

I. Pathway of aqueous outflow

- A. Anterior Chamber
- B. Uveal meshwork
- C. Corneoscleral meshwork
- D. Juxtacanalicular meshwork
- E. Schlemm's Canal
- F. Aqueous collector channels
- G. Aqueous veins
- H. Episcleral veins

II. Anatomy of the trabecular meshwork (TM)

- A. Lies between scleral spur and Schwalbe's Line
- B. Consists of connective tissue beams
- C. Covered by endothelial layer
- D. Three layers deep
 - 1. Uveal meshwork (Closest to anterior chamber, little resistance)
 - 2. Corneoscleral meshwork (Little resistance)
 - 3. Juxtacanalicular Meshwork (Closest to Schlemm's Canal)
 - 4. Likely location of part of the resistance to aqueous flow is juxtacanalicular meshwork

III. Anatomy of Schlemm's Canal (SC)

- A. Inner wall endothelium lies adjacent to juxtacanalicular meshwork
- B. Forms giant vacuoles in response to pressure gradients
- C. Endothelium likely location of part of the resistance to aqueous flow
- D. Outer wall lined with ~30 collector channels
- E. Collector channels route aqueous into the episcleral veins through the aqueous veins
- F. Once aqueous enters the canal, outflow only limited by episcleral venous pressure

IV. Pilocarpine

- A. Historically important drug that acts on trabecular outflow pathway
- B. Mechanism of action
 - 1. Stimulates the longitudinal muscle of the ciliary body
 - 2. Muscle inserts into the scleral spur
 - 3. Trabecular meshwork opens increasing outflow
- C. Clinical Aspects
 - 1. Side effects limit its use with today's other available alternatives
 - 2. Dosing requirements are less than ideal compared to available alternatives
 - 3. May have reduced efficacy with age
 - 4. May have reduced efficacy in patients with more iris pigment

V. Prostaglandin analogs

- A. Bimatoprost, Latanoprost, Travoprost
- B. Mechanism of action
 - 1. Primarily lowers IOP by increasing uveoscleral outflow
 - 2. Increasing evidence for smaller effect on trabecular outflow
- C. Evidence from the literature
 - 1. Action at the level of the juxtacanalicular TM and SC endothelium
 - 2. Has been proven to induce disassembly of junctions between SC endothelial cells
 - 3. Junctions between SC endothelial cells play role in outflow resistance

VI. Argon Laser Trabeculoplasty (ALT)

- A. Uses longer duration argon laser application
- B. Laser energy is absorbed primarily by the melanin contained within pigmented TM cells
- C. Heat dissipates to surrounding tissues resulting in coagulative damage to nonpigmented cells and trabecular beams
- D. Creates treatment crater within the trabecular beams
- E. Long-term, there is absence of giant vacuoles in the SC endothelium underlying burns
- F. Adjacent areas show herniation of juxtacanalicular TM into SC
- G. Mechanical theory of IOP Lowering
 - 1. Circumferential trabecular tension opens trabecular spaces
 - 2. Focal scarring creates contraction around burns opening spaces
 - 3. This excessive damage makes repeat treatment impossible
- H. Biochemical theory of IOP lowering
 - 1. Laser induces trabecular cell replication with improved phagocytosis ability that reduces resistance
 - 2. Laser induces increased levels of metalloproteinases that decrease resistance in extracellular matrix
- I. Evidence from Glaucoma Laser Trial
 - 1. Initial ALT was just as efficacious as initial topical therapy
 - 2. IOP was lower in ALT group compared to treatment group
 - 3. 44% of laser-first eyes did not require further intervention

VII. Selective laser trabeculoplasty (SLT)

- A. Uses a shorter duration frequency-doubled, Q-switched, 532 nm Nd:YAG laser
- B. No other ophthalmic application for this type of laser
- C. Pulse time less than the relaxation time of intracellular melanin, limiting collateral cell damage
- D. Damage essentially limited to melanin containing cells
- E. Short duration of laser application does not create the extent of structural damage to beams
- F. No treatment crater formed
- G. Effect likely not mechanical, but biochemical
 - 1. Similar biochemical effects as seen in ALT
 - 2. SLT induces the disassembly of junctions between endothelial cells in Schlemm's Canal
 - 3. SLT results in expression of several proteins within the TM/SC zone
- H. Evidence from the literature
 - 1. SLT has been shown to be repeatable
 - 2. Essentially equal efficacy to ALT
 - 3. Additional IOP lowering in eyes with previous ALT
- I. Biochemical mechanism of action may have overlap with prostaglandin analogs resulting in reduced efficacy

VIII. Steroid Response Ocular Hypertension

- A. Mechanism
 - 1. Increased extracellular matrix deposition in juxtacanalicular tissue
 - 2. Decreased MMP activity in trabecular meshwork
 - 3. Increased cross linking between TM cells
 - 4. Altered gene expression resulting in abnormal protein production
 - 5. Decreased phagocytosis
- B. Epidemiology
 - 1. Majority of patients will have at least a mild increase in IOP
 - 2. ~5% will have a large IOP response
 - 3. Evidence that IOP response can occur within a few days