CURRENT CHALLENGES
AND
CONCEPTS IN THE MANAGEMENT OF GLAUCOMA
<table>
<thead>
<tr>
<th>Abnormal</th>
<th>Normal</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP</td>
<td>Disc and VF</td>
<td>?? Glaucoma</td>
<td>+</td>
</tr>
<tr>
<td>IOP and Disc</td>
<td>VF</td>
<td>Glaucoma</td>
<td>+</td>
</tr>
<tr>
<td>IOP and VF</td>
<td>Disc</td>
<td>Glaucoma</td>
<td>+</td>
</tr>
<tr>
<td>Disc and VF</td>
<td>IOP</td>
<td>Wait for progression</td>
<td>+/-</td>
</tr>
</tbody>
</table>
A NEW BEGINNING TO AN OLD DISEASE

O.H.T.

INFLAMMATION

NO

YES

SEC INFLAMMATORY GLAUCOMA

Glaucoma Suspect

RAISED IOP

Established Glaucoma

FIELD CHANGES

NEUROLOGICAL LOCAL RETINAL LESIONS

Disc

Physiological Congenital Vascular

Normotensive Glaucoma
DEFINITION

“Multifactorial optic neuropathy” in which there is a characteristic acquired loss of optic nerve fibres.

AAO 1996
PRESSURE SENSITIVE OPTIC NEUROPATHY
RISK FACTORS

- I.O.P. DEPENDENT
- NON I.O.P. DEPENDENT

- Increasing age
- Family History
- African Heritage
- Hypertension
- Vascular & Endocrine disorders
- Myopia
- Diabetes
Newly identified Risk factors

- Systemic hypotension.
- Nocturnal hypotension.
- Cardiovascular disease.
- Vasospasm. (Migraine. Raynoud disease).
- Disregulation.
- Sleep apnea.
- Auto immune disease.
- Hemorrhagic abnormalities.
- Cerebral microvascular ischemia.
Current Concepts

Glaucoma pathology
Theories

- Mechanical theory.
- Vascular theory.
- Combined mechanism.
Glaucoma Pathogenesis.

- Interruption of axoplasmic flow at lamina cribrosa.
- Elastin present at L.C. Protects it from backward excavation.
- I.O.P. Damages it and facilitates backward stretching leading to poor capillary blood flow which inhibits axonal transport.
- In NTG, defective elastin is seen, low vasular flow may also contribute.
GLAUCOMA: OPTIC NERVE DAMAGE

Rise in IOP > 21 mm Hg

↓

Mechanical back pressure

↓

On the junction of optic nerve/retina

↓

Reduce the blood supply to the optic nerve (prolonged AVP time)

↓

Loss of blood supply (< in pOBF)

↓

Ischaemia

↓

RGC cell loss
A HYPOTHESIS FOR GANGLION CELL DEATH IN GLAUCOMA

Hypoxia to lamina cribrosa

Microcirculation in optic nerve head affected

Hypoxia to blood vessels

Hypoxia to astrocytes

Insult spread to all astrocytes in retina. Astrocytes electrically couple-spreading depression

Hypoxia to axons

Insult (lack of nutrients eventually affects all ganglion cell bodies

Release of glutamate and potassium

Release of glutamate

Released glutamate inactivated by Muller cell. These eventually become "overworked"

Muller cells no longer function normally so cannot inactivate "released" transmitters like glutamate and GABA

Glutamate / GABA eventually Deposited in vitreous

Glutamate and GABA receptors on ganglion cell overactivated and rate of death depends on numbers and type of receptors become "overworked"
**Retinal Ganglion Cell Destruction**

**Risk Factors**

- **Primary Insult**
  - Glutamate being released into surrounding medium
  - Toxic response in adjacent retinal ganglion cells (Secondary degeneration)

**Delivery of Neurotropins** (BDNF)

**Induction**

- Cells in the retina or to produce Neurotropins with gene therapy

**Ganglion Glutamate**

- Delivery of Neurotropins (BDNF)

**Excito toxicity**

- Blockade or receptor mediators

**Calcium**

- Activation of Nitric Oxide Synthetase

**Memantine**

- Block the Excito toxicity

**Calcium**

- Excessive levels of intra cellular

**Aminoguanidine**

- Blockade or receptor mediators

**Nitric Oxide Synthetase**

**Melatonin/Antioxidants**

- Scavenging of reactive Oxygen species

- Excess free radicals accumulation

**Death**

- Activation of catabolic enzymes (Apoptosis)
There is no POAG without vascular risk factors.

Ganglion cell apoptosis is increased by ischaemia.

Vascular disregulation makes the eye more sensitive to increased IOP or decreased blood pressure.

With normal auto regulation GON developed only if perfusion pressure is markedly decreased.

When disregulation occurred GON can occur without reduction in perfusion pressure.
Types of Neuronal death

- Necrotic.
- Apoptotic.
Mechanism of Retinal Ganglion cell death

- Neuroprotection with drawl due to retrograde axoplasmic transport block.
- Glutamate induced excitotoxicity.
- Free radical generation.
- Nitric oxide neurotoxicity.
- Apoptosis.
Steps Of Neuronal Death

- Axonal death.
- Death of injured neuron.
- Injury and death of previously intact neurons, through secondary degeneration.
Not all axons of O.N. Nor RGC die at the same time.

This occurs over a period of decades.

Groups of RGC similarly susceptible.

Field defects will not develop till 30% loss of axons.
Structure/Function in Glaucoma

% Loss

Time

VF

Disc

RNFL

This watermark does not appear in the registered version - http://www.clicktoconvert.com
Challenges in Diagnostic Tools

- Goldman appl.tonometry Vs central corneal thickness.
- SITA Vs SWAP / FDP.
- Estimation of RNF layer thickness.
- Measurement of ocular circulation.
Target of Glaucoma Therapy

• Preservation of visual function

• Maintenance of quality of life

• Affordable cost
Modes of Approach

- Lowering I.O.P.
- Increase out flow facility.
- Neuro protection.
- Vaso protection
Targets for Glaucoma Rx

1. Intraocular pressure
ELEVATED IOP

- Most important risk factor
- BUT still only a risk factor and not the disease itself
Aqueous Humor Dynamics
Aqueous Humor Dynamics

Glaucoma: not a disease of inflow; Normal fluctuations cause IOP spikes

Inflow

2-3 µL/min

1% min
Aqueous Humor Dynamics

Aqueous Outflow

1. Pressure insensitive
   (presumed uveoscleral)
2. Pressure sensitive
   (presumed trabecular)
Outflow Facility is Impaired in Glaucoma

• The cause of high steady-state IOP
• The cause of large diurnal IOP fluctuations

Glaucoma Management Percepts

- Quantify the damage
- Set an I.O.P. Goal
- Lower the I.O.P.
- Follow the course to establish that low IOP is maintained and damage is stationary
Patient Considerations

- Is the elevated pressure significant?
- Will the patient develop visual loss if untreated?
- Is treatment worth the risk of side effects?
Strongly RECOMMENDED For Treatment

- Poor reliability on visual field examination
- One eyed patient
- Poor compliance
- Patient whose optic nerve is difficult to visualize
- H/O of vascular occlusion
- OHT with IOP > 28 mmHg
- IOP progression is successive
Methods of IOP lowering

- Medications
- Laser
- Surgery
Managing IOP Dependent Risk Factors

- Decreasing aqueous formation
- Increasing outflow facility
- Increasing uveoscleral outflow
Medical Treatment

Aqueous Suppressors

Outflow Facilitators

**Produce less fluid**

- Iris
- Lens

Some medications reduce fluid secretion

**Drain more fluid**

- Iris
- Lens

Pupil contracts

Some medications open the trabecular meshwork, which allows fluid to drain more freely
Relationship Between IOP and Field Loss

- Pts with IOP > 30mm.Hg were over 38 times more likely to have glaucoma than with pts whose IOP is < 15mm.Hg.
- 4.7 times higher in patients with an IOP > 21mm.Hg.
- Odds of developing glaucoma were 2.8 times more in patients with IOP asymmetry between rt. And lt. Greater than 3mm.Hg.
Importance of lowering IOP

For every 1mm Hg drop in IOP, a 10% reduction in risk of glaucomatous progression is observed.

Reducing IOP in glaucoma patients limits disease progression & slows visual field loss.

Survey Of Ophthalmol 2003; 48 (Suppl 1)
Relationship between IOP & glaucomatous visual loss (Baltimore Eye Survey)

Risk of POAG at different IOP levels

Relative risk of POAG

IOP (mm Hg)

< 15 16-18 19-21 22-24 25-29 > 30

Eye 1996;10;295 -301
Survey Of Ophthalmol 2003, 48 (Suppl 1), S3-S7
Lower IOP Stabilizes Glaucomatous Damage

Percentage of Patients

<table>
<thead>
<tr>
<th>IOP (mm Hg)</th>
<th>12/13</th>
<th>14/15</th>
<th>15/17</th>
<th>16/19</th>
<th>20/21</th>
<th>25/23</th>
<th>24/25</th>
<th>26/26</th>
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</thead>
<tbody>
<tr>
<td>Glaucoma Stable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glaucoma Progressing</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>
Collaborative NTGS

- Treated: 80% survival, 20% progression
- No Rx: 60% survival, 40% progression
- NTG: 20% progression unrelated to IOP
How much should IOP be lowered
Individual susceptibility to IOP

6 months
Individual susceptibility to IOP

6 months
Target Pressure Range

“A range of IOP enough to limit progression of visual field loss to a rate that will preserve the patient visual function and maintain their individual patterns of daily living.”
Susceptibility to Damage By Pressure

(Hypothetical)

Rate of Ganglion Cell Death

IOP Risk Profile

Intraocular pressure
**Rationale of Therapy by Pressure Reduction**

- **Rate of Ganglion Cell Death**
  - Treated Pressure
  - Untreated Pressure

**Intraocular Pressure**

- Benefit of Therapy
Rationale of Therapy by Pressure Reduction

Rate of Ganglion Cell Death

No Benefit of Therapy in this Range

Threshold Pressure

Benefit of Therapy in this Range

Intraocular Pressure

Treated Pressure

Untreated Pressure

Treated Pressure

Untreated Pressure
Changing Susceptibility During Course of Glaucoma

Rate of Ganglion Cell Death

Early glaucoma

Late glaucoma

Benefit of Therapy

No Therapeutic Benefit

Treated Pressure

Untreated Pressure

Intraocular Pressure
Targets for Glaucoma Rx

1. Intraocular pressure
2. Facility of outflow
Facility of Outflow

- The only parameter that stabilizes IOP
- Abnormally low in glaucoma
- Accounts for large diurnal fluctuations in glaucoma
24-Hour IOP in Glaucoma and Normal Patients

Clock Time

IOP (mmHg)

WAKE

SLEEP

WAKE

Normal

Sitting

Supine

Glaucoma

Sitting

Supine

14
15
16
17
18
19
20
21
22
23
24
25
26
Aqueous Humor Dynamics

1. Pressure insensitive
   (presumed uveoscleral)
2. Pressure sensitive
   (presumed trabecular)
Importance of steady IOP.

- A diurnal variation of more than 11.8 mm Hg 88% develop further field loss, when compared to D.V <7.7 mm. With 57% loss.

- Large variation of IOP on multiple days found to be a significant risk factor for Glaucoma progression.

- Patients who have periodic or sporadic pressure spikes can lose visual field due to cumulative effects.
FACTORS CAUSING INCREASED RESISTANCE TO OUTFLOW

- Anatomical / Histopathological changes
- Altered Corticosteroid metabolism.
- Dysfunctional adrenergic control.
- Abnormal immunologic process.
- Oxidative damage of Trabecular meshwork.
CLASSIFICATION

- Inflow regulating Agents
  - Beta Blocker
    - Timolol
    - Betaxolol
    - Carteolol
  - CAIs
    - Dorzolamide
    - Brinzolamide
    - Acetazolamide

Reduces Aqueous Humor production
Outflow regulating agents (Increases drainage of Aq. Humor)

- Trabecular Outflow
  - Pilocarpine
  - Prostamides

- Uveo Scieral Outflow
  - Latanoprost
  - Prostamides

- Both
  - Alphagan
THERAPEUTIC AGENTS

SUMMARY

Non selective BBs

Selective BBs

Xalatan/Alphagan

Invisible / irreversible
Side effects

LOW Efficacy

High
THERAPEUTIC AGENTS
SUMMARY

- **Beta blockers**
  - (Non-Selective)
  - Xalatann

- **Selective Beta blockers**
  - Alphagan

- **High Efficacy**
- **Low Visible / Reversible Side effects**

- **Beta blockers (Non -Selective)**
- **Xalatann**
<table>
<thead>
<tr>
<th>Beta-Blockers</th>
<th>Inflow</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAI</td>
<td>Inflow</td>
</tr>
<tr>
<td>Alpha₂ Agonists</td>
<td>Inflow + US Outflow</td>
</tr>
<tr>
<td>Prostaglandins</td>
<td>US outflow + ?</td>
</tr>
<tr>
<td>Prostamides</td>
<td>US outflow + Increased</td>
</tr>
<tr>
<td>Cholinergics</td>
<td>Increased C</td>
</tr>
<tr>
<td>Adrenergics</td>
<td>Mixed</td>
</tr>
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</table>
# MEDICAL MANAGEMENT OF GLAUCOMA

<table>
<thead>
<tr>
<th>Aqueous Suppressors</th>
<th>Outflow facilitators</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Topical</strong></td>
<td><strong>Topical</strong></td>
</tr>
<tr>
<td>- β blockers</td>
<td>Cholinergics/ Miotics</td>
</tr>
<tr>
<td>- Timolol</td>
<td>- Pilocarpine</td>
</tr>
<tr>
<td>- Betaxolol</td>
<td></td>
</tr>
<tr>
<td>- Levobunolol</td>
<td></td>
</tr>
<tr>
<td>- α₂ agonists</td>
<td>Adrenergics</td>
</tr>
<tr>
<td>- Brimonidine</td>
<td>- Dipivefrin</td>
</tr>
<tr>
<td>Systemic CAIs</td>
<td>Prostaglandin analogues</td>
</tr>
<tr>
<td>CAIs (Carbonic Anhydrase Inhibitors)</td>
<td>- Latanoprost</td>
</tr>
<tr>
<td>- Acetazolamide Tablets</td>
<td>- Bimatoprost</td>
</tr>
</tbody>
</table>
Calculations (AAO Guidelines)

- **MILD DAMAGE (early or no field loss).**
  75-80% of IOP at which presenting damage occurs.

- **MODERATE DAMAGE (both hemi fields involved).**
  70-75% of IOP at which presenting damage occurs.

- **ADVANCED damage (fixation involved).**
  I.O.P. < 15mmhg.
ADJUSTMENTS

- **DOWNWARD**: For high risk factors
  - High myopia, family history
  - African, one eyed

- **UPWARD**: For mild damage in some patients
AAO Guidelines

- IN NTG 30% reduction in base line pressure.
- In OHT patients whose IOP is >30mm Hg with no signs of OD damage a target pressure low 20s with at least 20% reduction in baseline may be accepted.
Trial Medication Period

ASSESSMENT

- **Efficacy**
  IOP reduction during initial 2-3 weeks.
  Following with diurnal variability.

- **Safety**
  Ocular side effects
  Systemic side effects
  Acquiescence of primary care physician

- **Compliance**
  Technique of applying drops
  Use of medication schedule
  Rate of defaulting

- **Affordability**
## Guidelines For Follow Up

<table>
<thead>
<tr>
<th>Target IOP Achieved</th>
<th>Progress of damage</th>
<th>Duration of Control (months)</th>
<th>Follow up Interval (days)</th>
<th>ONH evaluation (months)</th>
<th>VF Evaluation (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
<td>NO</td>
<td>&lt;6</td>
<td>30-180</td>
<td>6-12</td>
<td>6-12</td>
</tr>
<tr>
<td>YES</td>
<td>NO</td>
<td>&gt;6</td>
<td>90-365</td>
<td>6-18</td>
<td>6-24</td>
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<tr>
<td>YES</td>
<td>YES</td>
<td>Not applicable</td>
<td>7-90</td>
<td>2-6</td>
<td>3-12</td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>Not applicable</td>
<td>7-90</td>
<td>2-6</td>
<td>3-12</td>
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<tr>
<td>NO</td>
<td>YES</td>
<td>Not applicable</td>
<td>1-30</td>
<td>1-6</td>
<td>3-12</td>
</tr>
</tbody>
</table>
Therapeutic Challenges

- Anti glaucoma treatment in pregnancy and lactation.
- Tailoring the treatment to the patient.
- Switching the therapy.
- First line of therapy.
- Improving compliance.
Guidelines of AAO

- Hypotensive lipid drugs as first line.
- Non-selective B blockers should not be used in NTG.
- Switching over to another drug, in the same class is recommended if there is no adequate response to initial therapy. If no response adjunctive therapy is advised.
Bimatoprost: Mechanism

 Increased outflow

1. Pressure insensitive
   (presumed uveoscleral)
2. Pressure sensitive
   (presumed trabecular)

35% reduction in IOP
(phase 3 FDA trial vs timolol)

*Brubaker et al AJO 2001;131

**35%**

*50%

**13% production**
Diurnal Mean IOP at Month 3

Data based on intent-to-treat patient population

*P < .038

Coleman et al, AAO, 2001
Targets for Glaucoma Rx

1. Intraocular pressure
2. Facility of outflow
3. Ganglion cells (Neuroprotection)
Treatment with Neuroprotection

Retinal Ganglion Cell
Categories of Ganglion Cells in Glaucoma Patient

- Normal healthy cells.
- Sick cells.
- Dead cells.
- Died and decayed.
MANAGING NON IOP DEPENDENT RISK FACTORS

- Delivery of neurotrophins
- Blockade of receptor mediated Excitotoxicity
- Scavenging of reactive oxygen species
Neuroprotection.

- Pharmacological intervention.
- Immunological intervention.
- Future possibilities.
Pharmacological Intervention

- Protection of undamaged cells.
- Rescue of marginally damaged cells.
- Regenerate/Regrowth/replacement of axons.
Protection of Undamaged Cells

- Blocking retinal exitotoxicity mediated by glutamate.
- Administration of neurotrophic factors (BDNF).
- Neuronal resistance to insult.
- Inhibition of nitric oxide synthetase 2 which will prevent axonal injury at LC.
- Ca2 channel blockers.
Rescue of marginally damaged ganglion cells

- Lazaroids/21-aminosteroids.
- UP-Regulation of antideath genes. (bcl-2/bcl-x; viral vectors).
- Antioxidants/Free radical scavengers.
- Ca2 channel blockers.
- Nitric oxide synthetase inhibitors.
Regeneration/Regrowth/Replacement of Axons

- Spanner neural grafts.
- Growth factors.
- Transglutaminases/Interleukin-2 Dimerizers/Oligodendrocytotoxins.
- Macrophage/cytokine/neuro immunological related factors.
- Astrocyte related factors.
Recently it has been suggested that COPL, a synthetic copolymer composed of amino acids, is known to be an immunosuppressive drug which can evoke T-cell mediated immunity that is neuroprotective.
FUTURE POSSIBILITIES

- Gene therapy.
- The hepatocyte growth factor.
- Heat shock proteins.
- Stem cell graft.
- Peripheral nerve graft.
- Optic nerve transection.
Neuroprotection

- By glutamate antagonists.
- Prevent calcium influx.
- Prevent sodium influx.
- Reduce formation of free radicals.
- Stopping formation of nitric oxide and preventing lipids peroxidation.
Neuro protecting agents.

- Antiglaucoma agents.
- Calcium channel blocking agents.
- Anti oxidants.
- Ginkgo bilopha extract.
- Cannabinoids.
- Melatonin.
- Aspirin.
Ginkgo biloba extract

- 60 known bioactive substances half of which are found nowhere in nature.
- Protective action against free radicals, and lipid per oxidation.
- Preserves mitochondrial metabolism, and ATP production in various tissues.
- Scavenges nitric oxide and reduce glutamate induced calcium conc.
Neuro rescue

- Restoration of viability of dead cells or sick cells.
- Under trials; Aminoguanidine an inhibitor of nitric oxide synthetase.
Retinal Ganglion Cell Destruction

Risk Factors

Primary Insult

Glutamate being released into surrounding medium

Toxic response in adjacent retinal ganglion cells (Secondary degeneration)

Excito toxicity

Block the Excito toxicity

Over stimulation of N-methyl-D-aspartate (NMDA) receptors

Excessive levels of intracellular Calcium

Activation of Nitric Oxide Synthetase

Delivery of Neurotropins (BDNTF)

Induction cells in the retina or to produce Neurotropins with gene therapy

Memantine

Blockade or receptor mediators

Aminoguanidine

Excito toxicity

Melatonin/Antioxidants

Vit.E

Scavenging of reactive Oxygen species

Excess free radicals accumulation

Activation of catabolic enzymes cell

Death (Apoptosis)
Considerations for Clinical Trials of Glaucoma with a Neuroprotective Agent

- Glaucoma is a slowly progressive disease. Clinical trials of neuroprotection will necessarily be of much longer duration than is required for determining IOP lowering effect.
- Large numbers of patients will be needed.
- No randomized controlled trial has been completed which evaluates patients with glaucoma.
While reduction of IOP remains the mainstay of medical therapy of glaucoma, other ocular effects of topical medications remain important.
Reduction of IOP is not always sufficient to prevent further optic disc changes and vision loss.

There is a direct evidence for deficient blood supply to the choroid, retina and optic nerve head in glaucoma patients.

*Am J of Ophthalmol* 2003; 135(2), 144 -147
Evidence suggests that vascular defects may be associated with optic nerve head damage in both normal tension and primary open angle disease

“Vasoprotection”

– May be effective in preventing damage resulting from vascular dysfunction of eye

– Can lead to improved visual function
VASOPROTECTION

- AVP time (Arteriovenous passage time): Difference between the time of appearance of blood in arteries and its appearance in their corresponding veins. (normal value = 1.45 secs)
- Optic nerve head blood flow: Blood flow to optic nerve
- Pulsatile ocular blood flow (pOBF): Blood supply to retinal layers
- Ocular perfusion: Passage of blood through ocular vessels
Contrast sensitivity

Treatment can be better managed if C.S is added to the evaluation process. (visual field, IOP, optic disc appearance)

Causes of improvement in C.S
Clinicians note changes in C.S following treatment are not correlated to changes in IOP.
- improvement in ocular circulation are related to improvements in Contrast sensitivity.
- **Dorzolamide**, besides improving ocular circulation, is thought to improve perifoveal circulation (nourishing RGCs near fovea), thereby improving visual function.

J of Ocular Pharmacology & Therapeutics 1999, 15, 189-197
www.vectorvision.com (31/01)
Parsons’ Diseases of the Eye, 19, 103-104
Dorzolamide: Vasoprotection

Results
- Patients visual fields significantly improved from MD – 11.71 to 8.06 dB (p < 0.05)
- Optic nerve head blood flow increased from 508 AU at baseline to 644 AU
- Pulsatile ocular blood flow improved from 542 to 676 μl/min (p < 0.05)

Conclusion
Dorzolamide has a significant effect on visual fields and pOBF in POAG patients and may significantly improve visual function

www.mednet.ca/html
## Glaucoma Treatment (Future)

<table>
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<th>Abnormal</th>
<th>Normal</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
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<tbody>
<tr>
<td>NFL*, Disc†, and VF**</td>
<td>Normal</td>
<td>Glaucoma</td>
<td>+</td>
</tr>
<tr>
<td>NFL and Disc</td>
<td>VF</td>
<td>Early glaucoma</td>
<td>+</td>
</tr>
<tr>
<td>NFL and VF</td>
<td>Disc</td>
<td>Early glaucoma (typical in small optic discs)</td>
<td>+</td>
</tr>
<tr>
<td>VF</td>
<td>Disc and NFL</td>
<td>Possible glaucoma (look also for other causes of VF defect)</td>
<td>Retest VF +/−</td>
</tr>
<tr>
<td>NFL</td>
<td>Disc and VF</td>
<td>Possible glaucoma</td>
<td>Wait for progression</td>
</tr>
<tr>
<td>Disc</td>
<td>NFL and VF</td>
<td>Disc anomaly? Early glaucoma?</td>
<td>Wait for progression</td>
</tr>
</tbody>
</table>

* Ophthalmoscopy, photography, scanning laser polarimetry, optical coherence tomography;
† Ophthalmoscopy, photography, confocal scanning laser ophthalmoscopy;
** Standard, short wavelength, frequency doubling, and multifocal objective perimetry;
HYPOThESIS FOR GLAUCOMA MANAGEMENT

- Maintainance
- Neuro Rescue
- Neuro Protection
- Control I.O.P.
- Eliminate Risk Factors
THERAPEUTIC GOALS

- Reduction in IOP
- Improvement in Blood flow of Optic nerve head and Retina
- Decreasing the damage caused by toxic metabolites such as Glutamate