A. Routes of Administration

1. **Topical**—most common route of administration
   Degree of penetration of topically applied medications depends on integrity of normal defense mechanisms of the eye. Drug absorption is greatly enhanced by ocular inflammation. Medications put in the conjunctival sac can penetrate the cornea or conjunctiva or be absorbed systemically via the nasolacrimal system. Topical administration is also affected by the vehicle, molecular size of the drug, drug concentration, pH, electrolyte composition, and preservatives.

   Corneal epithelium is the main site of resistance to drug penetration. The cornea may be thought of as a fat-water-fat sandwich. As a result, the epithelium and endothelium are relatively impermeable to electrolytes but are readily penetrated by fat-soluble substances. The stroma is readily penetrated by electrolytes but not by fat-soluble substances. Drugs that have the ability to exist in equilibrium in solution as ionized (water soluble; polar) and unionized (lipid soluble; nonpolar) forms are ideal for topical use, i.e., chloramphenicol, fluoroquinolones, alkaloids. Topical administration is used for treatment of eyelids, conjunctiva, corneal, iris, and anterior uvea.

2. **Subconjunctival (bulbar conjunctiva)**
   This technique requires only topical anesthesia and a tuberculin syringe with a 25- or 27-gauge needle. Volumes should not exceed 0.25 ml in cats and dogs and 1.0 ml in horses and cows. Subconjunctival medication reaches the cornea by slowly leaking out of the injection site. Intraocular drug levels are attained by diffusion through the cornea and sclera. Subconjunctival administration is used for diseases of the cornea, anterior, uvea, anterior vitreous, and sclera.

3. **Intravitreal**—used infrequently
   Antibiotics and antifungal drugs have been effectively used in microgram dosages. Generally injected at the pars plana for infectious endophthalmitis.

4. **Systemic**—P.O., I.V., I.M.
   Generally do not penetrate the anterior segment of the eye as well as topical or subconjunctival medications. Small molecular weight lipid-soluble drugs may penetrate the blood aqueous barrier. Drug penetration is also markedly increased with ocular inflammation. Systemic administration is required for treatment of diseases of the retina, optic nerve, and vitreous.

B. Mydriatics

Mydriatics cause dilation of the pupil by sympathomimetic or parasympatholytic action.

1. **Atropine**
   Direct acting—parasympatholytic, blocks the response of postganglionic cholinergic receptors to acetylcholine. Cycloplegic (paralyzes ciliary musculature).
   Strength—0.5%-4%.
   Duration—2–4 x day until mydriasis—then as needed.
   Lasts 12 weeks—dog.
   Lasts 4–6 weeks—horse.
   Use. Cycloplegic—uveitis/pain. May cause gut stasis in sensitized horses.

2. **Tropicamide (Tropicacyl®)**
   Synthetic parasympatholytic. Cycloplegic (weak).
   Duration—Works in ~ 15–20 minutes. Lasts ~ 2–4 hours.
   Use—Diagnostic evaluation.

C. Miotics

Topical administration results in pupillary constriction, ciliary muscle contraction, and increased aqueous outflow.
1. **Pilocarpine**  
   Direct acting—cholinergic, mimics acetylcholine.  
   **Strength**—0.05% - 4%.  
   **Duration**—4 – 6 hours  
   **Use.** Glaucoma, KCS limited. Often is topically irritating.

2. **Carbachol—Carbostat® 0.01%**  
   Used most commonly as an intracameral injection after cataract surgery to decrease potential intraocular pressure spikes.

3. **Latanoprost—Xalatan®**  
   Prostaglandin F 2α analog  
   **Strength**—0.005%.  
   Currently drug of choice for treatment (miosis) of glaucoma (increases aqueous outflow).

### D. Selected Antimicrobial Drugs

#### ANTIBACTERIAL

Topical antibiotics are indicated for the treatment of corneal ulcers, corneal perforations, conjunctivitis, and blepharitis. Ocular infections may result in ocular discharge, keratic precipitates, or cellular debris within the globe. Ideal choice of appropriate therapy begins with identification of the organism and its sensitivity. Culture or cytologic examination of material from the affected area is necessary. Minor bacterial conjunctivitis infection may not justify routine culture and may be amenable to initial therapy with broad spectrum antibiotics. Normal ocular flora is predominantly gram positive; a predominance of gram negative organisms is indicative of an abnormal condition.

1. **Chloramphenicol**  
   Broad spectrum, bacteriostatic.  
   Fat soluble—thus may be considered for initial treatment of intraocular infections (penetrates the cornea).  
   **Frequency of administration**—q 4 hours for full therapeutic levels.  
   **Toxicity**—in man—risk of aplastic anemia.

2. **Aminoglycosides**  
   a. **Neomycin**  
      Usually found in combination with other antibiotics.  
      Broad spectrum—bacteriocidal, impairs protein synthesis.  
      **Frequency of administration**—BID-TID.  
      **Toxicity**—Topical—localized sensitivity; conjunctival irritant.  
      Systemic—ototoxicity—possible head tilt.
   
   b. **Gentamicin**  
      Bacteriocidal. Very popular. Overused?  
      Broad spectrum of activity including *Streptococcus, Staphylococcus, Escherichia coli*, *Proteus* spp., and *Pseudomonas aeruginosa*.  
      Effective topically and subconjunctivally for external ocular infections.  
      Toxicity—Renal toxicity with concurrent oral therapy, may be toxic to surface epithelium.
   
   c. **Tobramycin**  
      Two to four times more effective against *Pseudomonas* sp. than gentamicin and effective against gentamicin-resistant microbes.  
      Use with caution. Indiscriminate use may lead to resistance that results in no viable effective antimicrobial agent.

3. **Polypeptides**  
   a. **Bacitracin**  
      Bactericidal, used in combination with other antibiotics.
Poor corneal penetration.
Gram + microorganisms.

b. Polymyxin B
Poor penetration.
Bactericidal.
Effective mainly against gram-negative bacilli and *Pseudomonas*.
Should not be given subconjunctivally.

4. **Cephalosporins, i.e., Cefazolin**
   Broad spectrum, first-generation cephalosporin.
   Topical use for gram + cocci resistant to other antimicrobials.
   Can be administered subconjunctivally–does penetrate intact cornea.
   Usually diluted to 50–100 mg/ml concentration.
   Mix with artificial tears to a concentration of 33 mg/ml for treatment of meibomitis.

5. **Fluoroquinolones, i.e., Ciprofloxacin HCl (Ciloxan®), Levofloxacin (Quixin®), Ofloxacin (Ocufox®), others**
   Broad spectrum, gram positive and gram negative.
   Drug of choice for *Streptococcus* and *Staphylococcus* corneal, conjunctival, and intraocular infections.
   Excellent corneal penetration.

**ANTIFUNGAL AGENTS**
Ocular antifungal agents belong to one of three classifications: polyenes, imidazoles, and pyrimidines. Topical antifungal agents are used more commonly to treat fungal keratitis in horses than in small animals. Penetration of the intact cornea is poor with all antifungals.

1. **Polyenes**
   a. Natamycin (Natacyn®–Alcon Laboratories)
      Used mainly against *Candida* sp. and *Fusarium* sp. (only approved agent in the market).

   b. Amphotericin B
      Fungistatic.
      Generally used systemically for fungal endophthalmitis.
      May be given as an intravitreal injection in mcg dosages.

2. **Imidazoles**
   a. Miconazole 1% (Monistat®)
      Was the drug of choice for most veterinary fungal keratitis cases but no longer readily available in IV preparation.
      Tolerated well as subconjunctivally injection. ~ 1 ml SID x 3–5 days if tolerated.
      Treatment frequency of a fungal keratitis may warrant 1- to 4-hour treatment intervals.

   b. Fluconazole (Diflucan®)
      Synthetic triazole, fungistatic.
      Strength—2 mg/ml IV preparation.
      Currently our drug of choice for topical use, subpalpebral lavage unit, and intracameral (100 µg) injection.
      Treatment frequency for fungal keratitis may warrant 2- to 4-hour treatment intervals.

**ANTIVIRAL AGENTS**
Antiviral agents are indicated for treatment of herpetic keratitis in cats.

1. **Idoxuridine**
   0.5% ointment and 0.1% solution (Stoxil® or Herplex®).
   Alters viral replication by substituting for thymidine in the viral DNA chain.
   Frequency of administration is approximately every 2 hours.
Poorn corneal penetration.
Greatest availability through compounding pharmacies.

2. **Vidarabine 3%**
   Ointment—Vira A®.
   Prevents extension of the DNA chain by causing a premature stop to DNA replication.
   Penetrates the cornea better than Idoxuridine.
   Frequency of administration is 4 to 6 times daily.
   Greatest availability through compounding pharmacies.

3. **Trifluridine 1%**
   Solution—Viroptic®.
   Current drug of choice for feline herpetic keratitis.
   Antiviral potency reported as over twice that of idoxuridine and 5 times greater than Vidarabine.
   Like idoxuridine, trifluridine is a pyrimidine nucleoside analogue and inhibits nucleic acid synthesis.
   Frequency of administration is 4 to 6 times daily.

4. **Others—Lysine, Acyclovir, Interferons**

**E. Anti-inflammatory Agents**

**CORTICOSTEROIDS**

Treatment of uveitis requires a corticosteroid that is capable of readily penetrating the intact cornea, e.g., 1% prednisolone acetate. Subconjunctival injection of corticosteroids provides a greater local anti-inflammatory effect than can be achieved by topical or systemic administration. Posterior segment inflammation requires systemic corticosteroid therapy. Regardless of route of administration, the lowest dosage necessary to control the inflammation is recommended. In general, topical therapy should be continued two weeks beyond resolution of clinical signs.

Local side effects of corticosteroid use include delayed corneal healing, increased corneal collagenase activity, and an increased incidence of bacterial and mycotic keratitis. In addition, topical corticosteroids may result in systemic changes. These include reduced baseline cortisol levels, suppression of the adrenocorticotropic hormone response curve, and altered carbohydrate metabolism.

1. **Anti-inflammatory potencies**
   Based on Prednisolone, e.g., Dexamethasone—1/10 strength of Pred.
   Penetration and effect is influenced by type of salt, frequency of application, and proximity to the site of involvement. Dexamethasone penetrates the cornea well—thus 0.1% Dex. is almost as potent as 1.0% Pred. (even though Pred. is 10x greater strength).

2. **Frequency of administration**—dependent on clinical signs and the type of steroid used.

3. **Subconjunctival doses and volumes**—mg vs. volume.

4. **Subconjunctival steroid durations**
   a. Prednisolone—24 to 48 hours.
   b. Triamcinolone—2 to 3 weeks.
   c. Methylprednisolone—3 to 4 weeks.
   d. Betamethasone—3 to 4 weeks.
   e. Dexamethasone—1 to 2 days.
NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

Categories of nonsteroidal anti-inflammatories include salicylic acids (aspirin), propionic acids (flurbiprofen), indomethacin, phenylbutazone (Butazolidin), and flunixin meglumine (Banamine). In contrast to corticosteroids, NSAIDs reduce prostaglandin synthesis by inhibiting production of cyclooxygenase. This inhibits production of endoperoxides, which are converted to prostaglandins and thromboxane. The lipoxygenase pathway is unimpeded, however, and products of the lipoxygenase pathway may actually enhance leukocyte response.

NSAIDs are available in both topical and systemic formulations. Systemic NSAIDs, at therapeutic levels, can markedly decrease renal blood flow, glomerular filtration rate, and sodium and water excretion. These effects are more pronounced in animals with preexisting renal insufficiency or animals in a vasoconstrictive state such as general anesthesia. Some degree of gastrointestinal intolerance may occur, such as gastroduodenal ulceration and hemorrhage, when NSAIDs are used systemically.

1. **Aspirin**
   - Most effective when used prior to prostaglandin release.
   - Dosages: dog—10 to 20 mg/kg, BID; cat—10 mg/kg, q 48 hours.

2. **Carprofen (Rimadyl®)**
   - Used in similar ways as aspirin. May have fewer side effects.
   - Do not use in Labrador retrievers—may cause liver disease.
   - Dosages: 1mg/lb BID. Not approved for use in cats.

3. **Etodolac (Etogesic ®)**
   - Dosage: dog—10–15 mg/kg, PO SID
   - Should not be used in dogs < 5 kg.
   - Monitor tear production—associated with development of KCS.

4. **Flunixin meglumine (Banamine®)**
   - Effective anti-inflammatory agent in the horse and dog (although not currently approved for use in dogs).
   - Dosages: dog—0.25 to 0.50 mg/lb, IV, SID, not to exceed 2 days; cat—do not use.
   - Commonly given 30 minutes prior to surgery to minimize postoperative swelling and inflammation (e.g., lens extraction).

5. **Flurbiprofen**
   - Cyclooxygenase inhibitor.
   - Used topically preoperatively to stabilize the blood-aqueous barrier in inflammation (especially when diabetes mellitus has been diagnosed), decrease production of ocular prostaglandins, and maintain pupil size. Can be used to treat anterior uveitis and in the presence of corneal ulceration.

F. **Topical Anesthetics**

Drugs suitable for use as local anesthetics cause a reversible block of conduction through nerve fibers by displacing calcium at binding sites in cell membranes. To be effective, local anesthetics must have properties similar to drugs that penetrate the cornea. They must be capable of existing in ionized (water-soluble) and nonionized (lipid soluble) forms. Increased membrane permeability exists in an alkaline state. Local anesthesia is less effective in inflamed tissue which has more acidic pH than normal.

Most topical anesthetics are effective within 30 seconds to 3 minutes to facilitate procedures such as tonometry, corneal and conjunctival scrapings, and subconjunctival injections. Microbial cultures should be taken prior to application of topical anesthetics, as inhibition of microorganisms has been attributed to topical anesthetic agents.

1. **Proparacaine (Ophthaine®) 0.5%.**
2. Tetracaine (Pontocaine®) 0.5% to 2%.
   Topical anesthetics should not be used on a regular basis with painful eyes because: (1) animal may scratch
   off corneal epithelium (feels no pain), and (2) topical anesthetics may inhibit mitosis (thus healing) in
   corneal cells.

G. Osmotic Agents (topical)
2 to 5 percent NaCl (hypertonic saline). Example: Adsorbon C 5%.
Indicated primarily for treatment of severe chronic corneal edema originating from superficial epithelial
disruption and for severe cornea bullae formation.
Side effect—localized irritation.

H. Tear Film Supplements
Many tear film supplements currently exist today. All are indicated to control keratitis sicca. May provide
temporary comfort to corneal irritation resulting from distichia, entropion, or sutures, and as a vehicle for
delivery of medications. Tear supplements are available in solution and ointment form and are intended to
replace the aqueous or lipid layer of the tear film. Preservative-free products generally recommended.

I. Lacrimogenics
These are drugs potentially capable of stimulating tear secretion.
1. Pilocarpine
   Has been used historically, but there is little evidence that it is effective when given either orally or
topically.
   May be effective in the rare case of neurogenic KCS.
   Prescribed as 2 drops of 2% Pilocarpine per 10 pounds body weight added to the food twice daily.
   Maintain therapy for at least 1 month prior to recheck.
   Side effect—emesis or anorexia—if this occurs—stop therapy for 24 hours and start again at one-half the
dose, gradually increasing to the starting dose.
2. Cyclosporine A 0.2% ointment (Optimmune®)
   Cyclosporine is a potent suppressor of T-cell growth factor and of the cytotoxic T-cell response to this
growth factor.
3. Tacrolimus 0.02%, 0.03% ointment or solution.
   Effective alternative to cyclosporine. T-cell suppressor with a distinct receptor site to cyclosporine.

J. Anticollagenase/Mucolytic Agents
Collagenase inhibitors are indicated for the treatment of melting corneal ulcers.
1. Acetylcysteine (Mucomyst®)
   Anticollagenase (e.g., Pseudomonas aeruginosa infection). Diluted from 10 to 20% with artificial tears to a
   5 to 8% concentration. Administered every 1 to 4 hours until desired effect is achieved.
   Mucolytic agent—I personally find no value for this perceived need in the treatment of KCS. Overuse may
result in localized inflammation and excessive lysis of normal mucus, thus worsening corneal exposure.
2. Autogenous serum—anticollagenase
   Questionable efficacy for treatment of melting corneal ulcers.
   Collect the animal’s blood in a clot tube. After clotting, spin down the serum and place in a dark dropper
   bottle. Use topically.
   MUST BE REFRIGERATED AND EACH BATCH USED FOR ONLY 7 DAYS—it is an excellent
growth medium for microorganisms.
3. Sodium EDTA
K. Pain Medication
   Topical
   Intracameral/intraorbital
   Parenteral/patch