAERT - Belgium

MCQs

1. **The best size and shape of a continuous circular capsulorhexis (CCC) to accommodate an intraocular lens (IOL) is:**
   a. CCC bigger than the optic of IOL
   b. CCC not overlapping & not centred on IOL optic
   c. Oval CCC overlapping IOL optic
   d. No shape is preferred but CCC must overlap IOL optic

2. **When pulling a continuous circular capsulorhexis (CCC), ending must be with:**
   a. Inside to outward movement
   b. Outside to inward movement
   c. Perfectly circular
   d. All of the above are acceptable

3. **These continuous circular capsulorhexis (CCC) techniques can be done without entering the eye**
   a. Femtosecond laser assisted cataract surgery (FLACS)
   b. CAPSULaser®
   c. Zepto®-rhexis
   d. Precision Pulse CCC

4. **White cataract continuous circular capsulorhexis (CCC) is best done with:**
   a. Dying the capsule, whatever the technique
   b. Femtosecond laser assisted cataract surgery (FLACS)
   c. CAPSULaser®
   d. High magnification, without dying the capsule

5. **When a radial tear begins to form your immediate action should be;**
   a. Continue pulling the CCC
   b. Stop and check reason with high magnification
   c. Use shearing force to recover CCC, if not yet zonular
   d. Remove zonulae in the area of the tear

CATARACT SURGERY is very old. The Codex Hammurabi (1795–1750 BC), an ancient book of law in the era of ruler Hammurabi of Babylon, included the fee for cataract surgery. For centuries a couching technique was performed. The French eye surgeon Daviel (1696–1762) learned from his 35% failures doing couching, and perfected removing the crystalline lens with a forceps through a corneal incision. This technique was described earlier by Blankaart (1669–1702).

It took nearly a century to transit from couching in the eye to intracapsular cataract extraction (ICCE) through a corneal incision from outside the eye. As always, when a new surgical technique emerges, many opponents line up against the progress. In the 20th century, ophthalmological schools were about equally divided between ICCE and extracapsular cataract extraction (ECCE). Admirers of the ICCE were the family *Barraquer who* further refined the technique. The cryoextraction made a point against ECCE technique. By the end of the 1980s, *Kelman* introduced us into the phacoemulsification era. This moved the majority of surgeons over to the ECCE technique. Opening of the anterior capsule was mandatory to this type of cataract surgery. Different capsule opening techniques appeared: linear downward or upward technique (*Pearce* 1976) then envelope capsulotomy (*Sourdille & Galand* 1980), Christmas tree, beer can opener capsulotomy, etc. All those non-linear and non-continuous techniques to open the capsule led to complications such as easy radial tearing of the capsule; a complication largely avoided by the continuous curvilinear capsulorhexis (CCC).

Gimbel and *Neuhann* both described the CCC technique simultaneously in a peer reviewed journal in 1991. Neuhann had published the technique first in 1987 in a German journal but he recognised his colleague Gimbel in what was called the nicest settlement between colleagues in centuries. Although these surgeons had a similar idea, their approaches as to how to create the CCC and the instruments they used differed. There was, however, a third surgeon Shimizu who used a bent 30G needle and did the CCC much as how we perform it today: a small flap was created and folded over onto intact capsule and with the needle advanced to a CCC. It seems that all three were beaten by Fercho in 1970 who developed, but never published, the CCC. Be as it may, CCC is considered a major breakthrough in phacoemulsification surgery.

1. CCC technique

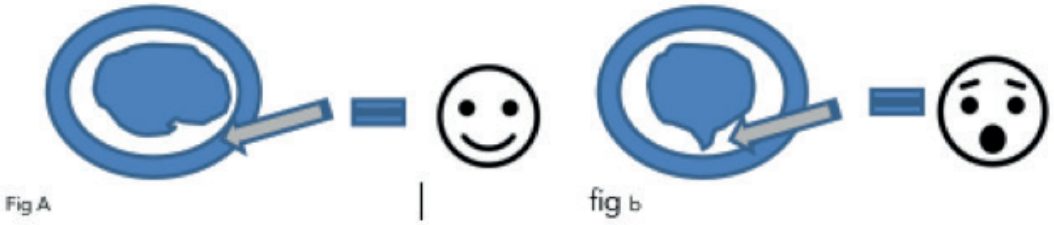
Manual technique

Bent 27G–30G needle: The needle is bend manually by the surgeon with the aid of a needle holder You can create a 2- or a 3-bend needle. Bend the hub region 120° up; this angle is necessary to avoid bringing your fingers in the field of view of the microscope while holding the needle.

Kelman CD. Phacoemulsificationand aspiration. A new technique of cataract removal. A preliminary report. Am J. Ophthalmol. 1967;64:23-35.
Gimbel HV, Neuhann T. Continuous curvilinear capsulorhexis. J Cataract Refract Surg. 1991;17:110-1.
Neuhann T. Theorie und Operationstechnik der Kapsulorhexis. Klin Monatsbl Augenheilkd. 1987;190:542-5.

STARTING THE CONTINUOUS CIRCULAR CAPSULOREXIS (CCC): It is imperative that the anterior chamber is filled with viscoelastics. Good filling or refilling as needed of the anterior chamber during the procedure causes flattening of the otherwise convex anterior capsule. Care needs to be taken to avoid letting the viscoelastic escape from the anterior chamber, because the anterior capsule will regain convexity and create a possible downhill trajectory of the anterior capsulorrhexis towards the capsular periphery. To begin the CCC, a puncture is made in the anterior capsule. Purkinje images projected by the operation microscope onto the eye can guide you towards centring the CCC on the visual axis. The sharp edge of the cystotome is used to create the first line in the capsule from the center towards the main incision position. At the end of this J-shaped line, a movement of the cystotome to the right or left of the surgeon's position creates a little triangular flap. This small triangular flap is folded over so that the underside of the capsule lies on top, and sharp edge of the cystotome is placed on the periphery of the folded flap. Pushing slightly so as not to perforate the flap, but firm enough, on the edge of this folded flap gives the cystotome a grip on the flap's edge and a guidance of the flap tear. The net result is sliding or gliding of the capsulorhexis flap over the intact capsule. Pushing too hard can let the capsulorhexis run to the periphery. Always keep the flap folded over so that the underside of the capsule is facing up. The position of the needle point needs to be close to the beginning of the flap edge. This ensures tearing the capsule and guiding it to the shape the surgeon wants. It is each surgeon's preference to do this clock or counterclockwise. Use the main port as a pivot point, and avoid pushing on the posterior lip of the wound because this facilitates escape of the viscoelastic from the eye.

COMPLETING THE RHEXIS: Always complete the rhexis outside-in (a). An outward finish (fig b) creates a weakness that can result in a radial tear.



Seibel BS. Phacodynamics. ISBN-13: 978-1556426889

Utrata forceps

The forceps designed by Utrata (1988) gives two modalities in making the CCC. The first is using shearing forces and the second is using tearing forces (as with the needle). **Shearing** means pulling the leading capsule edge in a centripetal way. The force vector created makes the capsulorhexis advance in a circular way around the force vector. **Tearing** is applying forces straight onto and in the direction of the wanted flap direction. It is guiding the CCC leading edge the way you intend the flap edge to go. It is much like tearing paper.

Most of the time it is a combination of the tearing and shearing techniques to complete the CCC. Cross-acting capsulorhexis forceps can be used in small incisions.

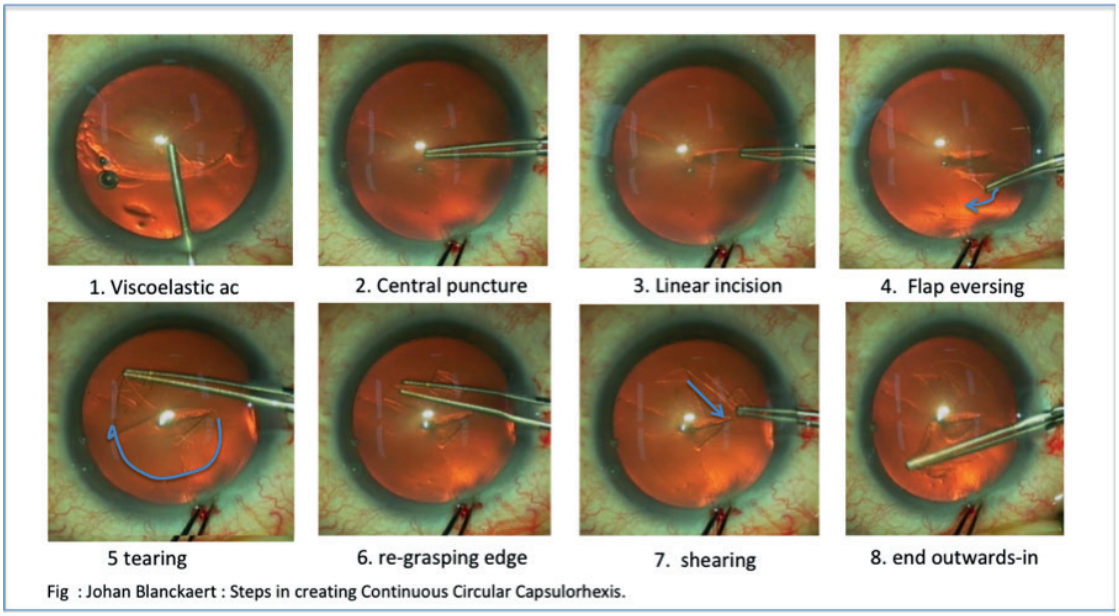
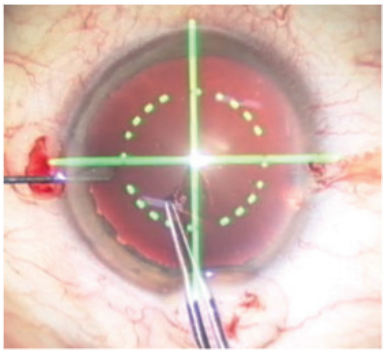


Fig : Johan Blanckaert : Steps in creating Continuous Circular Capsulorhexis.

Microincision capsulorhexis forceps

Vitrectomy-style microforceps provides the opportunity to create a capsulorhexis through a small incision. The same principles of shearing and tearing apply as with the Utrata forceps and the cystotome needle.

Visually guided manual technique



As an improvement to the purely manual technique, we have now the option to use guiding instruments intraoperatively. A projection in the eye piece gives the surgeon a template for CCC. The surgeon can use this projected template to position the centre of the manual CCC and to adjust the diameter to

the programmed diameter of the template. This way, a more consistent diameter and shape and centration of the CCC can be made. Because this is still a manual technique, the actual CCC intraoperatively can deviate from the projected template.

Two instruments can be mounted on the operation microscope and have this feature: Verion® astigmatic planner from Alcon and Calisto® from Zeiss.

Laser robot-based automated techniques

Femtosecond laser: Femto is a prefix of the international System of Units that stands for 10^{15}. This term comes from the Danish word "Fenten" which means power – 15. A surgeon using the Femto Laser Assisted Robot Laser has the opportunity to make a customised CCC. The size of the CCC can be adjusted and pre-programmed. Nagy introduced us to the precision and accuracy of making visual axis or limbal centred perfect CCC. The major difference with manual techniques is the fact that the eye is not openend before the capsulotomy can be done. Femto laser makes the CCC in a closed eye where normal anatomical features are not disturbed by viscoelastic filling.

CAPSULaser®: A small ergonomic microscope-mounted thermal laser creates, with laser precision for size and centration, a consistent CCC.

Electrical current based fixed-diameter CCC techniques

All these techniques need a viscoelastic-filled anterior chamber and have the same disadvantage as the manual technique.

Precision Pulse Capsulotomy: the device uses a highly focussed, fast, multi-pulse, low energy discharge to produce the capsulotomy instantaneously and simultaneously for 360°.

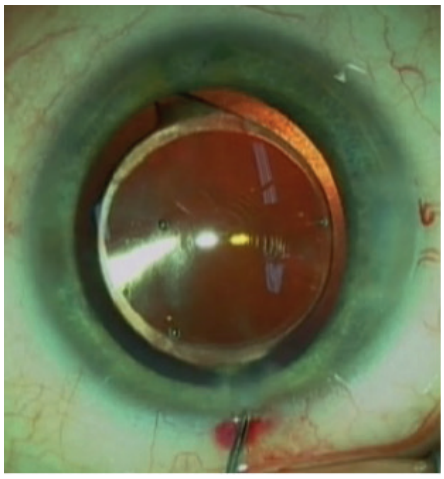
Zepto®-rhexis (Mynosys): Electric nanopulses are delivered to a nitinol cutting element ring to create the capsulotomy simultaneously for 360° with no cautery or burning of tissue. Vaporization of water molecules trapped between the capsule and the nitinol edges causes the stretched capsular membrane to split circumferentially all at once.

Haeussler-Sinangin Y, Dahlhoff D, Schultz T, Dick HB Clinical performance in continuous curvilinear capsulorhexis creation supported by a digital image guidance system J Cataract Refract Surg 2017;43:348–52.
Nagy, Z., Takacs, A., Filkorn, T., and Sarayba, M. Initial clinical evaluation of an intraocular femtosecond laser in cataract surgery. J Refract Surg. 2009;25:1053–60.

2. Sizing the CCC

- Caliper ring
- Forceps with ruler engraving
- Corneal impression (but be aware of the corneal magnification)
- Eyepiece video system projection, like Verion® and Calisto®
- Femtosecond laser
- Precision pulse Zepto®-rhexis

The net result should be a small overlap over the optic of the IOL.



Capsule dye

Trypan blue is the dye which was preferred in the study by Dr Mellis.
It's primarily used in white or brunescent cataracts.

(please see next page)

Daya S, et al. Br J Ophthalmol 2019. doi:10.1136/bjophthalmol-2018-313421
Chang DF, Mamalis N, Werner L. Precision pulse capsulotomy: preclinical safety and performance of a new capsulotomy technology. Ophthalmology. 2016;123:255-64.
Pandey SK, Sharma V. Zepto-rhexis: A new surgical technique of capsulorhexis using precision nano-pulse technology in difficult cataract cases Indian J Ophthalmol. 2018;66:1165–8.

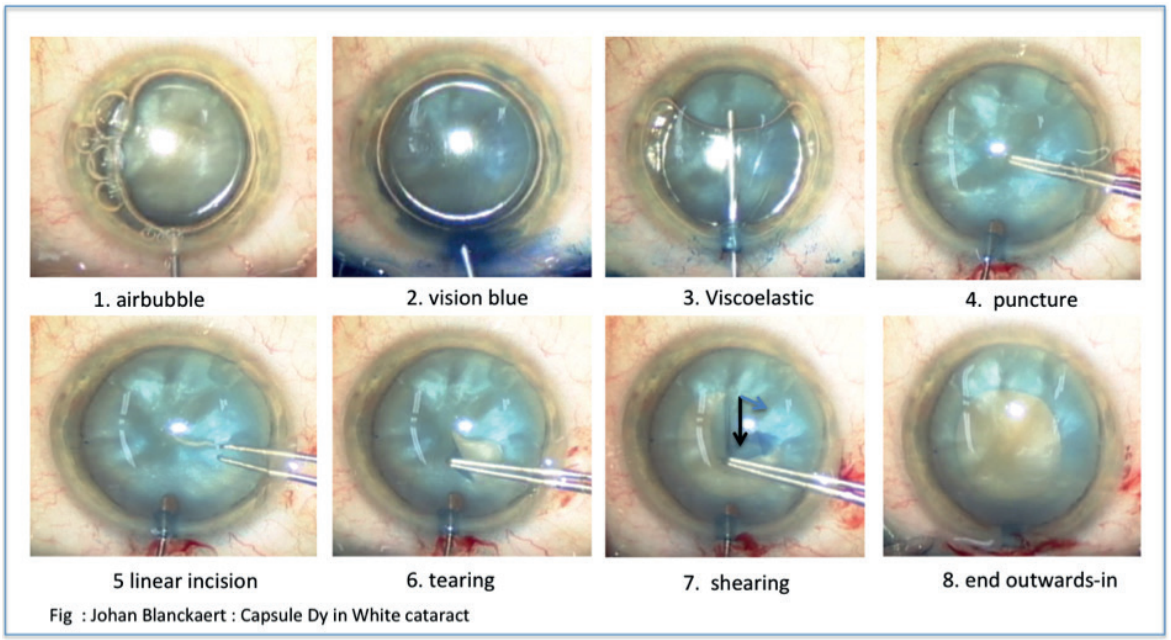


Fig : Johan Blanckaert : Capsule Dy in White cataract

3. Complications

Discontinuity of the capsular edge: When the capsulorhexis is inadvertly nicked with an instrument (phaco needle, second instrument) then an outward pointing discontinuity is present. This causes a major risk for a radial tear. Solution: converting the radial tear into a continuous circular capsulorhexis, this needs to be done immediately and with the highest priority before any manoeuvre that distends the capsule (e.g., hydrodissction) because it will cause radial tears running up to the posterior capsule. Sometimes a viscoelastic of high density (e.g., Viscoat, Healon 5) needs to be applied distal to the tear to be able to recover the tear and redirect the capsulorhexis. The only manoeuvre to recover is applying shearing vectors on the capsule. Therefore, you need to pull gently the capsule centripetal. This will make the capsulorhexis to bend towards the center and stop running outwards. Only centripetal forces can do the trick. So make sure to apply centripetal force all the way until you see the capsulorexis edge appearing again. However, if the tear extends into the zonular fibers then the chance to recover it is slim.

T*ear extending to the zonular fibers:* Sometimes anatomical abnormalities like centrally inserted zonular fibers exist. If the capsulorhexis encounters such fibers, then it cannot be continued without a risk to change its direction radially. *Solution*: When such fibers are present, it is probably safer to first remove them from the projected path the capsulorhexis is going to make (will need higher magnification from the microscope).

Diameter too small: Sometimes a capsulorhexis will be too small. *Solution* : Its better to continue in a spiral matter and enlarge the capsulorhexis until the desired diameter is reached.

Melles GR, de Waard PW, Pameijer JH, Beekhuis WH. [Staining the lens capsule with trypan blue for visualizing capsulorhexis in surgery of mature cataracts]. Klin Monbl Augenheilkd. 1999;215:342-4.

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Answers to MCQs on page 93

1. a. *False*
   b. *False*
   c. *True*
   d. *True*

2. a. *False*
   b. *True*
   c. *True*
   d. *False*

3. a. *True*
   b. *True*
   c. *False*
   d. *False*

4. a. *True*
   b. *True*
   c. *True*
   d. *False*

5. a. *False*
   b. *True*
   c. *True*
   d. *True*

15

Lens extraction techniques

Nic REUS - The Netherlands

MCQs

1. **Regarding lens extraction techniques:**
   a. With intracapsular cataract extraction (ICCE), the capsular bag is removed
   b. For soft lenses in children, the divide-and-conquer technique is the technique of choice
   c. The amount of surgery-induced astigmatism (SIA) with (manual) small incision cataract surgery is low
   d. Femtosecond laser-assisted cataract surgery (FLACS) is non-inferior to cataract surgery by phacoemulsification

2. **Regarding the chopping technique:**
   a. In horizontal chopping, two grooves are created before the lens is cracked
   b. The essence of horizontal chopping is that the phaco tip is lifted up while the chopping instrument is pressed down
   c. In eyes with smaller pupils, a vertical chopping technique can be advantageous
   d. The second instrument used in vertical chopping has a very sharp tip

3. **Regarding lens extraction techniques in special cases:**
   a. In an eye with a posterior polar cataract, it is best to perform a hydrodissection
   b. In an eye with a suspected posterior capsule rupture, it is advisable to inject a dispersive viscoelastic behind the lens after the first crack
   c. Cohesive viscoelastics are much more difficult to aspirate than dispersive viscoelastics
   d. In an eye with a generalised zonulolysis, it may be wise to use a chopping technique

IN MODERN CATARACT SURGERY, we routinely remove the opacified lens from the lens bag and implant a clear artificial intraocular lens (IOL). This is a form of **extracapsular cataract extraction** (ECCE). The reason that this is called *extracapsular* is that the lens is removed without the capsule; the Latin for without is *extra*. This is in contrast to **intracapsular cataract extraction** (ICCE) in which the lens is removed *including* the capsular bag. The size of the capsulorhexis should be so that at the end of surgery the margin of the anterior capsule completely overlaps the optic of the IOL. With an average diameter of the optic of 6 mm, the rhexis diameter thus should be 5 mm to 5.5 mm. The human lens has a diameter of approximately 10 mm. Therefore, in order to extract the lens through the smaller opening in the anterior lens capsule, we need to break up the lens in smaller parts which can then be emulsified with the phaco tip. This breaking up of the lens is called nucleofractis.

There are several techniques to extract the lens from the bag. Choosing which one to use depends on surgeon's experience, preference, density of the lens (a soft lens of a young patient with subcapsular posterior cataract versus a reddish brown cataract in a ninety-year-old), and any comorbidities. Often, however, a combination of various techniques is used.

1. Routine lens extraction techniques

The technique often first taught to residents is the **divide-and-conquer** technique. In this technique, two grooves at right angles are created in the nucleus after which the lens is cracked into 4 separate parts. These quadrants can then be emulsified with the phaco tip. This technique is actually the *in situ nucleofractis* technique described by Shepherd in 1990 (J Cataract Refract Surg 1990;16:436-440). The term *divide-and-conquer* was coined by Gimbel in 1986 to describe his technique in which a central crater was made to remove the nucleus after which the remaining peripheral rim could be fractured in multiple smaller pieces and subsequently emulsified (J Cataract Refract Surg 1991;17:281-291). Shepherd's technique, however, is the one we routinely use today. In general, it can be used in all cases (i.e., in routine, complex, and complicated cases).

For dense nuclei, a **chopping** technique may be preferred. In this technique, the nucleus is impaled by the phaco tip while a second instrument is used to push the lens towards the phaco tip thereby splitting the lens along its natural cleavage planes. There are two major types of chopping: horizontal and vertical. **Horizontal chop** was introduced by Nagahara in 1993. In this technique, a second chopping instrument is placed behind the nucleus. This instrument is then pulled toward the phaco tip in a horizontal movement. This allows cracking of the lens. The second technique, **vertical chop**, was described almost simultaneously by Pfeiffer, Dillman, Neuhann, and Vasavada in around 1996. In this technique, the second chopping instrument has a very sharp tip. It is placed adjacent to the phaco tip. Then, the chopper is pushed down while the phaco tip is being pushed up. With these vertical (and opposite) movements, the nucleus is cracked. In clinical practice, a combination of horizontal and vertical movements is often used. Advantages of chopping is that is requires less phaco-energy to emulsify the lens. In addition, it does not rely on a red reflex, it exerts less stress on the zonules and on the capsular bag, and it can be performed through smaller pupils.

For very soft lenses, it may be difficult to make grooves in the lens with the divide-and-conquer technique since it is very elastic. In addition, cracking of such a soft lens is challenging. In these cases, it is often easier to perform a hydrodissection and, possibly, a hydrodelineation in order to prolapse the lens into the anterior chamber and then aspirate the lens with the phaco tip. One could describe this as a **prolapse-and-flip** technique. This often prevents any phaco energy to be used which may be better for the endothelium and for the visual recovery after surgery.

2. (Manual) small incision cataract surgery

In areas where phacoemulsification systems are not affordable or are difficult to service, (manual) small incision cataract surgery (SICS) can be used. This is also a form of ECCE. The main incision is wider than for phacoemulsification (6-7 mm versus 2.2 mm), thereby increasing the amount of and variability in surgically induced astigmatism (SIA). After creating an opening in the anterior lens capsule (often triangular, but it can also be a continuous curvilinear capsulorhexis), the nucleus is expressed out of the capsular bag and then irrigated out of the eye. An IOL is implanted in the capsular bag. The main incision is self-sealing. Experienced surgeons can perform SICS as safely and as fast as experienced surgeons can perform phacoemulsification.

3. Intracapsular cataract surgery

Removing the lens, including the capsular bag, by means of ICCE is nowadays seldom performed. It might be used for cases in which there is a complete zonulysis. However, one might also use iris hooks to stabilize the lens, perform phacoemulsification, and then either remove the capsular bag or suture it to the sclera. With ICCE one removes the barrier between the anterior chamber and the vitreous cavity, resulting in a very high risk of vitreous loss with subsequent risk of retinal tear and retinal detachment, and risk of developing cystoid macular edema.

4. Femtosecond laser-assisted cataract surgery (FLACS)

In femtosecond laser-assisted cataract surgery (FLACS), a femtosecond laser is used to create cleavage planes via photodisruption in transparent/translucent tissues. Currently, it can be used to create incisions, arcuate keratotomies, anterior capsulotomy, and nuclear fragmentation. Because the lens is fragmented into smaller pieces, it requires less phaco energy to emulsify these parts than using the divide-and-conquer technique. It is, however, not widely used at this time because of the high cost associated with this technique and no conclusive evidence at this time that FLACS provides better results for the patient. Several randomized controlled trials are about to publish their results comparing the outcomes of cataract extraction with phacoemulsification versus FLACS.

5. Lens extraction techniques in special cases

The divide-and-conquer technique requires a hydrodissection of the lens because the nucleus has to be rotated to create the grooves. In some cases, a posterior capsule rupture may be pre-existent. For example, in posterior polar cataracts, after intravitreal injections of anti-VEGF medication for exudative macular degeneration, and after ocular injury. Hydrodissection in these cases may cause the nucleus to drop into the vitreous cavity. In these cases, an *in situ* nucleofractis technique may be performed. This means that the nucleus is left in its original position (*in situ*) where it is broken into smaller pieces. This can be done with a vertical chopping technique. However, a modified *in situ* nucleofraction version of the divide and conquer technique may also be used in which the lens is not rotated to create the trenches. After having created the first crack, it is advisable to inject a dispersive viscoelastic (such as 3% sodium hyaluronate or 3% sodium hyalorunate with 4% chondroitin sulfate) underneath the lens to provide a barrier between it and the vitreous cavity. In these cases, a dispersive viscoelastic is the viscoelastic of choice since it cannot be easily aspirated (in contrast to a cohesive one).

In cases with a generalised zonulolysis, the divide-and-conquer technique may also not be ideal. To create the groove, one pushes the lens away and also down, thereby stressing the zonules. If these are not strong, one may increase the risk of a dropped nucleus (including the capsular bag). In these cases, vertical chopping may be the preferred technique. This is because the nucleus is impaled by the phaco tip and the second instrument is used to give counterpressure in order to fracture the lens. This means that less stress is exerted on the zonules, thereby possibly saving the lens bag.

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Recent

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Classic

2. Steinert RF. Cataract Surgery. 3rd Edition. Saunders, 2009.

Answers to MCQs on page 102

1. a. *True*
   b. *False*
   c. *False*
   d. *True*

2. a. *False*
   b. *False*
   c. *True*
   d. *True*

3. a. *False*
   b. *True*
   c. *False*
   d. *True*

16

Paediatric cataract surgery

Christian BILLOTTE - France

MCQs

1. **Regarding paediatric cataracts:**
   a. Surgeons agree that the best time for surgery is 1 year of age or older.
   b. Both posterior capsule opacification and inflammation often cause postoperative problems.
   c. The intraocular lens power calculations need a correction factor in children younger than 3 years of age.
   d. The incidence is about 1-3 cases per 1,000 births.

2. **Regarding the so-called bag-in the-lens technique:**
   a. Includes always a posterior capsulorhexis in addition to an anterior one.
   b. Berger's space is evacuated with an anterior vitrector.
   c. The surgery can be successfully completed in only 50% of patients
   d. The frequency of postoperative glaucoma is about 1%.

THE INCIDENCE of paediatric cataract ranges from 1–3 per 10,000 births. Paediatric cataract surgery management involves specific difficulties before, during, and after surgery.

- There is no worldwide consent on the best time of surgery, age, and IOL implantion.
- The common cataract surgery technique in chidren is phakoaspiration, posterior capsulotomy associated with anterior vitrectomy. The main complications in children is the very high rate of posterior capsular opacification (PCO) and postoperative inflammation, so multiple surgeries can be necessary to maintain a clear visual axis, a key to successful amblyopia treatment.
- If implantation is realized, the calculation of the power of the lens in very young chidren is done under general anaesthesia, including a correction function of age under three years.

Bag-in-the-lens (BIL)

In our practice, since 10 years all chidren over three months of age are implanted with the bag-in -the-lens technique without anterior vitrectomy.

Technique:
- An anterior capsulorhexis well centered and sized 4.5 to 5.0 mm is first realised
- Phako aspiration of the lens and cortical cleaning
- Anterior chamber is filled with viscoelastic, avoiding filling the equator of the empty bag
- A small puncture in the center of the posterior capsule is done
- Berger's space is filled with viscoelastic, pushing back the anterior intact hyaloid
- A posterior capsulorhexis is realised at the same size than the anterior one
- The bag-in-the-lens IOL (Morcher 89A®) is injected, and the edges of the anterior and posterior rhexis are inserted in the peripheral grove of the IOL.
- Only the viscoelatic in the anterior chamber is removed.
- In our experience, the BIL technique was feasible in 90% of 76 eyes

Advantages:
- The main advantage is the complete lack of PCO even after 10 years, if the BIL is well placed
- The very low rate of post operative inflammation explains the lack of iris synechiae, absence of capsular fibrosis and retraction, and IOL displacement
- Only one surgery is needed and amblyopia treatment is immediately possible. No anterior vitrectomy is needed.
- Long term incidence of secondary glaucoma is in our experience 1.3%

The BIL way of implantation gives better results than the common paediatric cataract surgery. Implantation as soon as possible, not leaving the children aphakic. A short learning curve is needed

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3. Nyström A, Almarzouki N, Magnusson G, Zetterberg M,. Phakoemulsification and primary implantation with bag in the lens intraocular lens in children with unilateral and bilateral cataract. Acta Ophthalmol. 2018 ;96:364-70.
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5. Tassignon MJ, Ni Dhubhghaill S, van Os L. Innovative Implatation Technique. Bag In the Lens Cataract Surgery. Speringer, 2019.

Answers to MCQs on page 107

1. a. *False*
   b. *True*
   c. *True*
   d. *False*

2. a. *True*
   b. *False*
   c. *False*
   d. *True*

17

Toric IOLs, corneal marking

Nino HIRNSCHALL - Austria

MCQs not available

Abstract not available

18 Myth and reality about accommodative/EDOF IOLs

Rafael BARRAQUER - Spain

MCQs not available

18

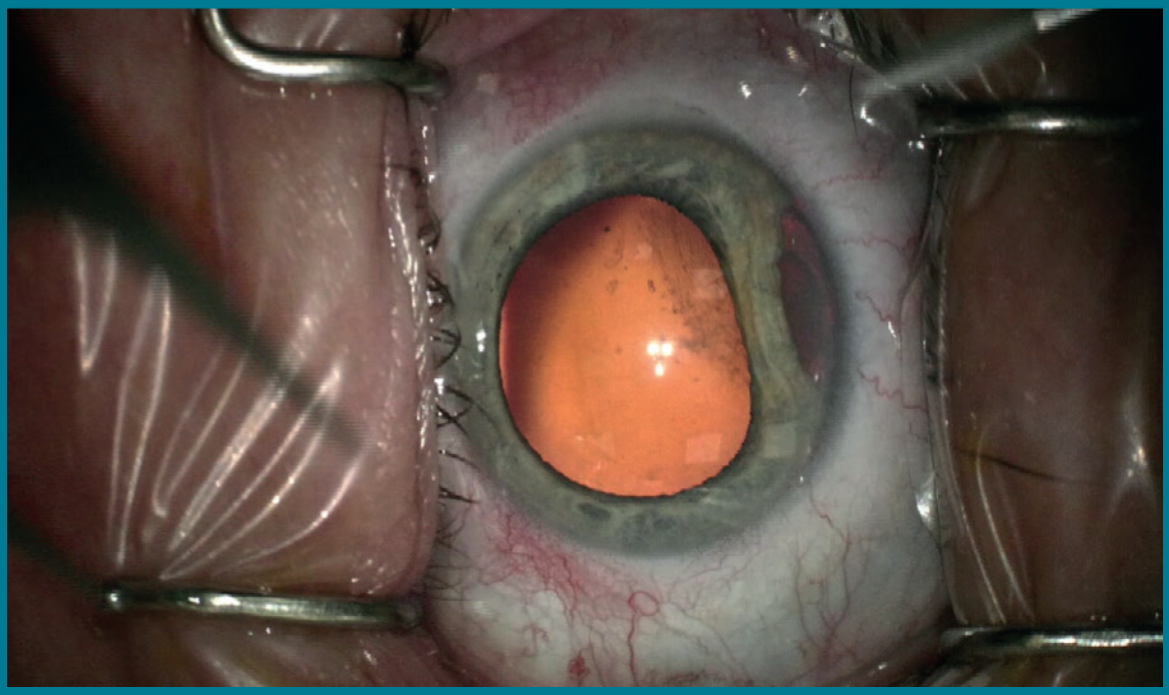
Myth and reality about accommodative/EDOF IOLs

BARRAQUER R - Spain

Abstract not available

C

How do I treat this patient?
Case 1 - Nic REUS



How do I treat this young patient with a traumatic cataract and iridodialysis

19

Laser treatment

Anton HOMMER - Austria

MCQs

1. **Regarding selective laser trabeculopasty (SLT) and argon laser trabeculoplasty (ALT):**
   a. SLT is more effective in IOP lowering than ALT
   b. In SLT the IOP lowering effect lasts longer than in ALT
   c. SLT makes less histopathological damage than ALT
   d. SLT can be repeated more often than ALT

2. **Regarding SLT:**
   a. It can be used in angle closure glaucoma
   b. The larger beam does not need that much of differentiating the structures of an open angle
   c. It is (probably) more cost effective than medical therapy when used as primary treatment in primary ope-angle glaucoma (POAG)
   d. After SLT, medical therapy is less effective

3. **Regarding Nd:YAG iridotomies:**
   a. The size of the iridotomy hole correlates with its IOP lowering effect
   b. Iridotomy can be performed easier if the area is pretreated with argon laser
   c. Iridotomy is helpful in chronic angle closure glaucoma
   d. The location of the iridotomy is irrelevant for the risk of side effect

4. **Regarding cyclodestructive procedures:**
   a. They can be performed by ultrasound, diathermy, cryo, or laser
   b. Diode laser provides less inflammation than other lasers in cyclodestructive procedures because of its wave length
   c. Because of their destructive character, they are not an option as first line therapy in early POAG
   d. They should not be combined with cataract surgery

LASER SURGERY has got a more and more important role in ophthalmology over the last few decades. In glaucoma, the preferred type of laser depends on the type of glaucoma and the stage of the disease. All these procedures aim to lower the intraocular pressure (IOP), the only evidence- based proven effective concept in glaucoma therapy.

We can differentiate among various laser-tissue interactions. Photothermal (photocoagulation) mechanism is used in glaucoma with argon, krypton, diode (e.g., 810 nm) and frequency doubled Nd: YAG lasers, whereas the photodisruption mechanism is used with Nd: YAG laser. The mechanism for IOP lowering can be either reduction of the production of the aqueous humour (e.g., transscleral cyclophotocoagulation) or improving the outflow of the aqueous humour (e.g., trabeculoplasty).

The delivery system can be either slit lamp-based, hand-held or endoscopic. Special lenses are required if the treatment is performed via slit lamp.

1. Laser trabeculoplasty (LTP)

Introduced in 1979 by Wise and Witter as *argon laser trabeculoplasty* (ALT) it was originally designed to be used in eyes in which medication alone is not effective enough to reach the target pressure. The mechanism is based on improving the aqueous humour outflow through the trabecular meshwork. Because of its safety profile, efficacy and compliance independence it became more and more popular. As a result, in the European Glaucoma Society (EGS) guidelines it became a primary treatment option in primary open-angle glaucoma (POAG) and ocular hypertension (OHT). *Selective laser trabeculoplasty (SLT)* uses minimal heat energy absorption and, therefore, is taken up only by selected pigmented tissue. It produces less scaring on histopathological level and seems to be safer. SLT claims to be repeatable. Its IOP lowering effect seems to be 20–30% from baseline. Repeatability depends on success of the first LTP. If the first LTP is not successful, it does not make sense to repeat a non-successful treatment. No data are available that a third or fourth repetition of ALT or SLT produces a meaningful IOP reduction. In addition, we have to consider that there are limitations regarding LTP in general. SLT, as well as ALT, is not indicated in any angle malformation, developmental, neovascular or angle recession (posttraumatic) glaucoma. ***Micropulse laser trabeculoplasty (MLT)*** is a similar procedure to ALT/SLT. It seems to be as effective in IOP lowering. It claims to produce less inflammation. No data are available about better repeatability. Neither SLT, nor ALT or MLT provide a cure for glaucoma.

In a recent study, patients with POAG and OHT were treated either with SLT or eye drops. The study was performed in the United Kingdom. The primary outcome was health-related quality-of-life (HRQoL) at 3 years (assessed by EQ-5D questionnaire). Secondary outcomes were cost and cost-effectiveness, disease-specific HRQoL, clinical effectiveness, and safety. Based on the UK health care system, SLT was more cost effective than eye drop therapy after 36 months. Because of limitations in the study, it is not possible to apply the suggestion to prefer SLT as first line treatment in other countries and health care systems.

2. Laser peripheral Iridotomy (LIT)

Performed to treat angle closure and angle-closure glaucoma. It may be useful in some cases of pigment dispersion syndrome as well. The aim is to reduce the risk of further angle closure attacks. It is performed with Nd:YAG-Laser, sometimes it is helpful to perform a pretreatment with argon laser. The procedure is considered to be safe. In some patients a surgical iridectomy has to be performed. Moreover, in some patients the angle closure is lens-induced, and a lensectomy is indicated.

3. Cyclodestructive procedures with laser

It is not a novelty to destroy the ciliary body, the structure where the aqueous humour is produced, to lower the IOP. After different but not so successful approaches in the past, like cryo, surgical, diathermy or ultrasound, laser technology was introduced in the seventies and eighties. After the use of ruby and Nd:YAG lasers, today diode laser is preferred over other wavelengths. It is achieved either transsclerally (TS-CPC) or endoscopically (ECP). The infrared wavelength (usually 810 nm) provides better absorption by the melanin-containing ciliary epithelium and as a result more targeted destruction and less inflammation is achieved. Indications are usually refractory glaucoma and eyes with poor visual outcome. ECP can be combined with cataract surgery.

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Answers to MCQs on page 116

1. a. *False*
   b. *False*
   c. *True*
   d. *False*

2. a. *False*
   b. *True*
   c. *True*
   d. *False*

3. a. *False*
   b. *True*
   c. *False*
   d. *False*

4. a. *True*
   b. *True*
   c. *True*
   d. *False*

20

Filtration surgery

Barbara CVENKEL - Slovenia

MCQs

1. **Trabeculectomy, the commonly performed filtration surgery:**
   a. increases aqueous outflow via Schlemm's canal
   b. is traditionally considered the gold standard of glaucoma surgery
   c. is currently the most effective IOP-lowering surgery
   d. is safe and predictable procedure in almost all types of glaucoma
   e. is successful (no medication required) in 80% of patients with primary open-angle glaucoma at 2 years

2. **Regarding use of antifibrotics/antimetabolites in glaucoma filtration surgery:**
   a. It improves outcomes of surgery
   b. It is associated with decreased incidence of bleb leak
   c. It delays healing and reduces scarring
   d. The delivery systems, concentration and exposure times are standardised
   e. Intraoperative treatment of larger areas may increase the chance for more diffuse blebs

3. **Risk factors associated with a higher failure rate of trabeculectomy include:**
   a. Younger age
   b. Previous incisional or intraocular surgery
   c. Older age
   d. Treatment-naïve eyes
   e. Uveitic glaucoma

4. **Early postoperative complications (during the first days to weeks after surgery):**
   a. Hypotony can be caused by overfiltration
   b. These include fibrosis of filtering bleb
   c. They may be reduced by releasable and/or adjustable scleral flap sutures that help to titrate aqueous flow in the early postoperative period
   d. Minor bleb leaks do not affect trabeculectomy outcome
   e. Encapsulated (encysted) blebs typically occur within the first 2 weeks after surgery

GLAUCOMA SURGERY is typically performed when maximal tolerated medical and laser therapy fail to sufficiently lower intraocular pressure (IOP) or to prevent progression. Trabeculectomy is one of the longest surviving glaucoma surgeries and has been traditionally considered the "gold standard" for filtration surgery. The goal of surgery is to bypass the conventional outflow pathways by creating a corneoscleral fistula that enables aqueous outflow to the subconjunctival space. Initially described by Cairns in 1968, trabeculectomy has since then undergone several modifications to improve outcomes and to reduce complications.

1. Trabeculectomy and lowering of IOP

Current trabeculectomy technique in the UK with antifibrotics and releasable sutures in patients with open-angle glaucoma *without previous incisional surgery* showed good outcomes with low rates of surgical complications. At 2 years, 80% of 342 patients achieved an IOP ≤21 mmHg and 20% a reduction of preoperative IOP without IOP-lowering treatment. An IOP ≤18 mmHg and 20% reduction of preoperative IOP were achieved in 78% without hypotensive medication. In another retrospective study, 80% of patients had a good IOP control 20 years after trabeculectomy.

Recently, new devices and procedures have emerged termed minimally invasive glaucoma surgery (MIGS) that are less invasive with minimal external dissection, short operating time, good safety profile, and rapid visual recovery. These devices target different aqueous outflow pathways: Schlemm's canal, the suprachoroidal, and the subconjunctival space. MIGS as a stand-alone procedure (without concurrent cataract surgery) may lower IOP and reduce the number of medications. However, there are many questions to be answered, such as the selection of the appropriate device for an individual patient for a given severity of glaucoma, cost-effectiveness, and quality-of-life. A clear need exists for good quality evidence from large randomised controlled trials with longer follow-up. In the Unietd States, the increasing popularity of MIGS has led to a decline in trabeculectomy procedures from 85% in 2008 to 60% in 2016.

2. Indications for trabeculectomy

- Open-angle and angle-closure glaucoma with uncontrolled IOP and documented visual field progression or progressive retinal nerve fibre layer or optic disc changes
- Documented progression of glaucoma at apparently controlled IOP
- Presumed rapid rate of progression without surgical intervention (very high IOP in ocular hypertension, unresponsive to medical or laser therapy)
- Poor compliance to medical treatment
- Intolerance to medical treatment

Before surgery, it is important to explain the aim of surgery, potential intra- and postoperative complications, postoperative treatment, and the importance of intense follow-up during first months after surgery.

3. Steps to achieve successful outcome

Preoperative risk assessment

Several risk factors are associated with a higher failure rate and with intra- and postoperative complications. These factors include younger age, higher preoperative IOP, prior incisional orocular surgery, uveitic and pigmentary glaucoma, thin sclera and conjunctiva, and ocular surface inflammation. Therefore, careful preoperative clinical examination is crucial.

Optimisation of operating environment

Surgery is performed on a quiet eye (whenever possible), choosing an area of mobile, non-scarred conjunctiva. Long-term topical drug treatment with added preservatives induces ocular surface inflammation with an increase of lymphocytes, mast cells, and fibroblasts. Stopping topical therapy before surgery reduces ocular surface inflammation. In the period before surgery either peroral systemic acetazolamide (if tolerated and safe for the patient) or preservative-free IOP-lowering therapy is prescribed. Starting topical anti-inflammatory therapy 4 weeks before surgery has been shown to improve survival of the filtering bleb.

Correct surgical approach and technique to improve predictability of surgery and to avoid early postoperative complications

Preferred **method of anaesthesia** is local (sub-Tenon's, peribulbar, retrobulbar, subconjunctival, topical, or intracameral). General anaesthesia is required for paediatric patients and in anxious and uncooperative adult patients. To expose the surgical site, superior corneal traction suture (6-0 or 7-0 Vicryl) is placed approximately 2 mm anterior to the limbus. Alternatively, a 4-0 superior rectus bridle suture can be used.

A fornix-based or limbus-based **conjunctival flap** is made with dissection through Tenon's capsule. The type of conjunctival flap does not influence the outcome of trabeculectomy. A fornix-based flap is commonly performed. It is easier to make, enables better exposure of the surgical bed, and no assistant is required, but it has a higher risk of early postoperative bleb leak.

To reduce scarring, **antifibrotics/antimetabolites** are applied under the conjunctiva, under scleral flap, or both. Both mitomycin C (MMC) and 5-fluorouracil (5-FU) have been used since the early 1990s and were shown to improve bleb survival. MMC has a direct cytotoxic effect and inhibits DNA-dependent RNA-synthesis. 5-FU inhibits the synthesis of thymine nucleotides and consequently DNA synthesis at the S (synthesis) phase of the cell cycle. MMC is a more potent agent as it inhibits DNA synthesis throughout the cell cycle. Application of antimetabolites (delivery systems, concentration, and exposure) is not standardised, but often MMC or 5-FU is delivered on polyvinyl corneal shields or methylcellulose sponges. It is important to place the sponges/shields posteriorly, to avoid contact with conjunctival border and to treat a large area to increase the chance for a diffuse bleb. Dosage of MMC varies

between 0.2–0.4 mg/ml (usually, 0.2–0.3 mg/ml) with an exposure time of 2–5 minutes. For 5-FU concentration of 50 mg/ml and exposure time 3–5 minutes are most common. Following application of antimetabolites, the area of the sclera and the underside of the conjunctival flap is irrigated with 10 ml of balanced salt solution.

Besides MMC and 5-FU, several other agents were proposed for decreasing episcleral healing after trabeculectomy. Only a few were evaluated in randomised clinical trials, and none other became generally accepted or widely used. Inhibitor of vascular endothelial growth factor (VEGF) bevacizumab (Avastin®) has shown efficacy and IOP reduction comparable to MMC, but it was associated with increased rate of bleb leak. The degradable collagen matrix implant (Ologen®) was also used and placed directly over the loosely sutured scleral flap to modulate the healing process and to improve bleb survival. Some studies showed that Ologen implants may be comparable to MMC, but the cost of the implant is a disadvantage compared to MMC.

The next step is dissection of the partial-thickness **scleral flap**. The size and shape of scleral flap may vary. The size ranges between 2–5 mm in length at limbus and between 2–4 mm in width, with rectangular, triangular, or trapezoid shape. Size and shape of scleral flap do not influence the outcome of trabeculectomy. It is important to dissect the half-thickness scleral flap anteriorly into clear cornea to avoid entering the anterior chamber over the ciliary body. Before entering the eye, a **paracentesis** away from the fistula is created to allow anterior chamber stability, adjust IOP, and ensure watertight wound closure.

Creation of the fistula is made by either excision of the tissue block or by using a punch technique. First an incision smaller than the flap is made anterior to Schwalbe's line to insert the punch. A small opening (0.5 mm) is created by taking 2–3 bites with the punch from the posterior lip of the incision, followed by peripheral iridectomy.

Meticulous **scleral flap closure** is important to prevent early postoperative complications. A tight closure is achieved with 10-0 nylon fixed and releasable or adjustable sutures. The early postoperative IOP depends on the number and tightness of sutures and the thickness of the scleral flap. Postoperative filtration can be titrated by adjusting or removing sutures at the slit lamp. The closure of the conjunctival-Tenon's flap should be watertight without damaging the conjunctiva. The fornix-based flaps have higher frequency of leakage at the limbus, but minor early postoperative leakage does not affect the outcome of trabeculectomy.

4. *Intense postoperative management to reduce scarring and preserve aqueous flow*

Postoperative therapy includes topical antibiotics for approximately 2 weeks and topical steroids, preferably preservative-free, over 3 months (with decreasing instillations). The best way to control scarring and to keep the fistula patent is by frequent visits. Early signs of scarring must be noticed and establishing flow is priority. This can be achieved by massage, removing releasable sutures or cutting them with laser (if only fixed sutures are used), and needling of the bleb as the very last resort.

5. Complications

While trabeculectomy is the most effective surgery to reduce IOP, it is associated with a number of postoperative complications. These can occur intraoperatively, in the early (the first few days or weeks after surgery) and late postoperative period. Some of the complications, those most common and vision-threating are described.

Blebitis is a bleb-related infection that is limited to the area of filtering bleb. The infection must be treated aggressively by topical antibiotics to prevent inflammation of the anterior and posterior segment: **endophthalmitis**. This is a rare complication with a high risk of visual loss. Risk factors for blebitis and endophthalmitis include thin ischemic blebs, bleb leaks, use of antifibrotics (MMC and 5-FU), and inferiorly placed trabeculectomy.

Hypotony is defined as an IOP of 5–6 mmHg or less. It can be divided in early (within 2 weeks after surgery) and late. Early hypotony can be due to overfiltration at the surgical site or decreased aqueous production (toxic effect of intraoperative antifibrotics, inflammation). Hypotony is often associated with shallow anterior chamber, choroidal detachment, and macular and disc oedema. Chronic hypotony can lead to maculopathy with choroidal folds, optic disc oedema, and transient or permanent vision loss.

Bleb leak is common in the early postoperative period, particularly with fornix-based conjunctival flaps. They can result from conjunctival button holes during surgery or from wound dehiscence (too loose sutures). If the leak is combined with hypotony, shallow anterior chamber, or both, this often requires surgical repair. Minor early bleb leak was found in 65% of fornix-based and in 24% of limbus-based flaps, and did not influence the outcome at 6 month of follow up. Bleb leaks can occur months to years after surgery and are more common after use of antifibrotics that result in thin, avascular blebs. If left untreated, they can cause hypotony maculopathy, shallowing of the anterior chamber, choroidal effusion, and endophthalmitis.

Encapsulated bleb is common (6-28%) and usually occurs several weeks after surgery. It is characterized by a localized dome-shaped elevation of the bleb with thickened and vascular Tenon capsule. Treatment depends on the level of IOP and whether it is acceptable for the individual's disease severity. Most of the blebs after conservative treatment begin to function well within a few months, but some require needling with subconjunctival injection of antifibrotics (MMC or 5-FU).

Bleb dysesthesia is characterised by symptoms including foreign body sensation, burning, tearing, and pain that are caused by the filtering bleb. The amount of discomfort is usually related to the area of the exposed bleb in the interpalpebral fissure and the height of the bleb. Risk factors for bleb dysesthesia are young age, poor eyelid coverage, superonasal bleb location, and distribution of the tear film in the area of the bleb that results in bubble formation upon blinking. If conservative methods (lubricants) fail to relieve the symptoms, surgical revision of the bleb may be necessary.

6. Other devices

ExPRESS® glaucoma shunt (Alcon) was introduced in 2002 as an alternative to trabeculectomy. It is a non-valved stainless steel device that diverts aqueous from the anterior chamber to the subconjunctival space. The surgical technique is similar to trabeculectomy except that the anterior chamber is entered with a needle and the shunt, preloaded on an inserter, is introduced into the anterior chamber. The goal of the device is to make surgery more repeatable with improved outcomes and fast visual recovery. Literature comparing ExPRESS with trabeculectomy found no significant difference in rates of success and early postoperative complications between the two filtration procedures. However, the cost of the shunt is an important disadvantage.

InnFocus MicroShunt® (Santen) is a synthetic tube that diverts aqueous from the anterior chamber to the subconjunctival space. It is implanted *ab externo* and requires conjunctival dissection. The results in a small number of eyes with up to 3 years of follow-up showed significant IOP lowering effect. Further clinical trials are required to establish its long-term efficacy and cost-effectiveness.

7. Conclusions

Despite the increasing popularity of MIGS, trabeculectomy is still a highly successful procedure for IOP lowering and it will have a role when greater IOP reductions (to lower teens) are necessary. Successful outcomes strongly depend on careful patient selection, optimisation of the operating environment, appropriate surgical approach and techniques, as well as on intense postoperative management to reduce scarring and to preserve aqueous flow.

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Classic

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Answers to MCQs on page 120

1. a. *False*
   b. *True*
   c. *True*
   d. *False*
   e. *True*

2. a. *True*
   b. *False*
   c. *True*
   d. *False*
   e. *True*

3. a. *True*
   b. *True*
   c. *False*
   d. *False*
   e. *True*

4. a. *True*
   b. *False*
   c. *True*
   d. *True*
   e. *False*

21

Alternative IOP lowering surgery

Gordana SUNARIC MEGEVAND - Switzerland

MCQs

1. **Regarding non-penetrating glaucoma surgery:**
   a. The IOP-lowering effect is equal to that of trabeculectomy
   b. The learning curve is short
   c. Results can be improved with Nd:YAG laser goniopuncture
   d. The safety profile is equal to that of trabeculectomy
   e. The mechanism relies only on external filtration

2. **The subconjunctival outflow pathway:**
   a. is the usual outflow pathway for trabecular minimally invasive glaucoma surgery (MIGS)
   b. can be enhanced by the use of antifibrotic agents
   c. may need repeated manipulation for adequate IOP control
   d. may increase the risk for bleb infection and endophthalmitis
   e. is an aim in all perforating filtration surgeries

3. **Trabeculectomy:**
   a. Is regarded as the gold standard for glaucoma surgery
   b. Its success depends mainly on the stage of the disease
   c. It has better IOP-lowering effect than most alternative surgeries
   d. It cannot be repeated in the same eye
   e. It is associated with better visual outcomes than other glaucoma surgeries

4. **Regarding MIGS:**
   a. Their cost-effectiveness is proven as compared to other glaucoma surgeries
   b. Only very mild postoperative complications are known today
   c. They cannot replace trabeculectomy in all cases
   d. They may damage the corneal endothelium after several years
   e. They are recommended for advanced glaucoma

21 Alternative IOP lowering surgery - SUNARIC MEGEVAND G - Switzerland

THE STANDARD TREATMENT of glaucoma consists of lowering intraocular pressure (IOP) with medical treatment or laser as primary therapy and of switching to surgery when the target intraocular pressure (IOP) is not achieved or optimal disease control is not obtained. Described by Crains in 1968, trabeculectomy is still the standard filtration surgery for glaucoma. Depending on patient selection, definition of success and length of follow-up, the success rate of modern trabeculectomy in experienced hands is high. However, complications such as hypotony, flat anterior chamber, choroidal detachment, and suprachoroidal haemorrhage or postoperative complications related to excessive filtration are not uncommon. Consequently, to avoid such vision-threatening complications, alternative innovative procedures have emerged. Deep sclerectomy, viscocanalostomy and canaloplasty are known under the name of non-penetrating glaucoma surgery (NPGS) whereas the *ab interno* approach and use of various devices is named minimally invasive glaucoma surgery (MIGS). These newer technics have aroused substantial interest among surgeons over the last few years because of their excellent safety profile and potential to be used at an earlier stage of the disease.

1. Non-penetrating glaucoma surgery

Three main technics are considered: deep sclerectomy (DS) with or without collagen implant, viscocanalostomy (VCS) with injection of Healon GV® into Schlemm's canal (SC), and canaloplasty (CP), considered to be an evolution of VCS.

All three surgical techniques have in common the dissection of a superficial and a deeper scleral flap (deep sclerectomy), the unroofing of SC, and the creation of a Descemet's window (DW). In addition, VSC and CP focus on the partial and complete dilation of SC and collector channels (CC) and distention either with a prolen suture or with a fenestrated stent.

Deep sclerectomy: As the DS relies on subconjunctival outflow, mitomycin C is used in most cases. A superficial scleral flap followed by a deeper flap is excised 1 mm into the clear cornea, removing the outer wall of SC and creating a DW as well as removing the fine juxtatrabecular tissue (JXT) from the inner wall of SC, thus allowing percolation of the aqueous. The excision of the deeper flap creates a scleral lake where the collagen implant or hyaluronic acid device is sutured to keep the scleral lake open. The superficial scleral flap is sutured loosely, allowing the aqueous to accumulate under the conjunctiva, thus creating a conjunctival bleb just as with trabeculectomy. In a high proportion of cases (up to 70%) post-operative (2 months to 2 years) Nd:YAG-laser goniopuncture is needed to lower IOP, transforming a non-penetrating procedure into a penetrating one[).

Viscocanalostomy: This procedure has the same initial steps as DS, but in addition to the unroofing of SC and the peeling of the JXT, the surgeon injects high molecular wight hyaluronic acid into the two ostia of the opened SC, thus creating a sectoral distention of the potentially collapsed SC and CC, and possibly also microperforations. After excision of the deep scleral flap, in the original version of the technique described by Stegman, the superficial flap is sutured watertight in order to allow the aqueous to drain via SC and via the intrascleral lake without depending on the conjunctival outflow pathway (bleb-independent). However, data

from previously published ultrasound biomicroscopy studies suggest that the subconjunctival outflow pathway is present in a significant number of eyes, resulting mainly from the evolution of the technique with looser suturing of the superficial scleral flap. Now it is generally believed that viscocanalostomy can decrease IOP by enhancing both conventional and uveoscleral outflow pathways.

Canaloplasty: This procedure combines non-penetrating DS with a modified VCS. Instead of partial dilation of SC, the canal is catheterised 360° using a microcatheter augmented with an illuminating tip (iTrack® & iLumen®; iScience International) and is then dilated by injecting circumferentially high molecular weight viscoelastics (Healon GV®)[]. Transtrabecular flow is thought to be enhanced by distending the circumference of the canal with a 10-0 Prolene suture tighetened under tension during surgery when the eye is still soft in order to stretch and dilate maximally SC and the trabecular meshwork circumferetially when the IOP returns to normal.

A fenestrated stent (Stegmann Schlemm's Expander®) is able to replace the 10-0 Prolene suture in order to standardise the amount of dilation of SC as the thightening of the suture can not be objectively controlled nor standardised during the procedure. A two-year follow-up reports promising results.[]

2. Results of non-penetrating glaucoma surgery

Long-term results of DS, VCS and CP are encouraging because their safety profile makes this type of surgery particularly attractive in patients with mild to moderate glaucoma while providing a better IOP-lowering effect than MIGS. They are also attractive in patients with advanced glaucoma in whom complications with fistulising surgery may compromise visual function. When considering patient satisfaction, CP is associated with better quality-of-life than trabeculectomy. Although NPGS is associated with less complications, a Cochrane systematic review has shown an inferior IOP-lowering effect of SD and VCS as compared to trabeculectomy.

3. Minimally invasive glaucoma surgery (MIGS)

MIGS is a relatively recently developed surgical approach, commonly defined as an *ab interno* approach inducing minimal trauma with very little or no scleral dissection, minimal or no conjunctival manipulation, good safety profile, and a rapid recovery. An important goal of MIGS is the individual approach to each patient, respecting the variability in risk profiles (age, stage of disease, rate of progression, anatomy, and existing pathology). Therefore, MIGS allows for a shift in decision making toward earlier surgical intervention to lower IOP in patients with mild to moderate glaucomatous optic neuropathy. This would mean that even a more modest decrease in IOP might suffice and could lead to enhanced outcomes with better safety profiles. MIGS is usually classified by the locus of action: trabecular, suprachoroidal, and subconjunctival. They can be performed in association with cataract surgery or as solo procedures.

Trabecular-based devices: These function by improving trabecular outflow through SC.

The Trabectome® system (Neomedix) performs a trabeculotomy under guidance of intraoperative gonioscopy: a disposable 19.5G handpiece with an insulated footplate containing electrocautery, irrigation, and aspiration functions is inserted into the anterior chamber and then through the TM into SC, treating usually 60°–120° of the nasal angle.

The iStent® (Glaukos) directly connects the anterior chamber to SC and creates a permanent opening and communication. The device is composed of one or two (iStent inject) heparin-coated, non-ferromagnetic, titanium stent(s), approximately 1×0.3 mm in size, presented with an inserter that is guided into a 1.7 mm corneal wound and implanted, under gonioscopic guidance, into SC.

The Hydrus Microstent® (Ivantis) is an 8-mm-long, crescent-shaped open structure with scaffold design, curved to match the shape of SC. It is made of nitinol and uses a preloaded injector via a clear corneal incision. It is inserted into the AC and sits within SC, in which it extends over 3 clock hours.

Gonioscopy-assisted transluminal trabeculotomy (GATT) is a form of *ab interno* trabeculotomy and a modification of the 360° suture *ab externo* trabeculotomy. In GATT, an illuminated iTrack® microcatheter (Ellex) is inserted via a pre-created goniotomy into SC nasally. The catheter is advanced circumferentially 360° and once the distal tip of the catheter has made all the way back to the initial goniotomy incision, it can be externalised through the temporal paracentesis. The same is done with the proximal tip, allowing for a 360° trabeculotomy.

Suprachoroidal stents

The suprachoroidal based devices should improve uveoscleral outflow through a connection between the anterior chamber and the suprachoroidal space.

The Cypass® polyamide implant, which is 6.35 mm in length and 510 µm in external diameter, is introduced into the supraciliary space, but has been withdrawn from the market in 2018 because of significant corneal endothelial damage observed after the 5 years follow-up.

Subconjunctival stents

Subconjunctival filtration creates an alternative outflow pathway for the aqueous huomour to the subconjunctival space and is the basis of the traditional trabeculectomy and aqueous shunt glaucoma surgeries

XEN® Gel stent (Aquesys) is a hydrophilic tube, 6 mm long with a lumen of 45 µm, composed of porcine gelatine crosslinked with glutaraldehyde. XEN is implanted *ab interno* via a clear corneal incision. The stent follows Poiseuille's law of laminar flow where the length of the tube and its inner diameter determine the rate of flow. Hypotony is avoided by the flow resistance

determined by the length and inner diameter of the XEN tube. As in other bleb-dependent interventions, mitomycin C is mandatory for the success of the procedure and it is injected prior to the surgery under the conjunctiva.

The Preserveflow® microshunt (previously named Innfocus, Santen) is an *ab externo* drainage device necessitating opening of the conjunctiva and Tenon's capsule and, therefore, not really adhering to the strict definition of MIGS. The use of mitomycine C is part of the procedure and concentrations of 0.02–0.04% for 2–3min are recommended. The material is SIBS (polystyrene-block-isobutylene-block-styrene) which has been developed specifically for medical implants such as cardiac stents. The 70 µm lumen of the device serves as a flow restrictor with the intention of avoiding hypotony yet dampening IOP spikes postoperatively.

4. Results of *ab interno* MIGS

There are only a few randomsied controleld trials on *ab interno* MIGS, and the existing literature has been extensively reviewed.

Trabecular-based devices: most studies report a modest reduction of the IOP, certainly less than in standard trabeculectomy, weather used in combined surgery or in solo procedures. They have, however, an excellent safety profile, with minimal complications and side effects. Globally, the use of medication postoperatively is significantly lower as compared with the preoperative use. It is suggested to use these devices mainly for combined surgeries in early and moderate glaucoma where the target IOP can be in the mid teens or the patient is intolerant to medication. Standalone use is acceptable, but results of long-term studies are not available.

Subconjunctival-based devices: XEN-Gel two-year follow-up results in a multicentre study showed a good IOP lowering result both in standalone and in combination procedures with phacoemulsification with an acceptable safety profile. In a comparison on the risk of failure and safety profiles between standalone XEN and trabeculectomy authors stated that there was no detectable difference between the two procedures, showing that XEN can also have some serious complications. Indeed, anecdotal reports have reported blebitis and endophthalmiis as a consequence of the implantation of the XEN-Gel device.

Preserveflow microshunt: this device should not be included in the MIGS family as the preparation of the conjunctiva takes an *ab externo* approach just as with trabeculectomy and other tubes. Only rare studies have been reported so far, we await with interest the 5-year follow-up results of the multicentre, randomised comparative trial with trabeculectomy that should be published toward end of 2019. Results from non-randomized and non-controlled studies may reveal that the devise has better IOP lowering efficacy than true MIGS.

The limitation of the current state of MIGS is the lack of standardised, long-term, high-quality data. Available are only limited data on cost effectiveness and, overall, a lack of knowledge on the ideal patient profile prevails. We need more robust studies to compare MIGS with more conventional surgeries.

5. Conclusion

A constant interest exists in searching for safer and more efficient glaucoma surgeries. The sub-conjunctival route was the principal type of filtering procedure exploited with trabeculectomy and tubes, but its potential bleb-related complications and fibrosis have initiated the surge for newer procedures. The interest raised with NPGS and trabecular MIGS interventions has mainly led to understand their inferiority as compared to trabeculectomy. Indeed, this has created an urge for better understanding of the anatomy, and new structural and functional assessments have arisen.

In recent years we have learned more about SC and CC and the individual behaviour of the ocular filetring procedures in each patient, but we still do not know which MIGS is the best for each given eye. Hopefully new diagnostic tools will be able to help us to better chose the appropriate surgical procedure for a given patient by targeting the appropriate filtering procedure.

Today, MIGS have already the potential to reduce the medication burden and to enhance patient's quality-of-life, to bypass or delay the need for more invasive surgery, and to preserve the conjunctiva if a more invasive intervention were to be required later on. Limited data on the cost-effectiveness of MIGS are available, and we need more studies to address all these questions before incorporating MIGS as a routine standard procedure.

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Answers to MCQs on page 128

1. a. *False*
   b. *False*
   c. *True*
   d. *False*
   e. *False*

2. a. *False*
   b. *True*
   c. *True*
   d. *False*
   e. *True*

3. a. *True*
   b. *False*
   c. *True*
   d. *False*
   e. *False*

4. a. *False*
   b. *False*
   c. *True*
   d. *True*
   e. *False*

22

Phacoemulsification in glaucoma

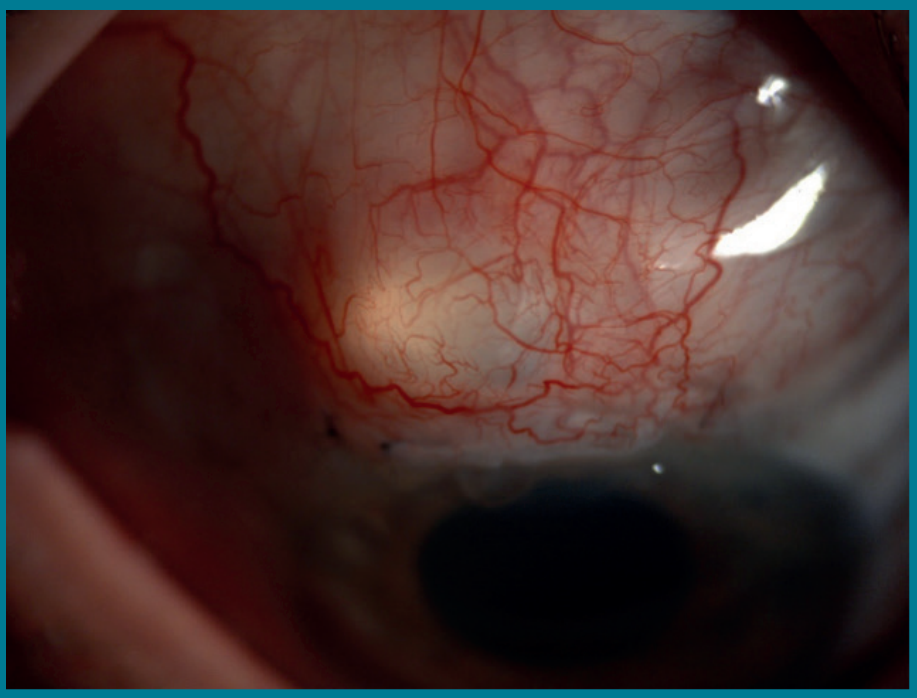
Carlo TRAVERSO - Italy

MCQs not available

Abstract not available

C

How do I treat this patient?
Case 1 - Barbara CVENKEL



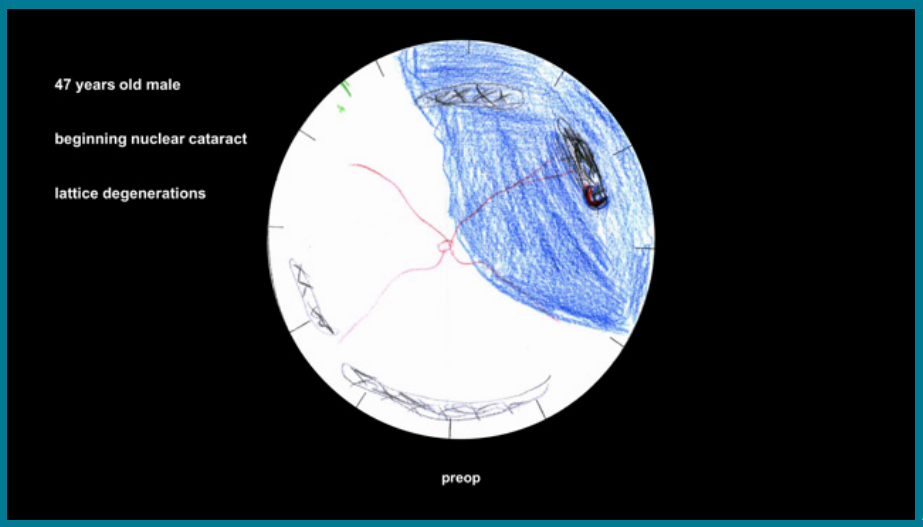
A 65-year-old male patient with advanced exfoliation glaucoma, OS, and uncontrolled IOP on maximum tolerated hypotensive medication underwent a trabeculectomy.

IOP at week 1 and 2 post-operarively was 12 mmHg. He was on topical preservative-free steroids and antibiotics. At 1 month, his IOP has increased to 30 mmHg.

- **What is the reason for IOP increase in this case after trabeculectomy?**
- **How would you treat this patient?**
- **Other treatment options and suggested follow-up?**

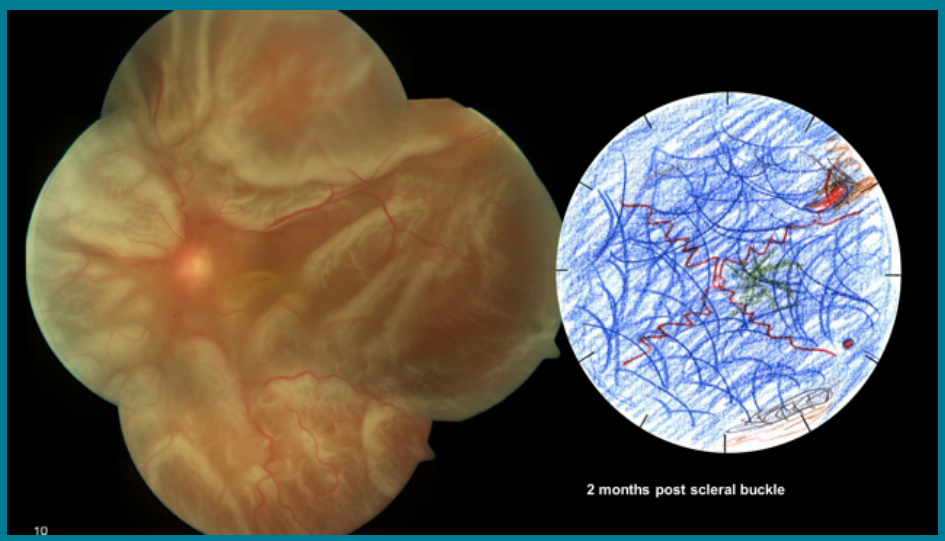
C

How do I treat this patient?
Case 1 - Eckert TILLMANN



A 47-year-old male patient with a rhegmatogenous macula-off retinal detachment, OS, from 11 to 4 o'clock from a horse shoe tear at 2 o'clock near one of four lattice degenerations. Best corrected visual acuity (BCVA) was 0.5, OD, and hand movements, OS. Beginning nuclear cataract, OU. Axial length 23.8 mm, OD, and 23.2 mm, OS. Detached macula.

- **How would you treat this case?**

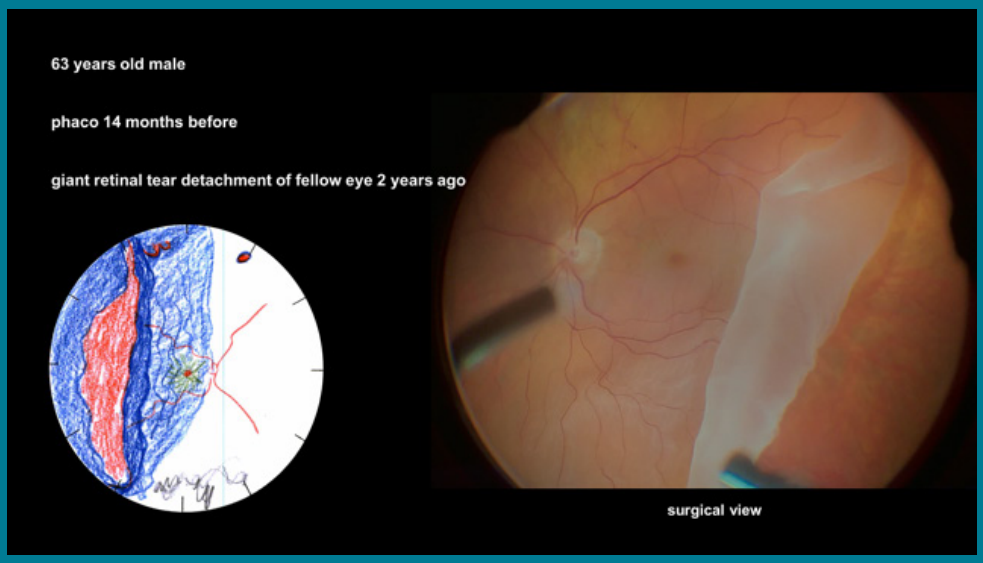


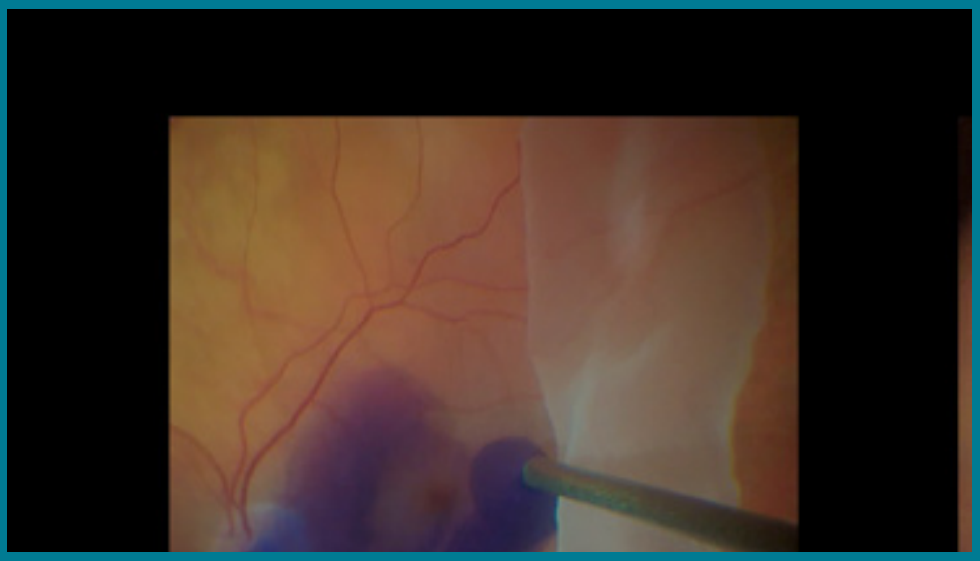
Two months later total retinal detachment ,OS, BCVA 20/300. The tear at 2 o'clock was open and marked wrinkling of the retinal surface could be seen.

- **What would you do now?**

C

How do I treat this patient?
Case 2 - Eckert TILLMANN





14 months after cataract surgery retinal detachment, OD, with a giant retinal tear between 6 and 11.30 o'clock and a full thickness macular hole. BCVA OD counting fingers.

- **Would you perform prophylactic laser treatment of the fellow eye before cataract surgery?**

Redetachment with beginning proliferative vitreoretinopathy.

- **What would you do now?**

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When to call the vitreoretinal surgeon?

Leigh SPIELBERG - Belgium

MCQs not available

23 When to call the vitreoretinal surgeon? - SPIELBERG L - Belgium

Abstract not avaialble

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Postoperative retinal detachment

Eckert TILLMANN - Germany

MCQs

1. **Regarding retinal detachment (RD) after cataract surgery:**
   a. Lincoff's rules apply only to phakic RD
   b. Breaks in pseudophakic RD are usually smaller than in phakic RD
   c. Vitreous haemorrhage is a common finding in pseudophakic RD
   d. In pseudophakic eyes, three-mirror contact lenses are better for visualisation of the peripheral fundus than indirect contact lenses
   e. 360° scleral indentation during indirect ophthalmoscopy is useful, because many retinal breaks in pseudophakic eyes are located near the ora serrata.

2. **Regarding the risk for pseudophakic RD (PRD):**
   a. The risk for PRD is higher in older than in younger patients because patients with a PRD are usually older than those with a phakic RD
   b. Cataract surgery increases the risk for a PRD by a factor of about 4
   c. The risk of PRD in patients with a posterior capsule rupture is high even if no vitreous loss occurs
   d. In highly myopic patients younger than 55 years the hazard ratio for PRD is as high as 25
   e. A refractive lens exchange in a young high myope is a relatively safe procedure, if prophylactic laser treatment of all peripheral degenerations is performed

3. **Regarding vitreoretinal surgery for PRD:**
   a. Scleral buckling is an option also in PRD
   b. In a PRD with multiple inferior breaks, vitrectomy should be combined with an encircling element
   c. A macula-on PRD should be operated on the same day, whereas a macula-off PRD can be postponed up to one week after presentation
   d. According to the Scleral buckling versus Primary vitrectomy in Rhegmatogenous retinal detachment (SPR) study, functional results in PRD are better with vitrectomy than with scleral buckling
   e. Prone positioning in the first postoperative hours is a means to prevent macular folds

4. **Regarding pars plana vitrectomy (PPV) for RD:**
   a. After PPV for macular pucker or hole, the incidence of RD is about 10%
   b. The larger the gauge (e.g., 20G vs. 25G), the higher the risk for sclerotomy-site related breaks
   c. Intraoperative retinal breaks are more common during macular hole surgery than during macular pucker surgery
   d. Lattice degenerations should be treated with photocoagulation before elective vitrectomy
   e. The progression of a post-vitrectomy RD is faster than in a non-vitrectomised eye

RHEGMATOGENOUS RETINAL DETACHMENT (RRD) is defined as separation of the neurosensory retina from the underlying retinal pigment epithelium (RPE), caused by at least one retinal break. Typically, vitreoretinal traction has created the break(s). Ageing of the vitreous body or certain conditions lead to an increasing liquefaction of the vitreous gel. This can be followed by an anomalous posterior vitreous detachment (PVD) with posterior separation of the vitreous cortex from the retina but persistent traction on the peripheral retina. If traction is greater than the physiologic forces keeping the retina attached (metabolic pump of the RPE, osmotic pressure of thechoroid), vitreous fluid will open the normally only virtual subretinal space via the break(s), leading to accumulation of subretinal fluid and an increasing RRD.

Common predisposing factors for a premature PVD and a subsequent RRD are high myopia, peripheral retinal degenerations (in particular lattice degeneration), genetic disorders such as Stickler's syndrome, direct ocular injury, and previous intraocular surgery.

The most frequent risk factor for a postoperative RRD is cataract surgery leading to pseudophakia (or rarely, aphakia). About a third of eyes with primary RRD are pseudophakic retinal detachments (PRD). Modern small incision phacoemulsification leads to less PRD than older techniques like intracapsular cataract extraction. The increasing rate of cataract surgery and a trend to operate earlier (at a younger age and at higher visual acuities) will lead to even higher rates of PRD in the future. This will be becaue of a high volume of cataract surgery and increasing life expectancy. Therefore, the characteristics and treatment of PRD will be the main topic.

Because "simple" vitrectomies for epiretinal membranes or macular holes or floaters can lead to detachment, postoperative RRD following macular surgery is also an issue.

The huge topic of proliferative vitreoretinopathy (PVR) and redetachment after vitreoretinal surgery for RRD or traction retinal detachment will not be discussed. The risk for PRD caused by corneal refractive procedures such as LASIK and after intravitreal anti-VEGF-injections is considered to be low or very low, and will not be discussed either.

1. Pseudophakic retinal detachment

Known risk factors for PRD: young age, male gender, long axial length, posterior capsule rupture with vitreous loss, vitreous strands around intraocular lens (IOL) and into surgical wounds, history of fellow eye with RRD.

***Risk of RRD following cataract surgery*:** Overall, the annual incidence of a RRD is approximately 10 (6–18 in different countries, continents and periods) per 100,000 (0.01% annually). After cataract surgery, the incidence is estimated to be 0.7–1% in the first 4 years, with a still increasing cumulative risk even after many years.

Recently, a large register-based study in Denmark (Bjerrum et al. 2013; between 2000 and 2010) and a national population-based study in France (Daien et al. 2015; between 2009 and 2013) found that previous cataract surgery increased the risk of RRD by a factor of about 4. The Danish study compared the rates of RRD after uneventful phacoemulsification in patients

with a fellow phakic eye. The risk for a PRD was 4.23 higher than the risk for a RRD in the phakic fellow eye and remained higher even after 10 years. The same group (Hajari et al., 2014) found a 100-fold higher risk of RRD for the fellow eye in Denmark if the first eye had sa RRD, and an increase in the incidence of RRD that was mainly attributed to the increasing number of cataract surgeries.In France, the odds ratio associated with increased risk of RD was 3.87. It was higher for younger patients (40–54 years), for high myopia, after vitrectomy for perioperative posterior capsular rupture (PCR), history of eye injury, extracapsular cataract extraction, male gender, and history of diabetes. Highly myopic patients (axial length 26 mm or higher) had the highest multiadjusted odds ratios (up to 25 in patients younger than 54 years).

PRD after Nd:YAG capsulotomy

According to a recent Canadian study (Wesolosky et al., 2017) the risk of retinal breaks (0.29%) and of PRD (0.87 %) is elevated in the first 5 months after a Nd:YAG capsulotomy. The increased risk seems to be relevant especially in younger and myopic patients in whom a PVD has not occured yet.

PRD after complicated cataract surgery with vitreous loss

A PCR with vitreous prolapse that necessitates anterior vitrectomy is a known high risk factor for PRD (increases risk by a factor of 10–40). A subanalysis of the United Kingdom National Ophthalmology Database Study of Cataract Surgery (Day et al., 2016) found that a PRD occurs earlier after cataract surgery complicated by PCR. The median time to PRD surgery was 44 days for eyes with PCR, and 6.3 months for eyes without PCR.

PRD after refractive lens exchange

Because refractive (clear) lens exchange (RLE) is usually performed in relatively young and highly myopic patients, the risk for a PRD is higher than for cataract surgery in older patients with shorter axial length.

PRD after paediatric cataract surgery

A recent Indian study (Agarkar et al., 2018) on the incidence of PRD in patients under 16 years found an overall risk of 5.5% at 10 years after cataract surgery in children with no known ocular and systemic anomalies. According to this study, the risk significantly increases in male, myopic, and intellectual disabled children. Long-term follow-up is needed in patients after paediatric cataract surgery.

Adult patients with a history of retinopathy of prematurity (ROP) have a high risk of retinal complications after cataract surgery (Kaiser et al., 2008).

Characteristic findings in PRD

In pseudophakic eyes, vitreous traction occurs more peripherally than in phakic eyes of generally younger patients. The horseshoe tears are often smaller and more peripheral (pre-equatorial) than in phakic eyes, include fewer ruptures of bridging retinal vessels and less vitreous haemorrhages, and are more often found also in the inferior quadrants. Despite these differences, gravitational forces are as important as in phakic eyes. Therefore, Lincoff's rules also apply for PRD and aid in searching for the primary break. Visualisation of the peripheral retina in pseudophakic eyes is often more difficult than in phakic eyes (smaller pupils, synechiae, opacification of anterior and posterior capsule, secondary cataract, rim of IOL optic). Three-mirror lenses are not as useful as in phakic eyes. Indirect contact lenses are more helpful. However, often scleral indentation during indirect ophthalmoscopy is necessary to localise the break(s).

2. Treatment of PRD

Vitrectomy has become the main treatment of PRD for most vitreoretinal surgeons, although some surgeons still perform buckling surgery with good results.

In the pseudophakic group of the Scleral buckling versus Primary vitrectomy in Rhegmatogenous retinal detachment (SPR) study (Heimann et al., 2007) the anatomic outcome after vitrectomy was significantly better, and the mean number of retina-affecting secondary surgeries was lower than after scleral buckling. Vitrectomy offers certain advantages over scleral buckling: removal of vitreous opacities and most of the peripheral vitreous traction, if vitrectomy is nearly complete; identification and selective laser treatment even of small peripheral breaks, even if they were undetectable with indirect ophthalmoscopy, thus avoiding cryocoagulation; removal of epiretinal membranes or subretinal strands if present; nearly complete tamponade with gas or silicone oil at the end of the procedure; no refractive changes. Primary success rates after vitrectomy usually range between 80–90%. In most cases, a gas tamponade with SF_6 is used. In PRD and manifest PVR with star folds, silicone oil tamponade for a few months is often necessary, as well as in giant retinal tear detachments. Postoperative positioning is important to attain sufficient closure of the breaks in the first postoperative days. In the first hours after the surgery, prone positioning helps to avoid a shift of subretinal fluid (SRF) into the central retina before complete absorption of central SRF. Shifting SRF could lead to deleterious retinal folds in the macula.

It was controversial whether a combination of vitrectomy and scleral buckling is safer than vitrectomy alone. The Vitrectomy with and without encircling band in the treatment of pseudophakic retinal detachment (VIPER) Study (Walter et al., 2016) confirmed that vitrectomy with gas is an efficient and safe treatment for uncomplicated PRD and that an additional encircling band does not significantly reduce the risk for any second procedure necessary to reattach the retina by 20G vitrectomy. A *post hoc* analysis revealed that this is also true of PRD with multiple inferior breaks (Baumgarten et al., 2018). In manifest PVR, an additional encircling element may still be a reasonable option, especially in redetachments.

Still controversial is whether the internal limiting membrane should be removed routinely in cases of RRD in order to prevent postoperative epimacular proliferations.

Timing of surgery

A RRD is an ophthalmic emergency, as long as the macula is threatened being detached, and if it has been only shortly detached. However, same-day surgery after presentation is often not feasible, even in a specialised vitreoretinal clinic. Postponing the surgery to the next day until an experienced surgeon and the whole team is available, is usually as safe or even better than immediately operating under suboptimal conditions.

Preoperative bed rest and appropriate positioning (on the side of the break) are helpful in flattening a highly detached retina and to prevent further progression of RRD by reducing eye and rotational head movements. A superior bullous RRD due to superior breaks will show rapid progression and should be treated as soon as possible, if the macula is still attached. In many cases, however, there is a shallow detachment of the fovea already at presentation. A detached macula should be attached within the first 3 days after central vision loss. After this period, the prognosis becomes worse because of a progressive irreversible loss of cones. If the macula has been already been detached for more than 6 days, the suregry is not urgent any more.

3. Postoperative RRD after pars plana vitrectomy (PPV) for macular diseaeses

Intraoperative retinal breaks and retinal detachment

If there has not been a PVD yet (e.g., in many macular holes, vitreomacular traction syndrome, young patients, asteroid hyalosis, proliferative diabetic retinopathy) retinal breaks can occur at or even central to the equator when the vitreoretinal surgeon detaches the posterior hyaloid (in up to 20 % of cases, independent of gauge). This risk is less pronounced if there has already been a partial PVD like in most eyes with macular pucker. Usually, immediate treatment with reattachment, laser photocoagulation, and gas tamponade is possible if the breaks have been noticed during the procedure. The same is true for peripheral breaks near the sclerotomies.

RRD after PPV

An increased risk for a postoperative RRD is present under the following conditions: core vitrectomy leaving much peripheral vitreous, especially if a gas tamponade is applied, which leads to traction on the inferior peripheral retina and early postoperative RRD; incarceration of peripheral vitreous, especially if larger gauges (i.e., 20G) are used or if multiple changes of instruments are necessary (e.g., in complex vitrectomies for proliferative diabetic retinopathy, inflammatory diseases, manifest PVR). Sclerotomy-site related RRD after vitrectomy tends to progress rapidly because these breaks are located superiorly and no tamponading effect of vitreous is present any more. An analysis using the IRIS registry (Parke et al., 2018) found 1-year rates of RRD after macular surgery to be 2% (macular hole) to 2.5% (macular pucker).

4. The role of peripheral retinal degenerations and prophylactic laser treatment

Until now, the only clear indication for prophylactic laser treatment is a symptomatic horseshoe tear that has to be treated completely, including the retina anterior to the flap. Because no randomised controlled trials exist, the value of treating asymptomatic retinal breaks to prevent RRD is still not clear (Wilkinson, 2014). Nevertheless, laser treatment of lattice degeneration is often performed though only rarely this common peripheral degeneration leads to RRD. In fellow eyes afetr RRD, treatment of lattice degenerations may be considered. However, although after an acute PVD the risk for a tear at a lattice site is high, additional breaks often occur in formerly healthy appearing areas of the retina. Fellow eyes of patients with idiopathic giant retinal tears (GRT) have a high risk for a GRT. A prophylactic 360° laser treatment of the fellow eye was found to provide a significant risk reduction for RRD and macular-off RRD (Verhoekx et al., 2019).

A multicenter retrospective study (Garg et al., 2018) compared patients undergoing pars plana vitrectomy for macular diseases with prophylactic 360° laser to those without such laser treatment and found no significant difference in the number of retinal breaks or RRD. More important seems to be the alertness of the surgeon during the creation of a PVD.

5. Conclusion

When counseling patients before cataract surgery, Nd:YAG capsulotomy, and vitrectomy, the individual risk of PRD should be discussed. Patients with a PCR and anterior vitrectomy should be informed openly about the complicated surgery and monitored closely after surgery since their risk of early PRD is very high. Referal to a vitreoretinal surgeon should be considered early, if vitreous is still in the anterior chamber or around the IOL, causing traction on the peripheral retina.

Patient education is very important: Explaining the possible symptoms of a PVD, retinal breaks or RRD is mandatory to achieve early treatment of symptomatic patients. Equally important is an immediate examination if patients develop suspicious symptoms. It is not a platitude: the earlier the diagnosis, the better the prognosis for patients with (postoperative) RRD.

RECOMMENDED READING

Recent

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Classic

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Answers to MCQs on page 144

1. a. *False*
   b. *True*
   c. *False*
   d. *False*
   e. *True*

2. a. *False*
   b. *True*
   c. *False*
   d. *True*
   e. *False*

3. a. *True*
   b. *False*
   c. *False*
   d. *True*
   e. *True*

4. a. *False*
   b. *True*
   c. *True*
   d. *False*
   e. *True*

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Pseudophakic macular oedema

Laura WIELDERS - The Netherlands

MCQs

1. **Pseudophakic cystoid macular oedema:**
   a. Develops within 1–3 weeks postoperatively
   b. Is characteriSed by fluid accumulation in the inner nuclear and outer plexiform layers of the retina and may involve subretinal fluid
   c. Causes visual complaints in essentially all patients affected by it
   d. Rarely resolves without appropriate treatment

2. **Which patients should you inform about an increased risk of cystoid macular oedema after cataract surgery:**
   a. A patient with diabetes mellitus type 2 without signs of diabetic retinopathy
   b. A patient who previously had a retinal vein occlusion in the eye that needs surgery
   c. A patient with dry age-related macular degeneration
   d. A patient with an epiretinal membrane in the eye that needs surgery

3. **What measures should be taken to optimally prevent the occurrence of cystoid macular oedema after cataract surgery:**
   a. Start with a personalised preoperative risk assessment
   b. Discontinue all glaucomatous eye drops at least 3 days prior to surgery
   c. Prevent complications and retained lens fragments
   d. Prescribe a topical corticosteroid and non-steroidal anti-inflammatory drug

4. **Treatment of pseudophakic cystoid macular oedema:**
   a. Is always needed, as it will never resolve spontaneously.
   b. Initially consists of corticosteroid and non-steroidal anti-inflammatory eye drops
   c. Will restore visual acuity, even in chronic cases
   d. Needs careful monitoring, because macular oedema may recur after cessation of treatment

PSEUDOPHAKIC CYSTOID MACULAR OEDEMA (PCME), also known as the Irvine-Gass syndrome, was first reported in 1953. Since then, its incidence has notably decreased because of improved surgical techniques. Incidence rates as high as 50–60% were reported after intracapsular cataract extraction (ICCE) in 1975, but gradually decreased to approximately 30% after extracapsular cataract extraction (ECCE), and further to 9% after phacoemulsification cataract surgery in 2003. **Currently, the incidence of PCME is estimated between 1–2%**, but incidence rates increase to 4–9% in patients with risk factors for developing PCME.

PCME usually occurs within 12 weeks after cataract surgery, with a peak incidence at 4–6 weeks postoperatively. Patients with PCME experience a reduced central visual acuity and reduced contrast sensitivity, and may complain of metamorphopsia.

1. Pathophysiology of PCME

PCME is the result of a postoperative inflammatory reaction. Manipulation during cataract surgery causes activation of phospholipase A2, which in turn deliberates arachidonic acid from cell membranes. Cyclo-oxygenase (COX) and 5-lipoxygenase catalyse the conversion of arachidonic acid to prostaglandins and leukotrienes. Most research on the pathogenesis of PCME has focused on the role of prostaglandins, but other inflammatory mediators, such as vascular endothelial growth factor (VEGF) and various cytokines have recently generated wide interest. Inflammatory mediators diffuse to the posterior segment of the eye and cause vasodilatation, increased vascular permeability, and disruption of the blood-aqueous and blood-retinal barrier (BRB). **PCME develops when transudate accumulates in the inner nuclear and outer plexiform layers of the retina**. Increased aqueous prostaglandin concentrations are also reported after femtosecond laser assisted cataract surgery (FLACS).

2. Risk factors for PCME

Prevention of PCME should ideally **start with a personalised preoperative risk assessment** for each patient. This risk assessment should be used to inform the patient about his postoperative risk of developing PCME, and it may influence pre- and postoperative anti-inflammatory treatment.

Diabetes mellitus is the best known risk factor for developing PCME, because of an impaired BRB. Large cohort studies have shown that the incidence of PCME is four times higher in diabetic as compared to nondiabetic patients, with an incidence rate of 4%. These studies have also shown a near linear trend between the severity of diabetic retinopathy (DR) and the risk of developing CME postoperatively. Nevertheless, it should be noted that even diabetic patients without any sign of DR have a significantly increased risk of developing PCME. A longer duration of DM and insulin dependence are additional risk factors. Previous panretinal photocoagulation (PRP) could not reduce the risk of developing PCME.

Retinal vein occlusion (RVO) is the second major risk factor for developing PCME, especially in patients who previously required treatment for RVO-associated CME. Other important risk

factors include an epiretinal membrane (ERM), macular hole, uveitis, and previous development of PCME in the fellow eye. Moreover, complicated cataract surgery and higher peroperative cumulative dissipated phaco energy levels increase the risk of developing PCME. Dry age-related macular degeneration (AMD), glaucoma, retinitis pigmentosa, status of the posterior vitreous membrane and high myopia were not identified as significant risk factors, nor were systemic factors such as hypertension and ischemic heart disease.

3. Diagnosis of PCME

Although the optimal definition of PCME remains to be identified, it is generally known that optical coherence tomography (OCT) is the most sensitive method to detect it. As CME is a hallmark of various retinal diseases, not all CME after cataract surgery should be named PCME. **Especially in case of chronic CME, it is crucial to determine its etiology**, becausetreatment strategies must be adjusted to the pathogenesis of the oedema. It has been shown that ophthalmologists are unable to differentiate PCME from other causes of CME based on the fundoscopic appearance alone. Historically, fluorescein angiography was used to differentiate DME from PCME, because PCME is characterised by disc oedema on fluorescein angiography. In recent years, however, OCT has become the preferred method to detect CME and to differentiate PCME from other causes of CME. The former is characterised by central and symmetric macular oedema, typically located in the central 1 mm of the macula. Central cystoid changes are confined to the inner nuclear and outer plexiform layers, and subretinal fluid is often seen.

4. Prevention of PCME

For many years, anti-inflammatory drugs have been used to prevent the occurrence of PCME, but the absence of solid evidence-based recommendations created remarkable differences between clinical guidelines of leading authorities. Recent systematic reviews and meta-analyses indicated that topical non-steroidal anti-inflammatory drugs (NSAIDs), with or without topical corticosteroids, are more effective in prevention of PCME than corticosteroids alone. Moreover, studies have shown that the incidence of PCME can be reduced if topical anti-inflammatory treatment is started 1–3 days preoperatively.

The European Society of Cataract and Refractive Surgeons (ESCRS) recently published its results of the PREvention of Macular EDema after cataract surgery (PREMED) study, a large European randomized controlled clinical trial comparing the efficacy of a topical NSAID (bromfenac 0.09%), topical corticosteroid (dexamethasone 0.1%), and their combination in nondiabetic patients. The PREMED study report 1 found that **the incidence of clinically significant macular oedema (CSME) was lowest in patients treated with a topical corticosteroid and NSAID**. The incidence rates of developing CSME within 12 weeks postoperatively were 3.6% in the NSAID group, 5.1% in the corticosteroid group, and 1.5% in the combination treatment group. Pairwise comparison showed that the odds of developing CME were significantly higher in the corticosteroid group as compared to the combination treatment group. However, statistical analyses could not identify a significant difference between the NSAID and combination treatment groups.

Currently no high-quality evidence exists to prefer bromfenac 0.09% over other NSAIDs such as diclofenac, ketorolac, or nepafenac. At this point, the optimal topical NSAID should be chosen based on patient satisfaction, frequency of drug administration, ocular comfort, and societal costs involved with various preparations. Dropless cataract surgery is a major current research focus that aims to improve these factors by eliminating the need for postoperative eye drops in cataract surgery. Studies on dropless cataract surgery investigate the efficacy of intra- and periocular corticosteroid and/or NSAID injections as an alternative to postoperative eye drops, to prevent PCME and to improve patient satisfaction and societal costs.

A combination of topical NSAIDs and corticosteroids is generally used to prevent the PCME in high risk patients. Only afew studies investigated the optimal prevention on PCME in patients with an increased risk because of an ERM, macular hole, or uveitis. Since DM is a well-known risk factor for developing PCME, the PREMED study report 2 investigated the efficacy of an additional subconjunctival injection of 40 mg triamcinolone acetonide (TA) at the end of cataract surgery. A **subconjunctival TA injection significantly reduced the risk of developing PCME in diabetic patients**. Nevertheless, it is not advisable to use subconjunctival TA in all diabetic patients undergoing cataract surgery, given an increased risk of developing an high intraocular pressure (IOP). At this point, a personalised risk assessment should be made for each patient, carefully weighing the risk of developing visual impairment from CME against the risk of developing a high IOP and the probability of developing glaucomatous visual field loss. In this study, an intravitreal anti-VEGF injection did not reduce the risk of developing PCME in diabetics without DR.

5. Treatment of PCME

Although acute PCME resolves spontaneously in most cases, chronic PCME may cause anatomic alterations and sustained visual impairment. This is the main reason for immediate attention and appropriate treatment of PCME. Previous research showed that adequate treatment of CME will lead to visual acuity improvement only as long as septae of healthy tissue persist between the cystic spaces, and if the photoreceptor inner segment/outer segment layer, or ellipsoid zone, remains intact on OCT. It is widely accepted that final visual acuity decreases if CME exists for a long period of time, but it remains unknown what the optimal timing for initiation of treatment is. Previous studies indicate that topical NSAIDs, with or without topical corticosteroids, improve visual acuity in patients with PCME. Further research is needed to investigate the efficacy of oral NSAIDs, acetazolamide, anti-VEGF, and intra- and periocular corticosteroid injections.

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Answers to MCQs on page 154

1. a. *False*
   b. *True*
   c. *False*
   d. *False*

2. a. *True*
   b. *True*
   c. *False*
   d. *True*

3. a. *True*
   b. *False*
   c. *True*
   d. *True*

4. a. *False*
   b. *True*
   c. *False*
   d. *True*

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Pre- and postoperative prevention of endophthalmitis

Ewa MRUKWA KOMINEK - Poland

MCQs

1. **The presenting features of endophthalmitis include:**
   a. decreased visual acuity and increased pain
   b. haziness of the cornea because of oedema
   c. decreased cellularity in the anterior chamber
   d. increased cellularity in the vitreous

2. **Preoperative prophylaxis of endophthalmitis includes:**
   a. povidone iodine disinfection
   b. topically administrated antibiotics
   c. systemic steroid administration
   d. irrigating water with cefuroxime

3. **Regarding proper prophylaxis of endophthalmitis:**
   a. 5% povidone-iodine for 3 minutes significantly reduced microorganisms
   b. 10% povidone-iodine did not reduce gram-negative cocci
   c. 10% povidone-iodine must be applied a minimum of 10 minutes for significant reduction of microorganisms
   d. Povidone-iodine is recommended in 10% solution for skin and in 5% solution for conjunctival application

4. **For prevention of postoperative endophthalmitis, the ESCRS study suggested:**
   a. Topical levofloxacin eyedrops 4 times daily postoperatively for 6 days
   b. Intracameral injection of 1 mg vancomycin at the end of surgery
   c. Intracameral injection of 1 mg cefuroxime at the end of surgery
   d. Intracameral injection of 1 mg gentamycine at the end of surgery

CATARACT SURGERY remains one of the most commonly performed surgeries around the world. Endophthalmitis following cataract surgery is a destructive complication, thus it is very important to prevent it. Its incidence is reported to be 0.023%–0.26%, depending on the report. Significant money is spent to find the best way of prevention. Commonly known risk factors include older age, diabetes, posterior capsular tear, necessity of suturing during surgery and, although controversial, a silicone intraocular lens (IOL), among others.

Presenting features include decreased visual acuity, pain, swelling and redness of the eyelids, redness of the conjunctiva, haziness of the cornea due to oedema, and increased cellularity of fluid in the anterior chamber with or without a hypopyon. Observed signs of infection and inflammation of the retina and vitreous are seen.

The microorganisms most commonly identified in postoperative endophthalmitis vary with regions of the world. The most common causative bacteria are Gram-positive species, such as coagulase-negative *Staphylococcus* (CoNS), *Streptococcus viridans*, and *Staphylococcus aureus*. Gram-negative organisms such as *Pseudomonas* or *Haemophilus* are less common; fungi and *Nocardia* are rare.

Endophthalmitis is a rare infection and it often results in significant long-term morbidity, even when treated appropriately. Approximately 50% of people do not regain vision of 0.5 (20/40) or better despite treatment, and often nearly one third has a visual acuity worse than 0.1 (20/200) after treatment. Endophthalmitis cannot be completely prevented but certain steps may significantly reduce its incidence. The severity and clinical course of postoperative endophthalmitis is related to the virulence and inoculum of the infecting bacteria, as well as to the time to diagnosis and the immune status of the patient.

1. Preoperative prophylaxis

The basis for the analysis and legitimacy of use of perioperative prophylaxis was the Swedish National Cataract Register. Preoperative prophylaxis includes: povidone iodine disinfection, application of topical antibiotic, and systemic administration (in special cases). In addition, to standard sterile techniques, sequestration of the lids and eyelashes by proper draping and antisepsis of the operative field with 5% povidone-iodine are common.

An antiseptic that is used for disinfecting skin of patients and hands of healthcare workers is povidone iodine. A very important feature is that it has minimal toxicity but produces powerful antimicrobial effect after only one minute of skin contact. This effect is attributed to the release of free iodine and it persists for at least one hour. Povidone iodine is recommended in 10% solution for skin and 5% solution for conjunctival application. Ideally, it should dry after skin preparation and the conjunctival cul-de-sac should not be irrigated before one minute contact time. It is contraindicated in people with iodine allergy and hyperthyroid disease. Use of 5% povidone iodine for 3 minutes resulted in a statistically significant reduction in percentage of culture-positive swabs (87% vs. 30%, $p<0.001$), mean number of bacterial species (0.96 vs 0.30, $p<0.001$), and growth of CoNS (heavy: 30% vs. 0%, moderate: 23% vs. 6%, light: 47% vs. 94%, $p=0.004$).

Do not forget that all instruments for surgery should be sterile. Limitation to single-use is even more important, as incidents have occurred where instruments were not washed properly prior to sterilisation, which may itself have been faulty. Single-use of tubing and other equipments that become wet during surgery is always preferable, if cost allows. Bottles of solution, such as balanced salt solution, should never be kept or used for more than one operating session.

2. Perioperative prophylaxis

Publications exist from numerous large retrospective studies and the multicenter randomised controlled trial sponsored by the European Society of Cataract and Refractive Surgeons (ESCRS) that supports the efficacy of intracameral (IC) cefuroxime. The use of intraocular antibiotic prophylaxis at cataract surgery increased following publication of these studies. According to the American Society of Cataract and Refractive Surgery (ASCRS), the percentage of surgeons using routine intraocular antibiotic prophylaxis increased from 30% in 2007 to 50% in 2014.Antibiotic prophylaxis is a common preventive measure. The antibiotic agents used vary widely (e.g., fluoroquinolones, aminoglycosides, cephalosporins, chloramphenicol) as do administration routes (topical, intraocular, subconjunctival, oral), and the timing (preoperative, intraoperative, perioperative, postoperative).

The ESCRS study evaluated effects of an intracameral injection of cefuroxime 1 mg at the end of the surgery, and compared postoperative endophthalmitis rates with other study groups that included perioperative antibiotic drops, and controls. All 4 study groups received standard preoperative povidone iodine, as well as topical levofloxacin drops 4 times daily for 6 days postoperatively. The group that received only these basic treatments was considered the "control" group, because ethical principles mandated this as a "minimum treatment" group rather than an non-treated control. The variables were 1) the intracameral injection of 1 mg cefuroxime at the end of surgery, and 2) the administration of an intensive pulsed dose regimen of 3 drops levofloxacin, each drop separated by 5 minutes, also given at the end of surgery along with 2 drops given preoperatively 30 minutes apart (at 30 and 60 minutes before surgery). The study design permitted cross-comparisons of the 4 groups. The endpoint of the study was infectious endophthalmitis, whether proven or presumed.

The ESCRS study suggested administration of intracameral cefuroxime (1.0 mg in 0.1 ml) at the time of cataract surgery for prevention of postoperative endophthalmitis. Cefuroxime is a second-generation cephalosporin that is active against Gram-positive cocci. The ESCRS study showed a nearly 5-fold reduction of endophthalmitis rate. The drug is now available for commercial use (Aprokam®, Thea) and it is increasingly used both in Europe (where the drug is approved) and in the United States (off-label use).

Moxifloxacin is a fourth-generation fluoroquinolone that is active against Gram-positive cocci, including MRSA, and against selective Gram-negative bacilli. In some countries (e.g., India), moxifloxacin is registered for perioperative prophylaxis.

Discussion is ongoing whether routine use of an intracameral antibiotic reduces or eliminates the need for a postoperative topical antibiotic. Some authors consider using an intracameral antibiotic injection only in high-risk patients (i.e., posterior capsule break, anterior vitrectomy, prolonged surgery, difficult surgery with excessive iris manipulation, corneal surface disorders, elderly individuals, and immunocompromised individuals). When prophylaxis with intracameral injection of 1 mg cefuroxime before cataract surgery was initiated, a reduction of postoperative endophthalmitis rates was noticed.

3. Treatment

For treatment of bacterial endophthalmitis after cataract surgery, two antibiotics are currently recommended: vancomycin (1.0 mg in 0.1 ml) that acts against Gram-positive cocci and ceftazidime (2.25 mg in 0.1 ml) that acts against Gram-negative bacilli (the Endophthalmitis Vitrectomy Study [EVS]). Vancomycin is a glycopeptide that inhibits the synthesis of the precursor units of bacterial cell wall and inhibits the RNA synthesis. It is highly effective against Gram-positive but essentially ineffective against Gram-negative bacteria. This antibiotic should be reserved for cases of resistant Gram-positive strains, such as methicillin-resistant *Staphylococcus aureus* (MRSA). It should not be used casually or for widespread prophylaxis, although intracameral use is reasonable in MRSA carriers who require cataract surgery. Gentamicin has activity against many Gram-negative strains, notably *P. aeruginosa*, and also against some *Staphylococci*, but it has poor activity against *P. acnes* and *Streptococci* (the latter being important, virulent, and toxin producing strains among endophthalmitis isolates). Ceftazidime is a third-generation cephalosporin that inhibits peptide crosslinking of polysaccharide chains of peptidoglycan and affects the cell wall synthesis. It is active against many Gram-negative organisms including P. *aeruginosa*. The Vitrectomy Study Group stated that there was no statistical difference in final visual acuity or media clarity between patients who received systemic antibiotics or not during endophtalmitis management.

4. Postoperative prophylaxis

Antibiotics could be administered immediately (within an hour) preoperatively or postoperatively as a single or repeated applications. Some suggestions exist regarding postoperative fourth generation fluorocinolon administration for 6 days after cataract surgery. The use of a systemic antibiotic is without justification for prophylaxis in a standard surgery. It may be justified only in high risk patients (e..,g rosacea) in extremely special situations.

5. Summary

Three publications significantly influenced our current thinking of reduction and management of post-cataract surgery endophthalmitis:

- Speaker's and Menikoff's study on povidone iodine preparation of the eye
- Endophthalmitis Vitrectomy Study (EVS) guidelines for infective endophthalmitis
- ESCRS study on application of intracameral cefuroxime for prevention of endophthalmitis

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Pre- and postoperative prevention of endophthalmitis

MRUKWA KOMINEK E - Poland

Many prophylaxis strategies illustrate the wide variety of guidelines followed around the world. This variability may be related to economic factors, the availability of certain antibiotics, local standards of care, and surgeon preferences. We should remember that predominant ocular flora and bacterial resistance may differ in different locations in the world. Prophylaxis patterns still change as ongoing studies report data on different approaches.

RECOMMENDED READING

Recent

1. Haripriya A, Baam ZR, Chang DF.. Endophthalmitis prophylaxis for cataract surgery. Asia-Pac J Ophthalmol. 2017;6:324–9.
2. Chang DF, Braga-Mele R, Henderson BA, et al. Antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery: results of the 2014 ASCRS member survey. J Cataract Refract Surg. 2015;41:300-5.
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Classic

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10. Barry P, Gardner S, Cordoves L. ESCRS Guidelines for Prevention and Treatment of Endophthalmitis Following Cataract Surgery: Data, Dilemmas and Conclusions, 2013
11. Behndig A, Cochener B, Guell JL. Endophthalmitis prophylaxis in cataract surgery: overview of current practice patterns in 9 European countries. J Cataract Refract Surg. 2013;39:1421-31
12. Endophthalmitis Vitrectomy Study Group. Results of the Endophthalmitis Vitrectomy Study. A randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. Arch Ophthalmol 1995;113:1479-96.

Answers to MCQs on page 160

1. a. *True*
   b. *True*
   c. *False*
   d. *True*

2. a. *True*
   b. *True*
   c. *False*
   d. *False*

3. a. *True*
   b. *False*
   c. *False*
   d. *True*

4. a. *True*
   b. *False*
   c. *True*
   d. *False*

27

Cataract and uveitis

Luc VAN OS - Belgium

MCQs

1. **Regarding pre-operative planning in face of uveitis:**
   a. The preferred minimum interval between the last activity of inflammation and cataract surgery is 3 months
   b. The inflammation-free interval has to be followed by a treatment-free interval
   c. A work-up to reveal an underlying aetiology has to be done before performing cataract surgery
   d. Polymethylmetacrylate (PMMA) is the preferred biomaterial for IOL

2. **Regarding cataract and uveitis:**
   a. In juvenile inflammatory arthritis (JIA), treatment with ≤ 3 drops daily topical steroids markedly decreases the risk of cataract as compared to higher dosages
   b. Patients with cataract and uveitis are generally younger than routine cataract patients
   c. Patients with uveitis have less zonular fragility than routine age-related cataract patients
   d. Cataract surgery in a patient with uveitis should be performed as soon as possible

3. **Regarding surgical technique in a uveitis patient:**
   a. Sphincterotomies are a good way of achieving mydriasis
   b. A small rhexis carries a higher risk of postoperative capsular phimosis
   c. A clear corneal incision is preferable in patients with scleritis
   d. Intravitreal triamcinolone can be used at the end of surgery to lower the postoperative inflammatory response

4. **Regarding cataract surgery in a uveitis patient:**
   a. In case of steroid-induced ocular hypertension ('steroid responder'), steroids should be stopped and replaced by immunosuppressant (e.g., methotrexate)
   b. Nd:YAG-capsulotomy is a risk-free procedure
   c. In case of lower than expected visual outcome, an optical coherence tomography (OCT) scan should be done to detect cystoid macular oedema (CME)
   d. Inflammatory cell deposits on the intraocular lens (IOL)must be surgically removed to improve vision

SEVERAL REASONS are known why patients with uveitis are at a higher risk for cataract and why they develop cataract earlier in life. On one hand, the inflammation itself will cause cataract, but on the other hand the treatment with steroids will also result in lens opacities. Chronic uveitis induces cataract more frequently than acute uveitis. This is especially true in patients who have an asymptomatic uveitis, such as children with juvenile inflammatory arthritis (JIA)-associated uveitis and patients with Fuchs' heterochromic uveitis. The induction of cataract by corticosteroids is dose-dependent and occurs more often with high doses. Any route of administration, however, can cause a cataract: eyedrops, periocular, intraocular, and systemic steroids alike. It is important to bear in mind that cataract formation can also be minimised by avoiding overdosage of steroids and earlier administration of immunosuppressants or biologicals. The exact mechanism that results in the formation of cataract in uveitis is not yet fully known.

On the other hand, patients who did not have uveitis earlier can develop uveitis because of an overly mature cataract or a damaged lens capsule. Lens proteins start to leak through the capsule and will induce an inflammatory response (phacoantigenic uveitis). In these cases, removing the lens will remove the primary reason for the uveitis.

The outcome of cataract surgery in patients with uveitis is worse than in routine surgeries. Important causes for a suboptimal postoperative outcomes are cystoid macular oedema (CME), posterior capsule opacification (PCO), flare-up of the uveitis, glaucoma, and damage to the retina because of inflammation and hypotony. Reliable data concerning cataract surgery in patients with uveitis are difficult to find. Sample sizes are usually rather small and very heterogeneous, and surgery can be performed in many different ways and with many different implants. This makes it very difficult to draw solid conclusions from these studies. However, there are some reliable data available and some concepts that are generally accepted:

- Cataract surgery in patients with previous uveitis can never be considered as 'routine' surgery. The risk of complications is incresed, both per-and postoperatively, and patients often need extra care and attention in the perioperative period.
- The surgery needs careful planning. **An interval of 3 months between the last period of activity and the surgery is generally accepted as a minimum requirement.**

When confronted with a uveitis patient with a cataract, it is necessary to think and plan.

1. Preoperative considerations

Aetiology of the inflammation

- Some aetiologies have a better prognosis than others (e.g., Fuchs' heterochromic uveitis usually has a good prognosis, whereas Behçet's disease often has a poor visual outcome).
- If an infectious cause is found, proper treatment should be administered before planning cataract surgery. Prophylactic treatment can be indicated to prevent postoperative flare-ups in cases of *Herpes simplex*, varicella zoster, and *Toxoplasma*.

- The history of the uveitis is also important: an eye that has had one course of easily controlled uveitis 20 years ago is less likely to cause problems than an eye that needs considerable doses of treatment to attain an acceptable level of inflammation.
- Making sure a proper work-up to reveal the aetiology of inflammation has been performed is mandatory before proceeding with surgery.

Control of inflammation

- It is of paramount importance that the uveitis is adequately controlled before starting surgery. A good perioperative control of inflammation is the key to avoid complications as far as possible, and it offers the best chance for a good visual outcome. To achieve good control, both topical (corticosteroids, non-steroidal anti-inflammatory drugs [NSAIDs]), local (subconjunctival, sub-Tenon, intravitreal corticosteroids) and systemic treatments (corticosteroids, immunosuppressants, biologicals) can be used, according to the severity of uveitis.
- In case of uveitis related to *Herpes simplex* or varicella zoster: start aciclovir or valacicovir at least one week prior to surgery to prevent a flare-up.
- In case of *Toxoplasma* uveitis, consider antibiotic prophylaxis to prevent a flare-up, depending on the severity and extent of the disease.
- In standard cases: start topical steroids and NSAIDs 4 times daily at least one week before surgery, with a higher dosage of steroids depending on the history of the patient. In case of more serious inflammation, consider a short course of oral steroids starting 1 to 2 weeks before surgery; the dose can be tapered after surgery.

Extent of the inflammation

- Be sure you have fully examined the eye; do not let posterior segment involvement go unnoticed.

Identify complicating factors

- Synechiae, both anterior and posterior, can complicate the surgery and should be addressed peroperatively.
- Band keratopathy can be removed with EDTA or phototherapeutic keratectomy (PTK), but remember to repeat your keratometry before calculating the IOL.
- Cyclitic membranes can exert traction on the ciliary body and result in ciliary detachment, predisposing to postoperative hypotonia. A preoperative ultrasound biomicroscopy (UBM) provides information on the condition of the ciliary body
- A dense vitritis or extensive retinal scarring can influence the red reflex during surgery
- Zonulolysis is more frequent in patients with uveitis. Look for signs of phakodonesis and prepare to use a capsular tension ring when necessary.
- Take care of patient positioning in ankylosing spondylitis.
- Take the precautions and be sure that the necessary instruments and implants are available.

IOL selection

- In case of very severe inflammation, leaving the patient aphakic can be the safest option.
- No hard evidence in available regarding the best biomaterial to use (see 'Recommended reading'): hydrophobic acrylate (less uveal biocompatibility, more giant cell deposits); hydrophilic acrylate (better uveal biocompatibility, but possibly more PCO because of less capsular biocompatibility); heparin-coated polymethylmetacrylate (PMMA); or silicone (more PCO, not compatible with silicon oil).
- A standard in-the-bag design can be used, preferably with a sharp optic edge and a narrow haptic-optic junction. Other lens designs such as bag-in-the-lens, iris fixated lenses and scleral sutured IOLs can also be used.
- Be mindful that positioning a lens in the sulcus or the anterior chamber might increase the postoperative inflammatory response.
- Patients with uveitis cannot be considered universally good candidates for IOL types with complex optics. Increased incidence of macular problems such as recurrent macular oedema and less stable IOL position over time exist because of more active proliferation of lens epithelial cells. You do not want to do more surgery than is necessary in a uveitis eye, so an IOL exchange is better prevented from the start.

Anaesthesia

- Consider which kind of anaesthesia you are going to use. In a case that is expected to be straightforward, topical anaesthesia can suffice, but in a complex case both the surgeon and the patient may be more at ease with general anaesthesia.

Patient expectations

- Try to assess the contribution of lens opacities to total visual impairment. If other factors (such as vitreous haze) seem more important, cataract surgery may not result in a significant improvement of visual acuity.
- Sometimes cataract surgery is mainly performed to enable a better visualisation of the fundus and the optic disc. In these cases in particular, the functional result after cataract surgery can be disappointing.
- In case of lens-induced (phacoantigenic) uveitis, counsel the patient that the main goal is to eliminate the source of inflammation - vision improvement is not always possible if other comorbities are present.
- It is also important to stress to the patient that additional surgeries might be needed, such as vitrectomy (e.g., in the presence of an epiretinal membrane or glaucoma).

2. Peroperative considerations

Wound construction

- Do not use a scleral tunnel in after a history of scleritis.
- Avoid making an incision through a vascularised scar in the cornea.
- Beware of possible future glaucoma surgery: a temporal approach can make the glaucoma surgeon's life easier. A clear corneal incision can be preferred for the same reason.

Strive for good pupillary dilation

- Use preoperative topical mydriatics.
- Use intracameral mydriatics at the beginning of surgery.
- Release posterior synechiae. This can be done by viscodissection and with the help of a Lester hook, or a similar instrument.
- Remove pupillary membranes (but be careful, they can extend further than you would think at first sight).
- Use additional tools such as pupillary expanders or iris hooks, if necessary.
- On the other hand, limit unnecessary iris manipulation because this will contribute to postoperative inflammation and may result in bleeding.

Create a properly sized capsulorhexis

- If the rhexis is too small, the risk of developing capsular phimosis is higher.
- Consider using a device such as a ring caliper or projection caliper through the microscope.
- Be careful as the younger the patient, the more elastic the capsule will be. Regrasping the rhexis edge will help in exerting better control of the rhexis.
- Because of longstanding inflammation, the capsule might not behave the way you expect it to. Be careful and be prepared to regrasp more often than you would in a routine case.
- Use vision blue when visualisation is limited.

Remove the lens

- Lenses are often rather soft because the patients are usually younger than other patients.
- Zonules can be more fragile, be prepared to use a capsular tension ring.

Additional anti-inflammatory treatment

- Peroperative iv Solu-Medrol® can be administered in severe cases
- Peroperative intracameral, subconjunctival or intravitreal steroids can be used as well.

3. Postoperative considerations

In the immediate postoperative period

- Carefully monitor the inflammation.
- These patients often need more topical corticosteroids than routine patients.
- Consider using a mydriatic drop postoperatively.
- Increase systemic uveitis treatment when inflammation is difficult to control.
- CME is an important reason for suboptimal visual outcomes. Monitor patients with OCT and adapt the anti-inflammatory medications.
- Monitor the intraocular pressure. Add pressure lowering drops if necessary.
- In case of steroid responder, lower the corticosteroid dose only if the level of inflammation permits this.

On longer term

- PCO develops earlier and more often in these patients, mostly on account of their younger age. Nd:YAG-laser capsulotomy can be performed, but this can also incite a flare-up of inflammation.
- Deposits on the lens can occur. These can be treated by intensifying the anti-inflammatory treatment, or in case of limited effect on vision, can be followed up without treatment.

4. Take home messages

- Careful preoperative planning is very important.
- Timing: at least 3 months of quiet inflammation.
- Precise assessment of possible complications.
- Plan peri-operative treatment according to the history of the patient and the aetiology and course of the uveitis.
- Careful postoperative follow-up is needed.
- Increase treatment if necessary.
- Communicate realistic goals to the patient and counsel them about the need for possible additional follow-up and interventions.

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2. Leung TG, Lindsley K, et al. Types of intraocular lenses for cataract surgery in eyes with uveitis. *Cochrane Database Syst Rev.* 2014;(3):CD007284.
3. Chan NS, Ti SE, et al. Decision-making and management of uveitic cataract. *Indian J Ophthalmol.* 2017;65:1329-39.

Answers to MCQs on page 167

1. a. *True*
   b. *False*
   c. *True*
   d. *False*

2. a. *True*
   b. *True*
   c. *False*
   d. *False*

3. a. *False*
   b. *True*
   c. *True*
   d. *True*

4. a. *False*
   b. *False*
   c. *True*
   d. *False*

RT

Round table: My job is difficult!
Case 1 - Laura WIELDERS

A 69-year-old woman presents to you with bilateral cataract. She complaints of slowly progressing blurry vision and glare. Her best corrected visual acuity decreased to 0.5 (20/40), OD, and 0.7 (20/30), OS, respectively. Her medical history includes a transient ischemic attack, hypertension, and hypercholesterolemia, for which she uses appropriate medications. She has never visited an ophthalmologist before, but she reports good visual acuity in both eyes in the past.

- **What measurements can be taken to minimise her risk of developing cystoid macular oedema (CME) after cataract surgery?**
- **What preventive treatment would you prescribe?**
- **When and how do you follow-up this patient after cataract surgery?**

RT

Round table: My job is difficult!
Case 2 - Laura WIELDERS

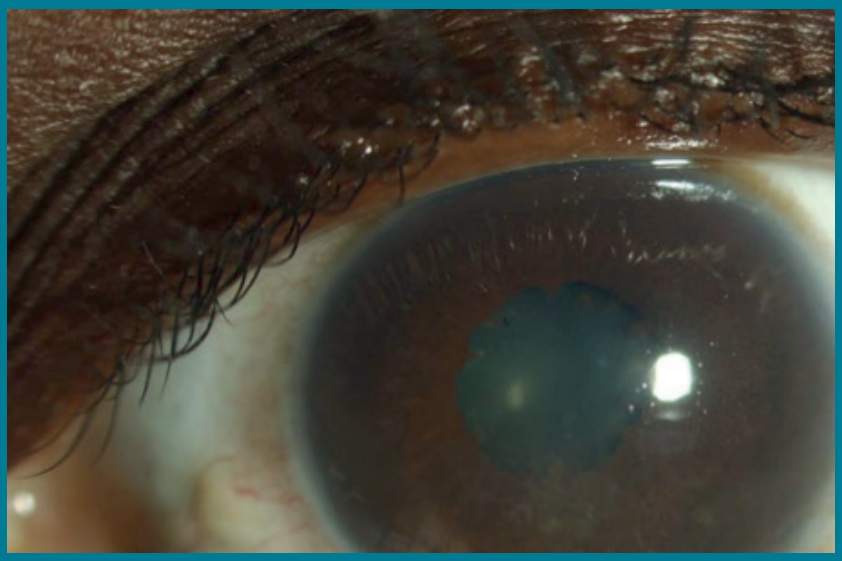
A 71-year-old-man presents with bilateral cataracts. He has visited your practice for many years and has been diagnosed with diabetic macular oedema (DME), OS, for which he has received several intravitreal injections of bevacizumab (Avastin®). Six years ago, he received adequate panretinal photocoagulation in both eyes.

For the past 6 months, he did not need any additional treatment for DME and his optical coherence tomography (OCT) images are stable. Today, he complaints of blurry vision and glare in both eyes. His best corrected visual acuity has decreased to 0.5 (20/40), OS, and 0.6 (20/63), OS, respectively, and his ophthalmic examination shows visually significant bilateral cataract.

- **Do you have any further questions with respect to his medical history?**
- **What measurements can be taken to minimise his risk of developing pseudophakic cystic macular oedema (CME) after cataract surgery?**
- **When and how do you follow-up this patient after cataract surgery?**

RT

Round table: My job is difficult!
Case 1 - Luc VAN OS

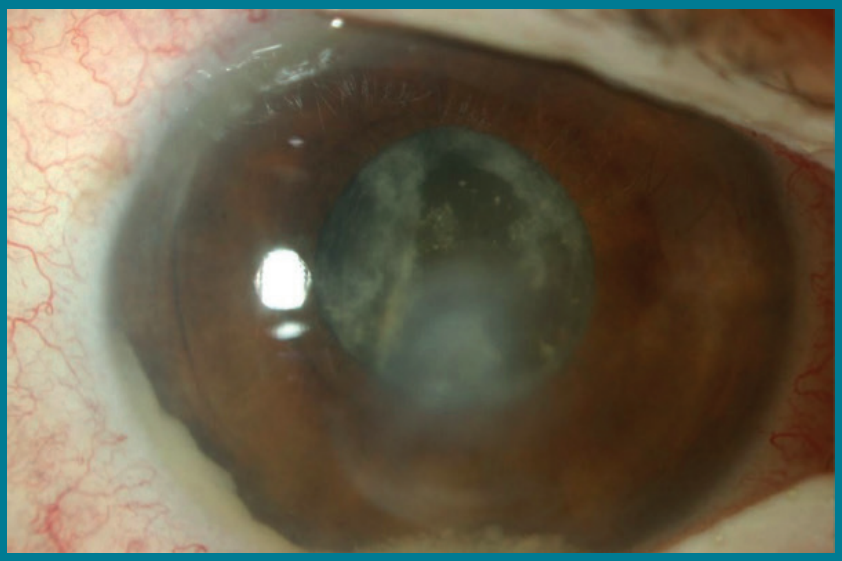


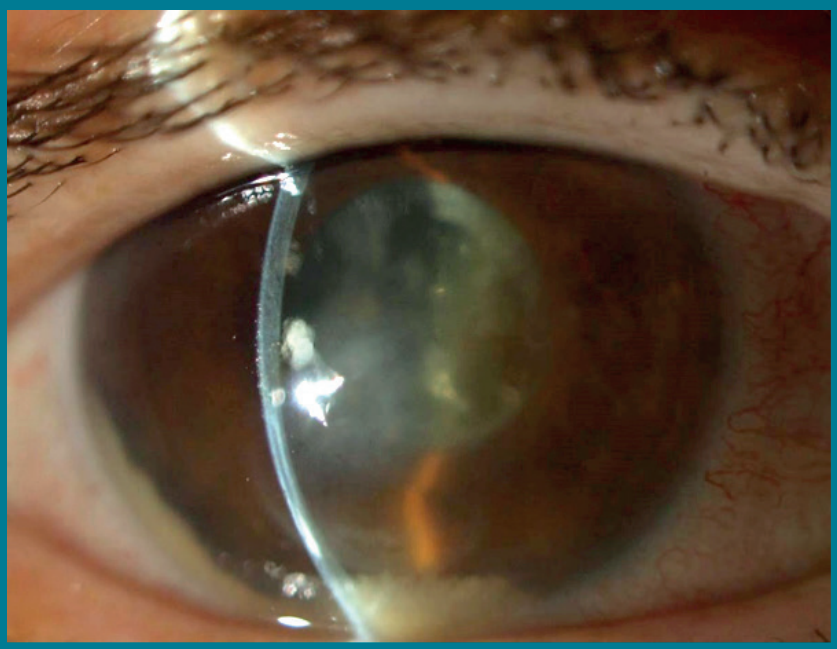
A 30-year-old man is referred to your clinic because of recurrent uveitis in the left eye, now persisting since 6 months. Since a few weeks, the right eye has started to be inflamed as well. The best correcetd visual acuity (BCVA) is 1.2 (25/20), OD, and 0.3 (20/60), OS.

- What is your further work-up?
- Which treatment will you consider? Medical? Surgical?

RT

Round table: My job is difficult!
Case 2 - Luc VAN OS





An 83-year-old lady comes to the emergency department complaining of pain and photophobia in her right eye. The visual acuity is poor, but it has been like that for a long time.

- What is your further work-up?
- Which treatment will you consider? Medical? Surgical?