Principles and Complications of Medical Therapy of Glaucoma

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By

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Definition: ---

Treatment: Medical or surgical

Principle [n.]: A settled rule of action; a governing law of conduct;

A rule (usually, a right rule) of conduct consistently directing one's actions

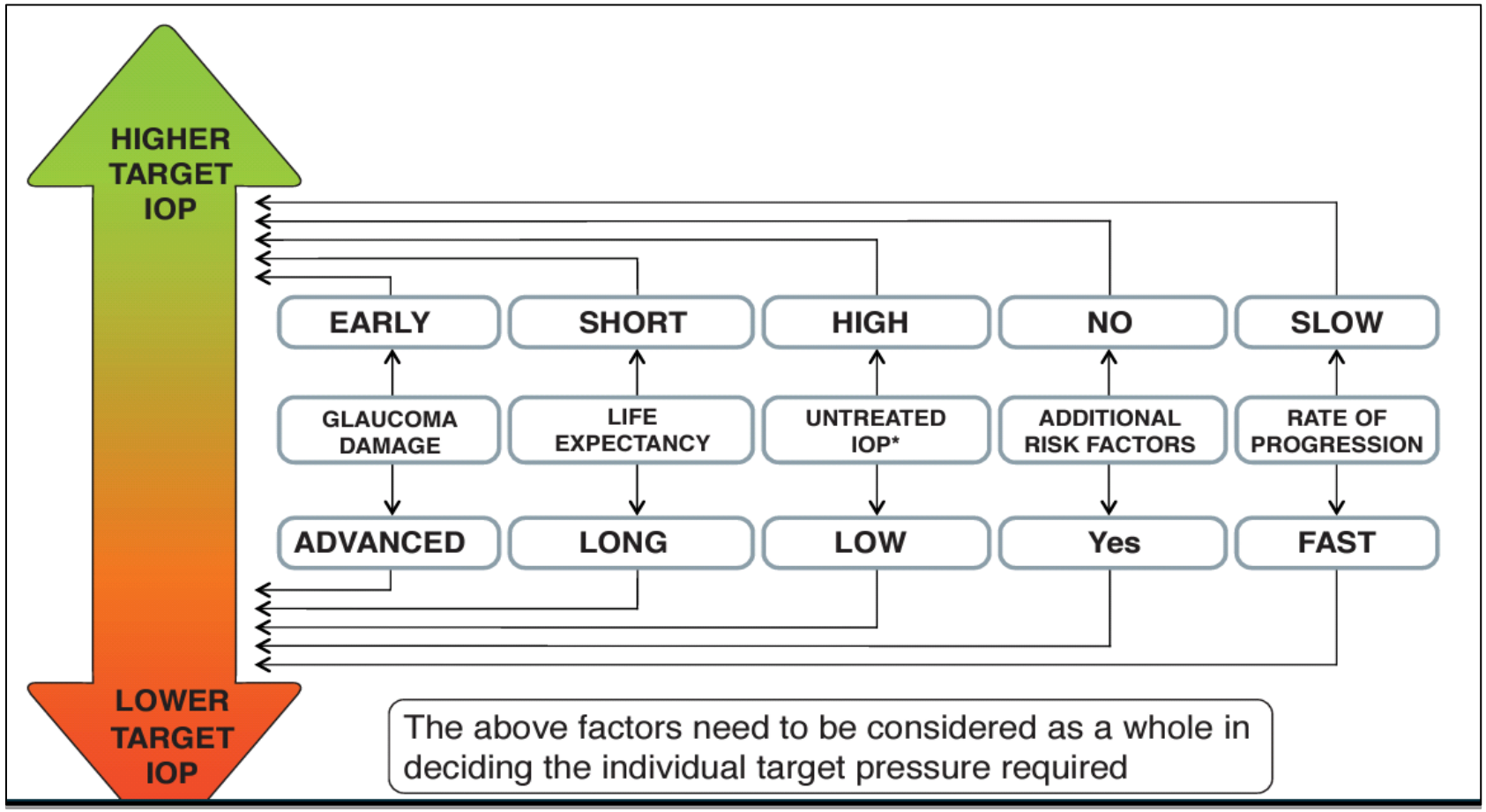
Why do we need principles

To standardize treatment, to avoid overtreatment and under treatment

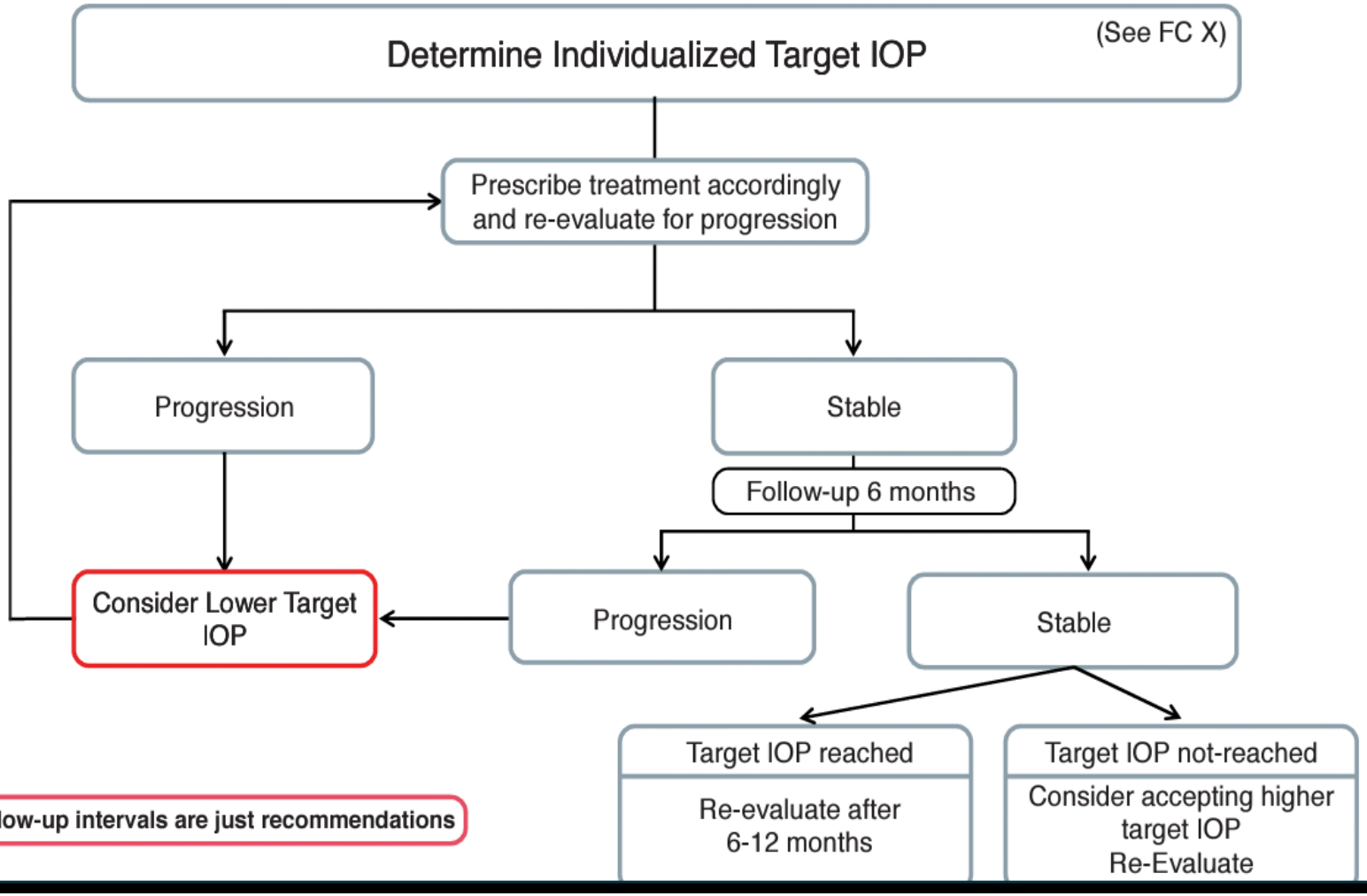
- Our tools for detecting and following glaucomatous disease have improved but are ‘not yet there’.
- Not precise enough to prospectively predict which patients will do better or worse than other
- Principles:
    - “Monocular therapeutic trial,”
    - “maximal medical therapy.”
    - “target intraocular pressure (IOP),” and
    - “Optimal Medical therapy”

- Target IOP is at best an educated guess

- Setting a target IOP is exaggeration of the importance of IOP instead of visual preservation.



Readjusting Target IOP



- Treatment decisions are based upon the risk versus benefit of the next step (in all areas of medicine)
- Treatment goals include preservation of visual function and structural (optic disc, RNFL) outcomes and QOL by lowering lOP to a level that is likely to prevent further damage

- Getting several IOP measurements on different days and times may be very useful prior to initiating medical therapy, (practically, without putting the patient at risk for vision loss).
- The treatment regimen chosen should achieve this goal with the lowest risk, fewest adverse effects, and the least amount of disruption to the patient's life, taking into account the cost of treatment.

- Optimal medical therapy (generally two or three medications, has replaced the concept of maximal medical therapy.

- Take into account the presence of coexisting ocular conditions, general health status, his/her perceptions and expectations about treatment

Who How and When to treat.

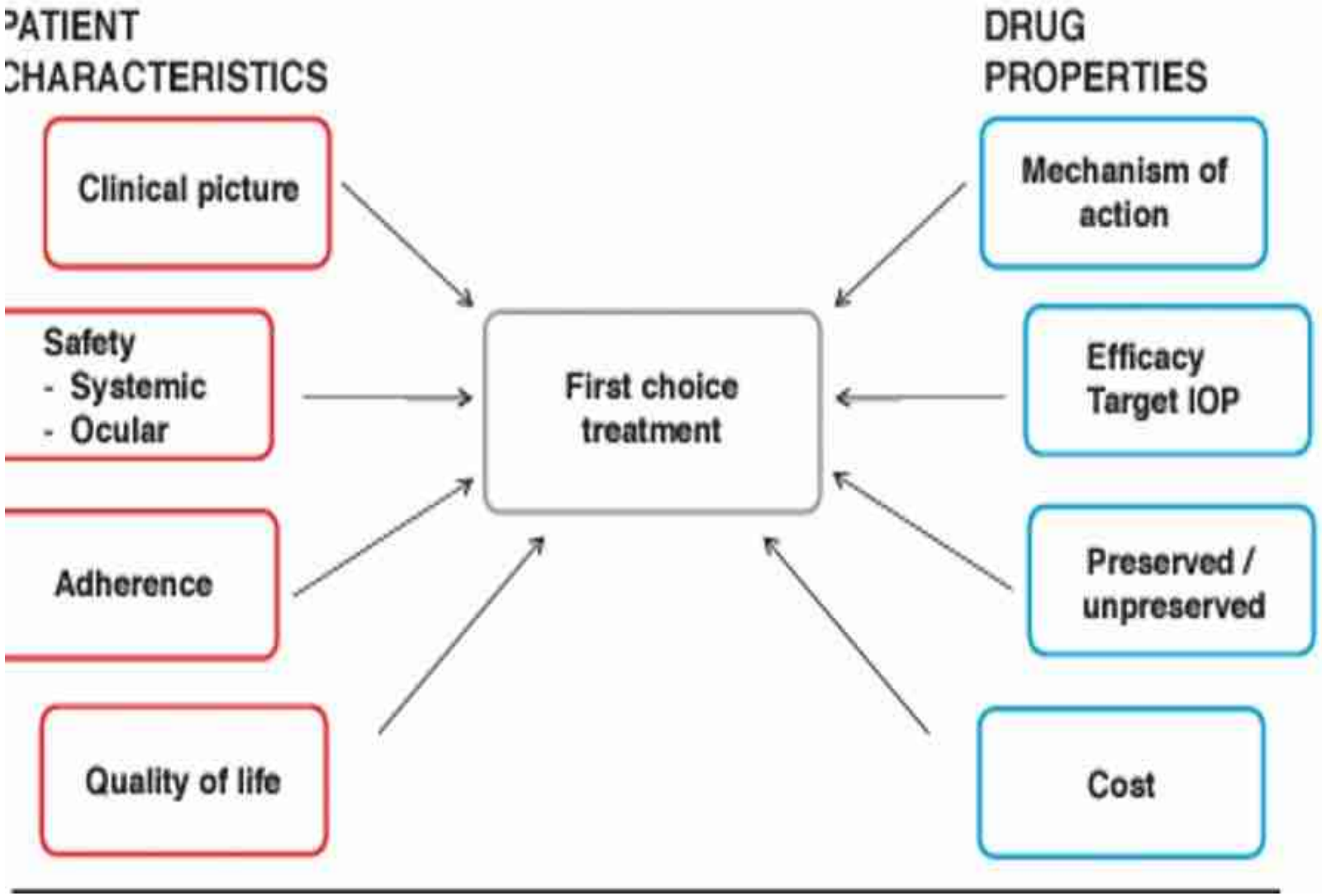
- In established glaucoma, 3 principal factors guide the decision to treat and how aggressively:
  - Life expectancy of the patient,
  - Stage of disease at the time of presentation
  - Rate of disease progression.
- Others:
  - family history
  - degree of lOP elevation,
  - presence or absence of optic disc hemorrhages,
- The stage of disease: a patient who is converting from ocular hypertension to mild glaucoma / advanced glaucoma

Glaucoma suspects: To treat or not to treat?

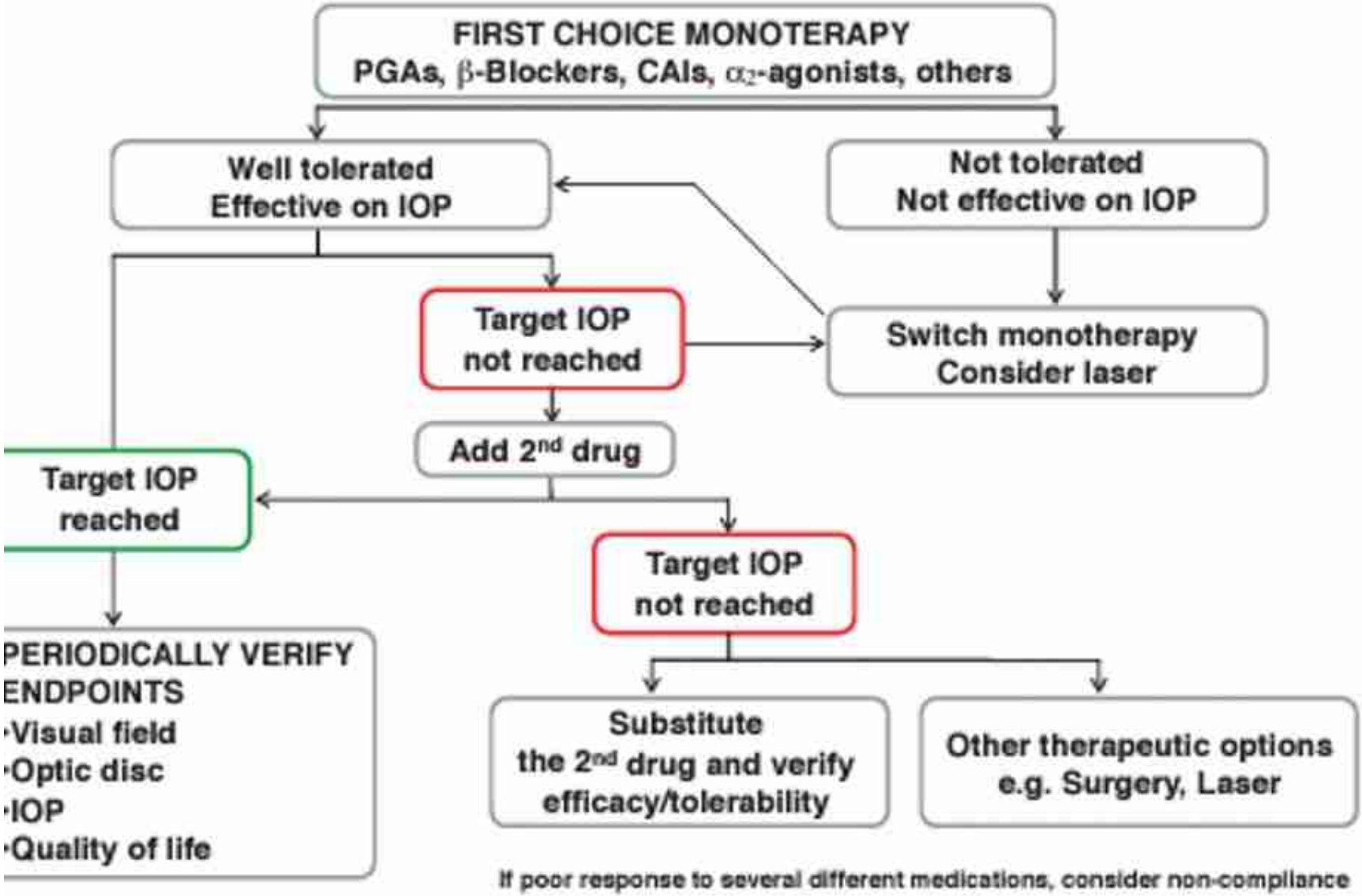
- Consider risk factors for disease development:
  - family history
  - age
  - IOP level
  - central corneal thickness
  - presence of pseudoexfoliation,
  - disc hemorrhages
  - structural and functional integrity of the optic nerve head and retinal nerve fiber
- Imaging of the optic nerve head and retinal nerve fiber layer can provide useful predictive information about the risk of developing functional loss from glaucoma and can serve as a surrogate predictor of vision loss

- How To Treat
- The prostaglandin analogs are the preferred first agents.
  - The diurnal and nocturnal IOP lowering of prostaglandin analogs is superior to all others
  - lowers IOP beyond 24 h thus compensating, for occasional missed doses.
  - Few side effects (during pregnancy, contraindicated: potential risk of miscarriage)

FC XII - Considerations on First Choice Treatment



FC XIV - Therapeutical Algorithm in Glaucoma
Topical Therapy



If poor response to several different medications, consider non-compliance

- Generally best to use the two agents separately prior to using combined medications,
- Given diminishing returns with each additional medication, it is rarely beneficial for a patient to be receiving two or more glaucoma drugs at the same time.
- Difficult to get an additional 2 mmHg IOP lowering when adding a second agent to a prostaglandin and the third agent likely adds less.
- Neuroprotection
- SLT

- **Length of follow-up visits**
- Determined by:
  - Severity of disease and
  - Degree of control

Generally

- Patients in whom a medication has been added or removed should routinely be seen within approximately 1 month of the change
- Ocular hypertensive patients with normal optic nerves and visual fields should be followed at 6- to 12-month intervals.

- Those Under treatment for ocular hypertension, those followed without change for many years should be seen less frequently than newly diagnosed

- Examine optic nerve and visual field at least once a year (more frequently in cases with severe disease and/or rapid progression).

- Obtain three (or at least two) baseline, IOP, visual field tests at the time of initial diagnosis.
- Stereodisc photographs remain the gold standard for disease staging and for following structural optic nerve progression.

- OCT.

3.3.3 First Line Drugs

Table 3.3 Class: PROSTAGLANDIN ANALOGUES

	Compound	Mode of action	IOP reduction	Contra-indications	Side effects
Prostaglandin analogues	Latanoprost 0.005% Tafluprost 0.0015% Travoprost 0.003% - 0.004%	Increase in uveo-scleral outflow	25-35%	Contact lenses (unless reinserted 15 minutes following administration of the drugs)	**Local:** Conjunctival hyperaemia, burning stinging, foreign body sensation, itching, increased pigmentation of periocular skin, periorbital fat atrophy, eyelash changes. Increased iris pigmentation, (in green-brown, blue/ grey-brown or yellow-brown irides). Cystoid macular oedema (aphakic/ pseudophakic patients) with posterior lens capsule rupture or in eyes with known risk factors for macular oedema, reactivation of herpes keratitis, uveitis **Systemic:** Dyspnea, chest pain/angina, muscle-back pain, exacerbation of asthma.
Prostamide	Bimatoprost 0.03% Bimatoprost 0.01%	Increase in uveo-scleral outflow	25-35%		

Table 3.4 Class: Beta-RECEPTOR ANTAGONISTS

	Compound	Mode of action	IOP reduction	Contra-indications	Side effects
Nonselective	Timolol 0.1-0.25-0.5% Levobunolol 0.25% Metipranolol 0.1-0.3% Carteolol 0.5-2.0% Befunolol 0.5%	Decreases aqueous humour production	20-25%	Asthma, history of COPD, sinus bradycardia (< 60 beats/min), heart block, or cardiac failure	**Local:** Conjunctiva hyperaemia, SPK, dry eye, corneal anesthesia, allergic blepharo-conjunctivitis **Systemic:** Bradycardia, arrhythmia, heart failure, syncope, bronchospasm, airways obstruction, distal oedema, hypotension, Hypoglycemia may be masked in insulin dependent Diabetes Mellitus (IDDM), nocturnal systemic hypotension, depression, sexual dysfunction
Beta-1-selective	Betaxolol 0.5%	Decreases aqueous humour production	±20%	Asthma, history of COPD, sinus bradycardia (< 60 beats/min), heart block, or cardiac–coronary failure	**Local:** Burning, stinging more pronounced than with non-selective compounds **Systemic:** Respiratory and cardiac side effects less pronounced than with non-selective compounds, depression, erectile dysfunction

Table 3.5 Class: CARBONIC ANHYDRASE INHIBITORS

	Compound	Mode of action	IOP reduction	Contra-indications	Side effects
Topical	Brinzolamide 1% Dorzolamide 2%	Decreases aqueous humour production	20%	Patients with low corneal endothelial cell count, due to increased risk of corneal oedema	**Local:** Burning, stinging, bitter taste, superficial punctate keratitis, blurred vision, tearing **Systemic:** Headache, urticaria, angioedema, pruritus, asthenia, dizziness, paresthesia and transient myopia
Systemic	Acetazolamide Methazolamide Dichlorphenamide	Decreases aqueous humour production	30–40%	Depressed sodium and/or potassium blood levels, cases of kidney and liver disease or dysfunction, suprarenal gland failure, hyperchloraemic acidosis	**Systemic:** Paresthesias, hearing dysfunction, tinnitus, loss of appetite, taste alteration nausea, vomiting, diarrhoea, depression, decreased libido, kidney stones, blood dyscrasias, metabolic acidosis, electrolyte imbalance

Table 3.6 Class: Alpha-2 SELECTIVE ADRENERGIC AGONISTS

	Compound	Mode of action	IOP reduction	Contra-indications	Side effects
Alpha-2-selective	Apraclonidine 0.5-1.0%	Decreases aqueous humour production	25-35%	Oral monoamine oxidase (MAO) inhibitor users Pediatric age Very low body weight in adults	**Local:** Lid retraction, conjunctival blanching, limited mydriasis (apraclonidine), allergic blepharoconjunctivitis, periocular contact dermatitis, allergy or delayed hypersensitivity (apraclonidine and clonidine >brimonidine) **Systemic:** Dry mouth and nose (apraclonidine). Systemic hypotension, bradycardia (clonidine), fatigue, sleepiness (brimonidine)
	Brimonidine 0.2%	Decreases aqueous humour production and increases uveo-scleral outflow	18-25%		
	Clonidine 0.125 -0.5%	Decreases aqueous humour production			

3.3.4 Second Line Drugs

Table 3.7 Class: NON SELECTIVE ADRENERGIC AGONISTS

	Compound	Mode of action	IOP reduction	Contra-indications	Side effects
Non-selective	Epinephrine 0.25-2.0% Dipivefrin 0.1%	Decreases aqueous humour production and may increases uveo-scleral outflow	15-20%	Occludable angles (Iridotomy needed) Aphakic patients (macular oedema)	**Local:** Conjunctival hyperemia, conjunctival pigmentation. Burning, stinging, ocular pain, blurred vision, macular oedema **Systemic:** systemic hypertension, headache, anxiety, confusion, chest pain, shortness of breath, tachycardia, sweating

Table 3.8 Class: PARASYMPATHOMIMETICS (CHOLINERGIC DRUGS)

	Compound	Mode of action	IOP reduction	Contra-indications	Side effects
Direct-acting	Pilocarpine 0.5-4% Carbachol 0.75-3%	Facilitates aqueous outflow by contraction of the ciliary muscle, tension on the scleral spur and traction on the trabecular meshwork	20-25%	Post-operative inflammation, uveitis neovascular glaucoma. Patient at risk for retinal detachment, spastic gastrointestinal disturbances, peptic ulcer, pronounced bradycardia, hypotension, recent myocardial infarction, epilepsy, Parkinsonism	**Local:** Reduced vision due to miosisand accommodative myopia, conjunctival, hyperaemia, retinal detachment, lens opacities, precipitation of angle closure, iris cysts **Systemic:** Intestinal cramps, bronchospasm, headache
Indirect-acting	Demecarium bromide 0.125-0.25% Ecothiophate Iodide 0.03% Diisopropyl fluorophosphates 0.025-0.1%		15-25%	Same as direct acting drugs	**Local and systemic:** Side effects are similar but more pronounced than with direct acting compounds

Table 3.9 OSMOTICS

	Compound	Mode of action	IOP reduction	Contra-Indications	Side effects
Oral	Glycerol Isosorbide Alcohol	Dehydration and reduction in vitreous volume Posterior movement of the Iris-lens plane with deepening of the AC	15-20%	Cardiac or renal failure	Nausea, Vomiting, dehydration (special caution in diabetic patients). Increased diuresis, hyponatremia when severe may lead to lethargy, obtundation, seizure, coma. Possible increase of blood glucose. Acute oliguric renal failure. Hypersensitivity reaction
Intravenous	Mannitol Urea		15-30%		

- References.
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- Medical management of Glaucoma Chapter 7. AAO series 10.
- World Glaucoma Association 7th Consensus Meeting: Medical Treatment of Glaucoma Fort Lauderdale, FL, May 1, 2010

- Thank You for your time