

There Are Multiple Routes By Which a Drug Can Get to the Eye

SYSTEMIC:

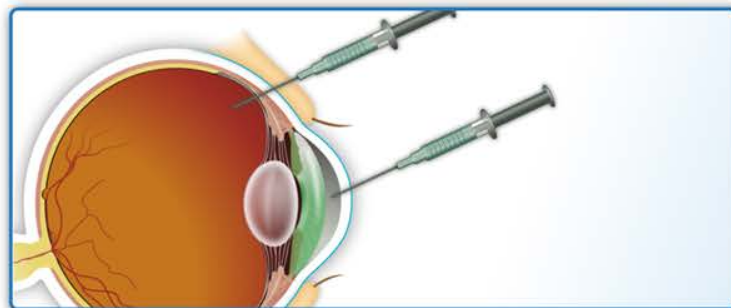
Drug is administered so that it gets into the bloodstream.

- **Oral:** Drug is given by mouth.
- **I.V.:** Drug is injected directly into the blood.



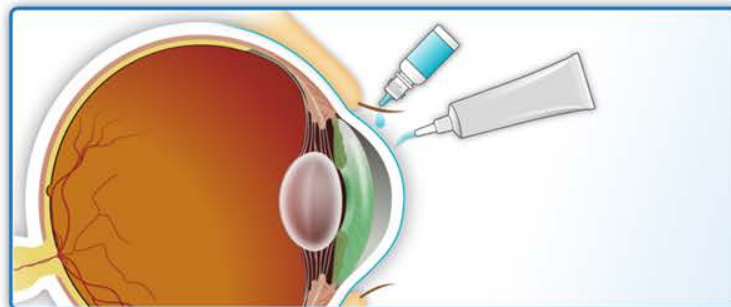
LOCAL INJECTION:

Drug is injected directly into the eye tissue.

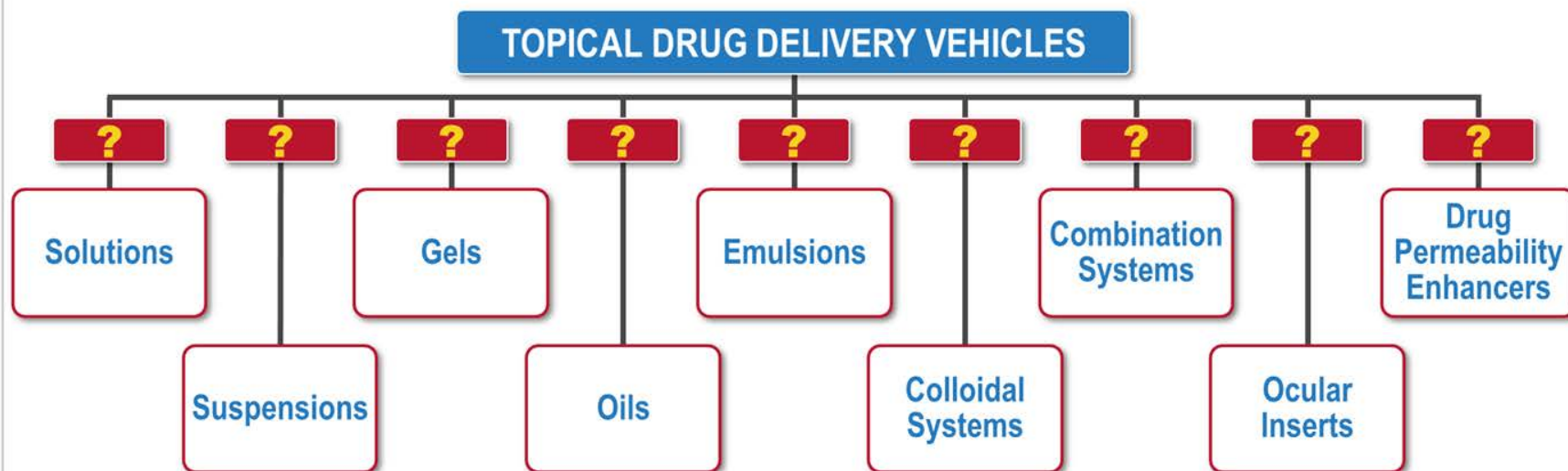


TOPICAL:

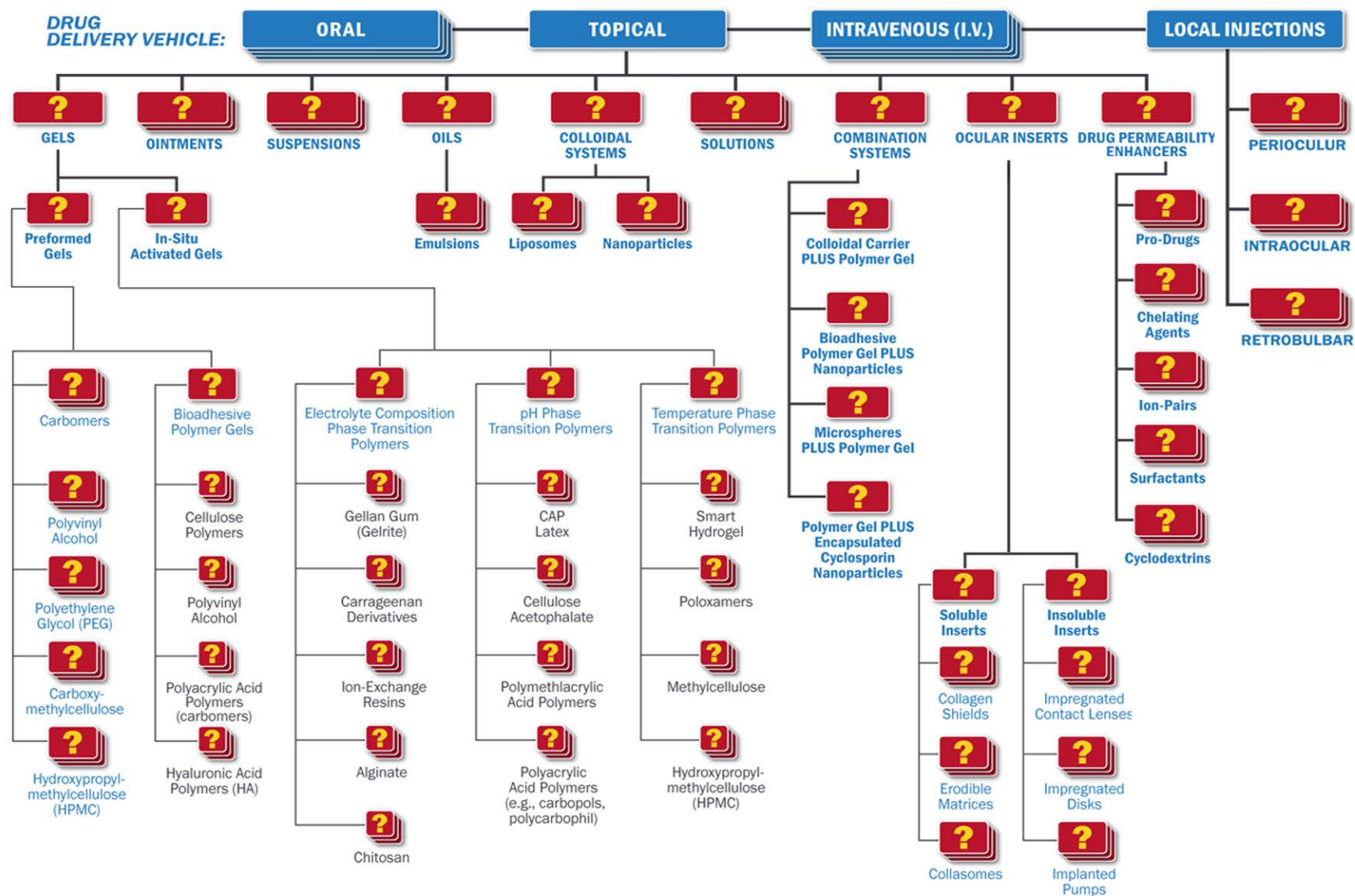
Drug is applied to the surface of the eye.



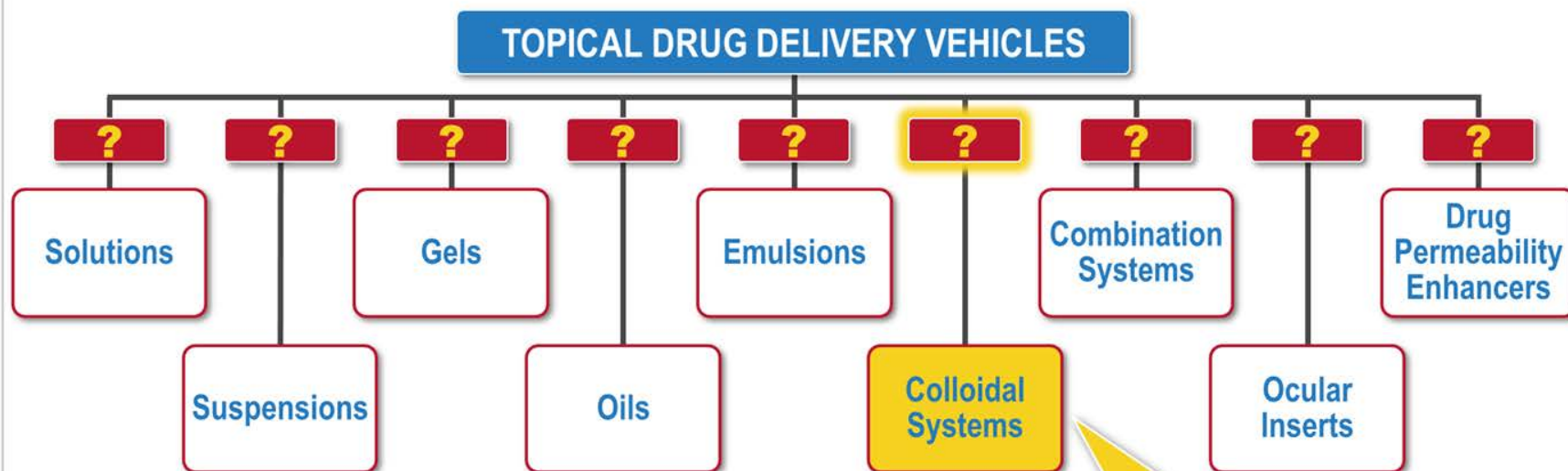
Formulation Options



Ocular Delivery Systems



Formulation Options



EXAMPLES OF COLLOIDAL SYSTEMS

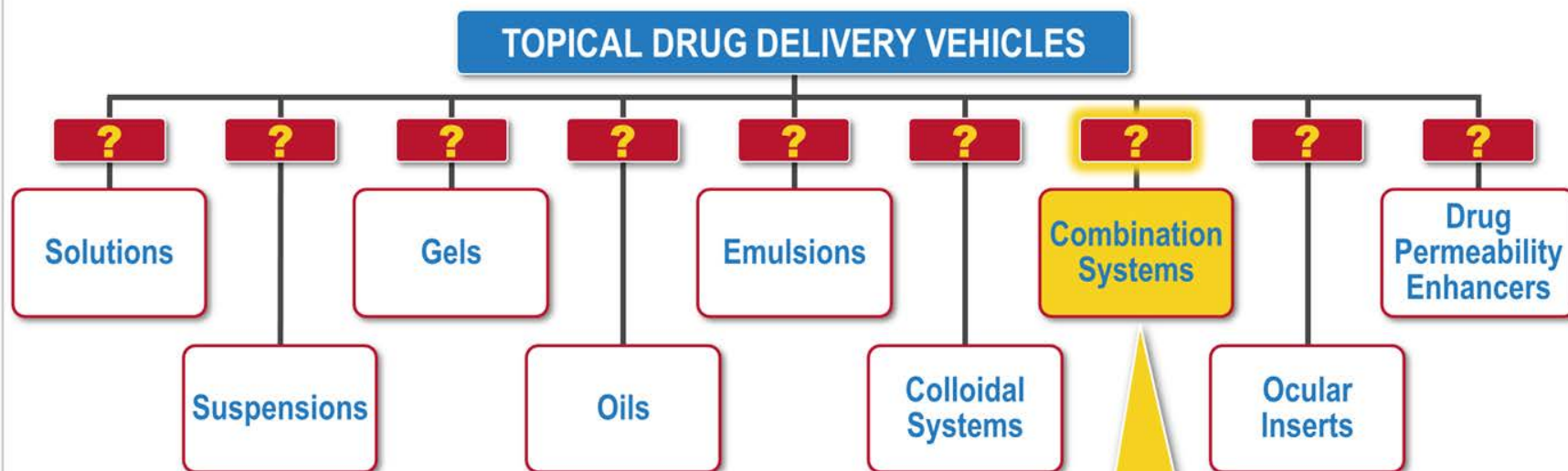
? Liposomes:

- ? Dipalmitoyl choline
- ? Dipalmityl lechtin
- ? Phosphotidyl choline
- ? Phosphotidyl serine
- ? Phosphotidyl inositol

? Nanoparticles:

- | | |
|-------------------------------|--|
| ? Ethyl cellulose | ? Albumin |
| ? Cellulose acetate phthalate | ? Polyamide |
| ? Ethylene vinyl acetate | ? Poly-isobutylcyanoacrylate (<i>PBCA</i>) |
| ? Polyethylene oxide | ? Poly-caprolactone (<i>PECL</i>) |
| ? Polyvinyl alcohol | ? Poly(lactic acid-co-glycolic acid) |
| ? Polyalkyl-cyanoacrylate | ? Gelatin |
| ? Polylactic acid | ? Polymethylmethacrylate |

Formulation Options

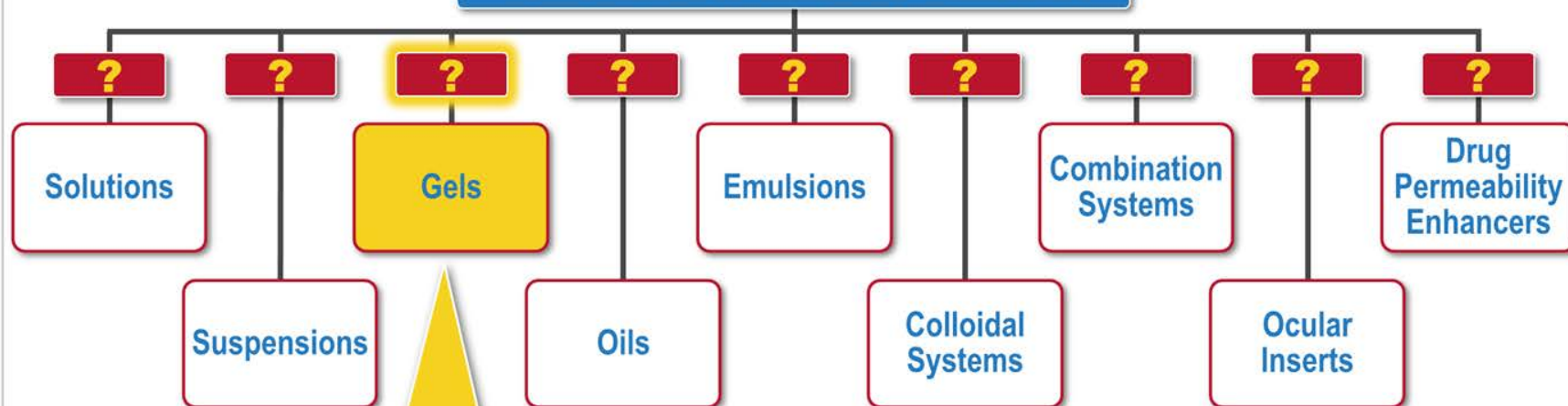


EXAMPLES OF COMBINATION SYSTEMS

- ?** Colloidal Carrier **PLUS** Polymer Gel
- ?** Bioadhesive Polymer Gel **PLUS** Nanoparticles
- ?** Microsphere **PLUS** Polymer Gel
- ?** Polymer Gel **PLUS** Encapsulated Cyclosporin Nanoparticles

Formulation Options

TOPICAL DRUG DELIVERY VEHICLES



EXAMPLES OF GELS

? Polyvinyl Alcohol	? Methylcellulose	? κ-Carrageenan	? Dextran 70
? Polyethylene Glycol	? Polygalacturonic Acid	? ι-Carrageenan	? Cellulose Acetate Phthalate
? Carboxymethylcellulose	? Hyaluronic Acid Polymers	? Ion-Exchange Resins	? Poly(methacrylic) Acid
? Hydropropylmethylcellulose	? Gellan Gum	? Alginate	? Carbomer
? Hydroxypropyl Cellulose	? λ-Carrageenan	? Chitosan	? Polycarbophil
? Hydroxethyl Cellulose	? Eudragit	? Pectin	? Poloxamers
? Polyethylene Oxide	? Acacia	? Sodium Alginate	? Polyvinyl Pyrrolidone
? Polypropylene Oxide	? Poly (methylvinyl ether-maleic anhydride)	? Pluronic Acid	? Ethylhydroxyethylcellulose
? Polyacrimide			

Topical vs. Oral Administration: Different Environment–Size

► Surface Area/ Volume

► pH

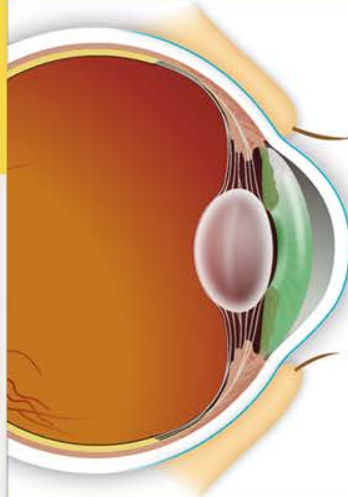
► Residence Time

► Epithelium

► Toxicity and Sensitivity

► Mode of Delivery

THE EYE DEFENDS



► Surface Area: **VERY SMALL**

- Conjunctiva $\approx 0.0016\text{m}^2$
(2.48 sq. in.)
- Cornea is
5 to 6 times smaller

A QUARTER



► Volume: **SMALL**

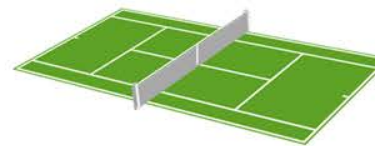
THE GUT ABSORBS



► Surface Area: **LARGE**

- Intestines $\approx 200\text{m}^2$ **(310,000 sq. in.)**

COMPARED TO A TENNIS COURT



► Volume: **LARGE**

Topical vs. Oral Administration: Different Environment–pH

► Surface Area/
Volume

► pH

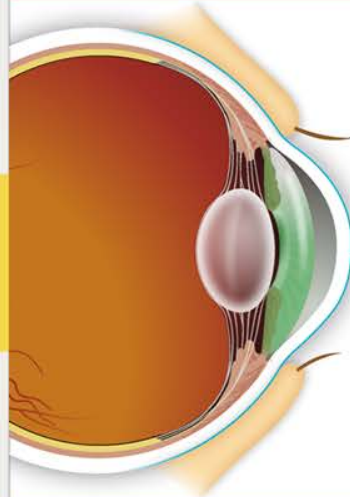
► Residence
Time

► Epithelium

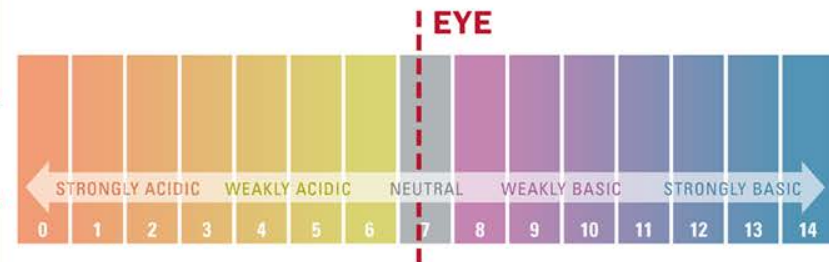
► Toxicity and
Sensitivity

► Mode of
Delivery

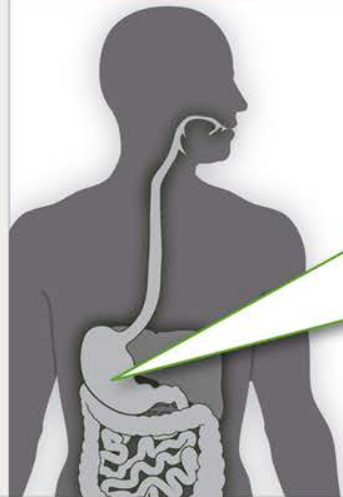
THE EYE DEFENDS



NEUTRAL pH ≈ 7.4



THE GUT ABSORBS



ACIDIC pH $\approx 1.0-2.0$



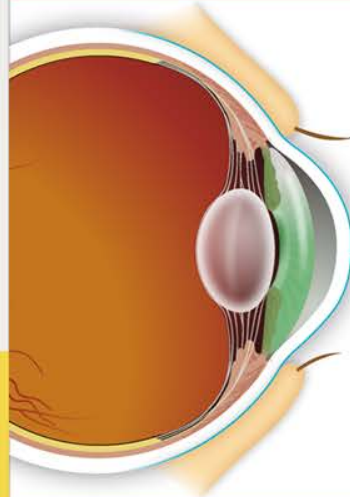
Topical vs. Oral Administration: Different Environment–Residence Time

THE EYE DEFENDS

► Surface Area/
Volume

► pH

► Residence
Time



EYE RESIDENCE



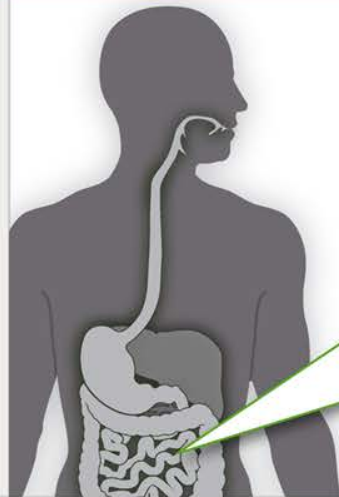
**A FEW
MINUTES**

THE GUT ABSORBS

► Epithelium

► Toxicity and
Sensitivity

► Mode of
Delivery



GI TRANSIT TIME



**SEVERAL
HOURS**

Topical vs. Oral Administration: Different Environment–Cells

► Surface Area/
Volume

► pH

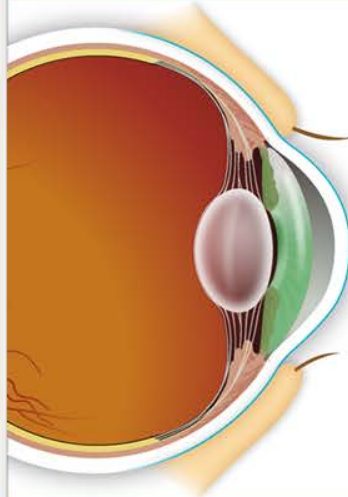
► Residence
Time

► **Epithelium**

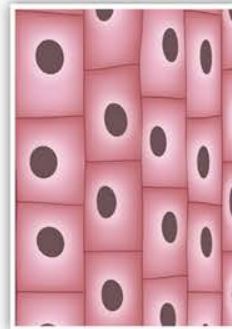
► Toxicity and
Sensitivity

► Mode of
Delivery

THE EYE DEFENDS



GEARED TOWARDS PROTECTION

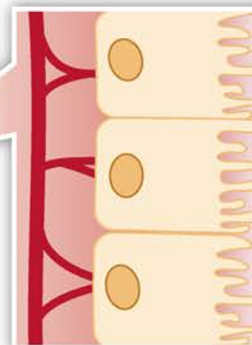


Conjunctival/
Corneal Epithelium:
MULTILAYERED,
Squamous shape

THE GUT ABSORBS



GEARED TOWARDS MAXIMUM ABSORPTION



**SINGLE
LAYER**,
Columnar
shape
(small intestine)

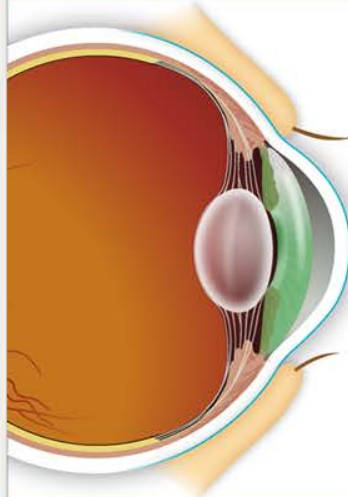
Topical vs. Oral Administration: Different Toxicity/Sensitivity

THE EYE DEFENDS

► Surface Area/
Volume

► pH

► Residence
Time



- Narrow tolerance
(grapefruit juice, lemon juice, hot sauce)

Lemon
Juice



Hot
Sauce



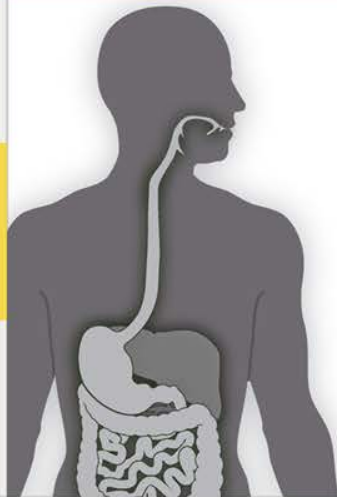
- Unique safety issues: FDA requires specialized safety testing (e.g., Draize Test)

THE GUT ABSORBS

► Epithelium

► Toxicity and
Sensitivity

► Mode of
Delivery



- Wider tolerance

Lemon
Juice



Hot
Sauce



- Systemic toxicity testing

Topical vs. Oral Administration: Different Delivery/Barriers

▸ Surface Area/
Volume

▸ pH

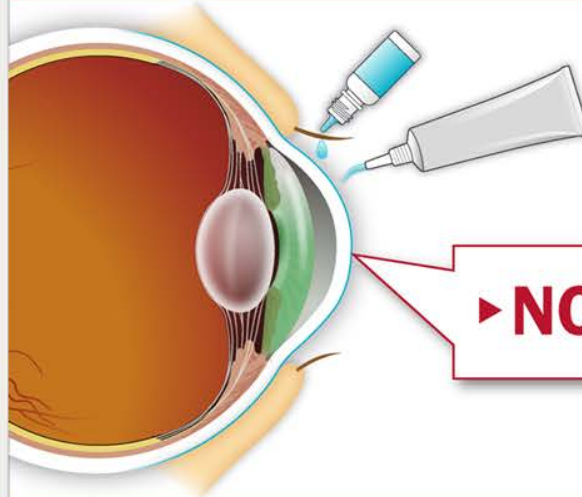
▸ Residence
Time

▸ Epithelium

▸ Toxicity and
Sensitivity

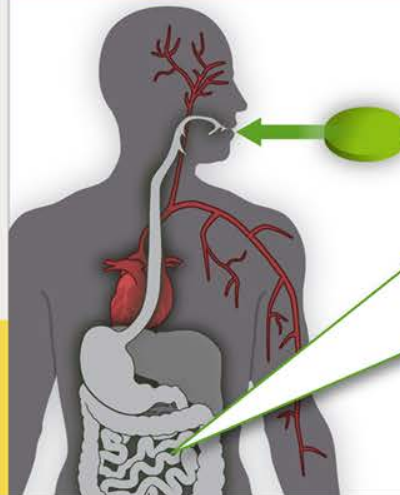
▸ Mode of
Delivery

THE EYE DEFENDS



▸ **NO** blood delivery

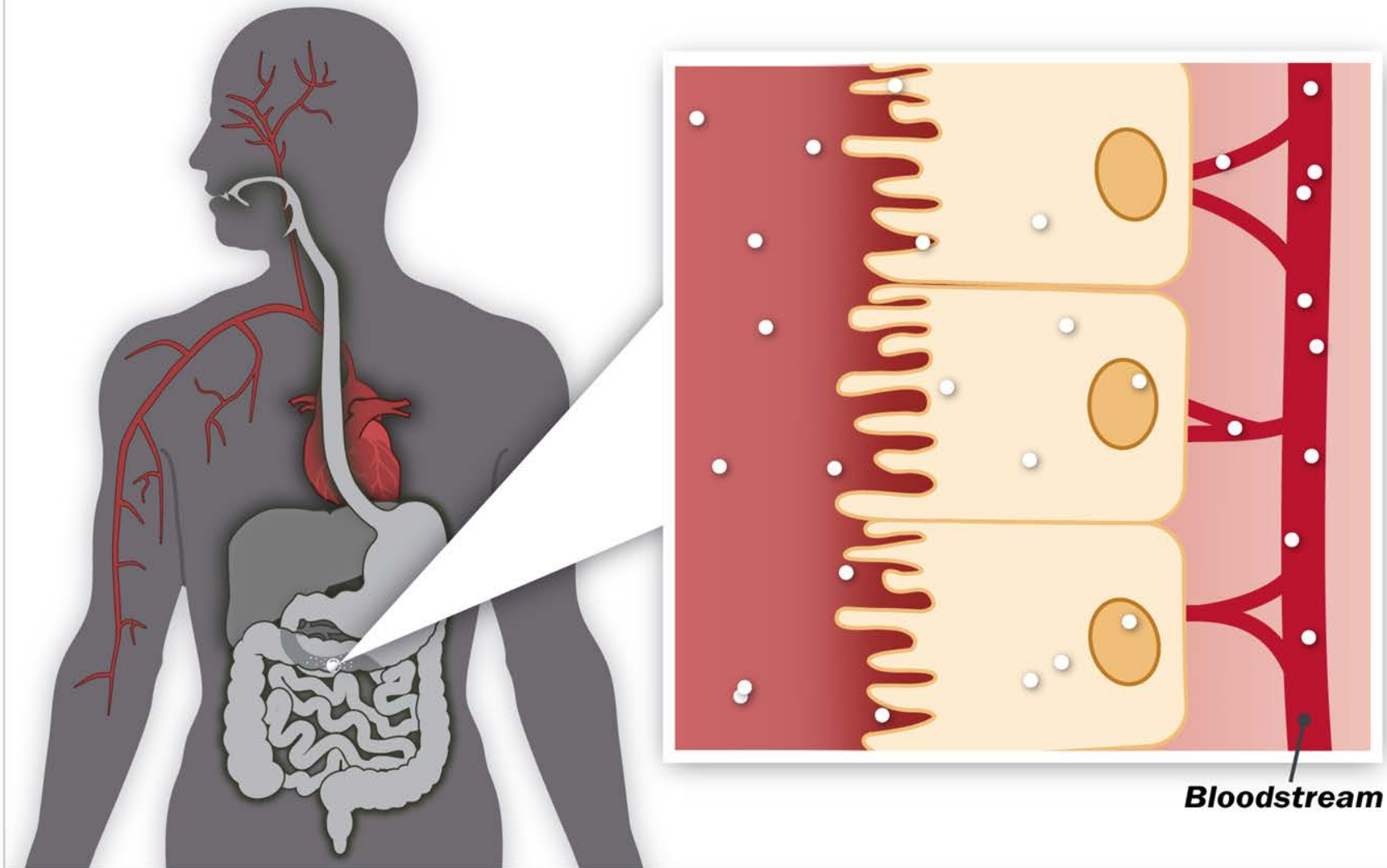
THE GUT ABSORBS



▸ **BLOOD DELIVERY**

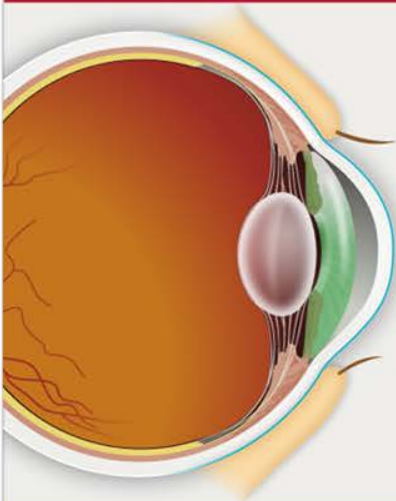
▸ **Phagocytosis** –
orally administered
azithromycin

Orally Administered Drugs Are **ABSORBED in the GI Tract and Carried by the Bloodstream to the Site of Infection**

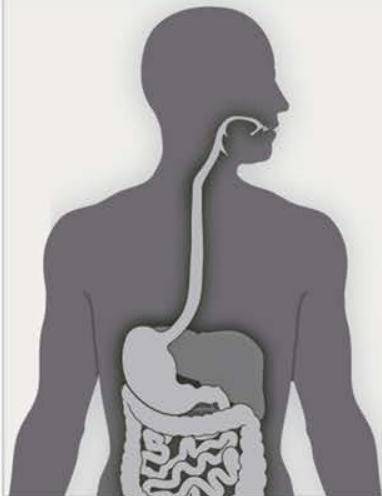


Topical **DOES NOT EQUAL** Oral

THE EYE DEFENDS



THE GUT ABSORBS



DIFFERENCES IN:

➤ Mode of delivery

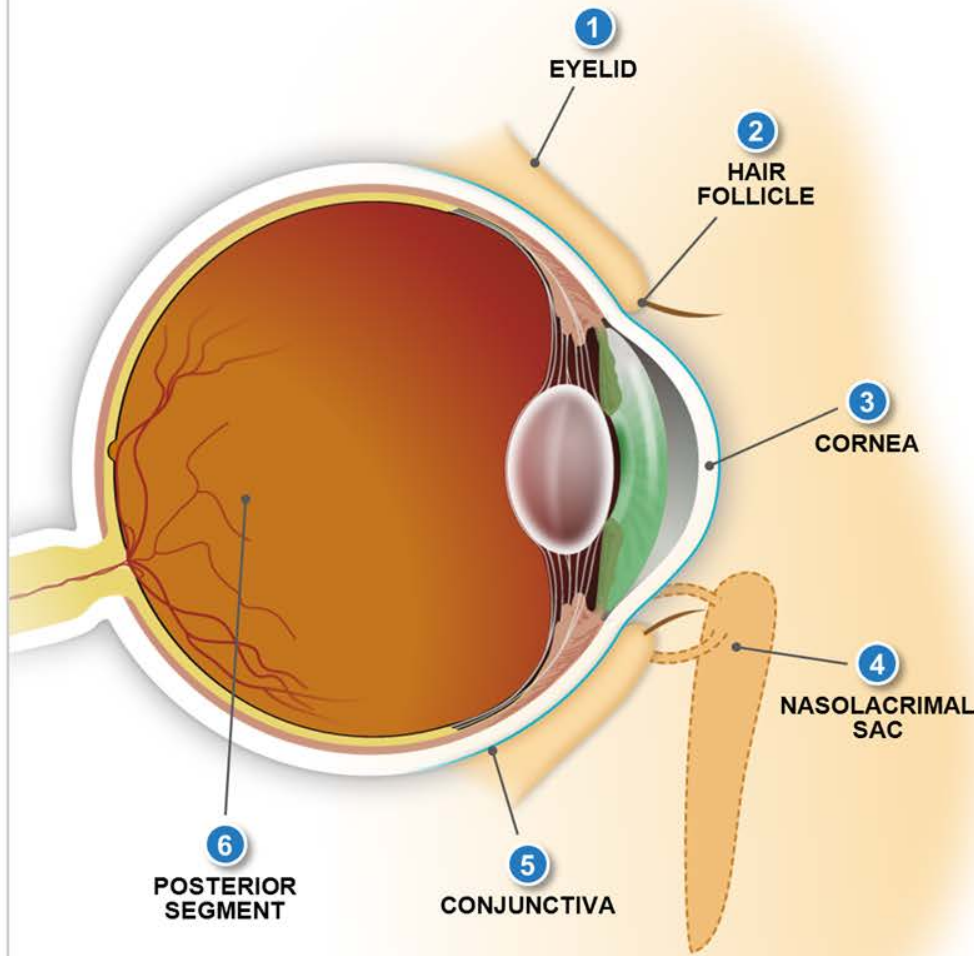
➤ Environment:

- Surface area and volume
- Epithelium
- pH
- Fluid composition
- Residence time

➤ Dosage regimen and form

➤ Toxicity and sensitivity

Ocular Infections Can Affect Many Ocular Structures



1 Eyelids:
Blepharitis

2 Hair Follicle:
Hordeolum

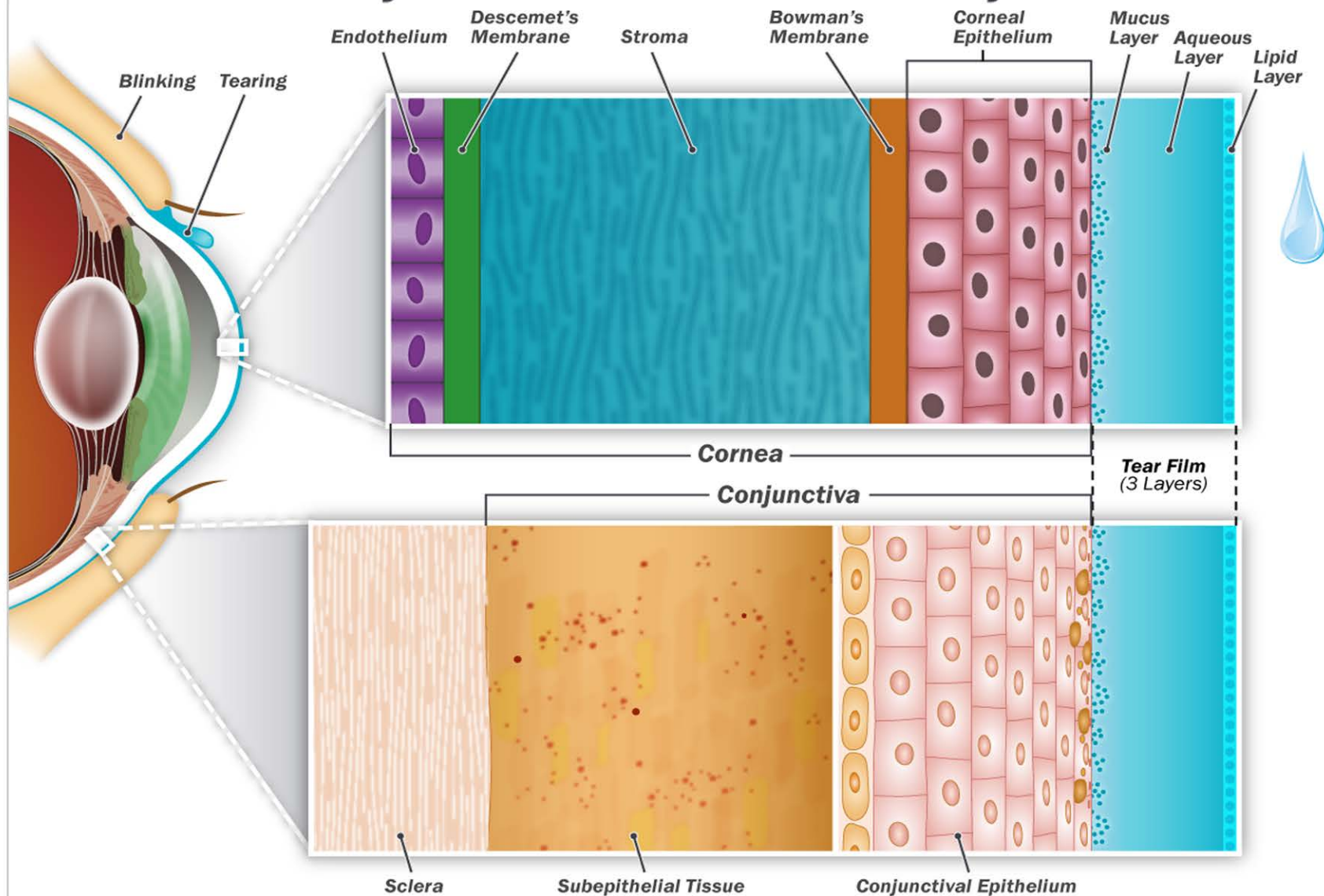
3 Cornea:
Keratitis, Abrasions, Ulcers

4 Nasolacrimal Sac:
Dacryocystitis

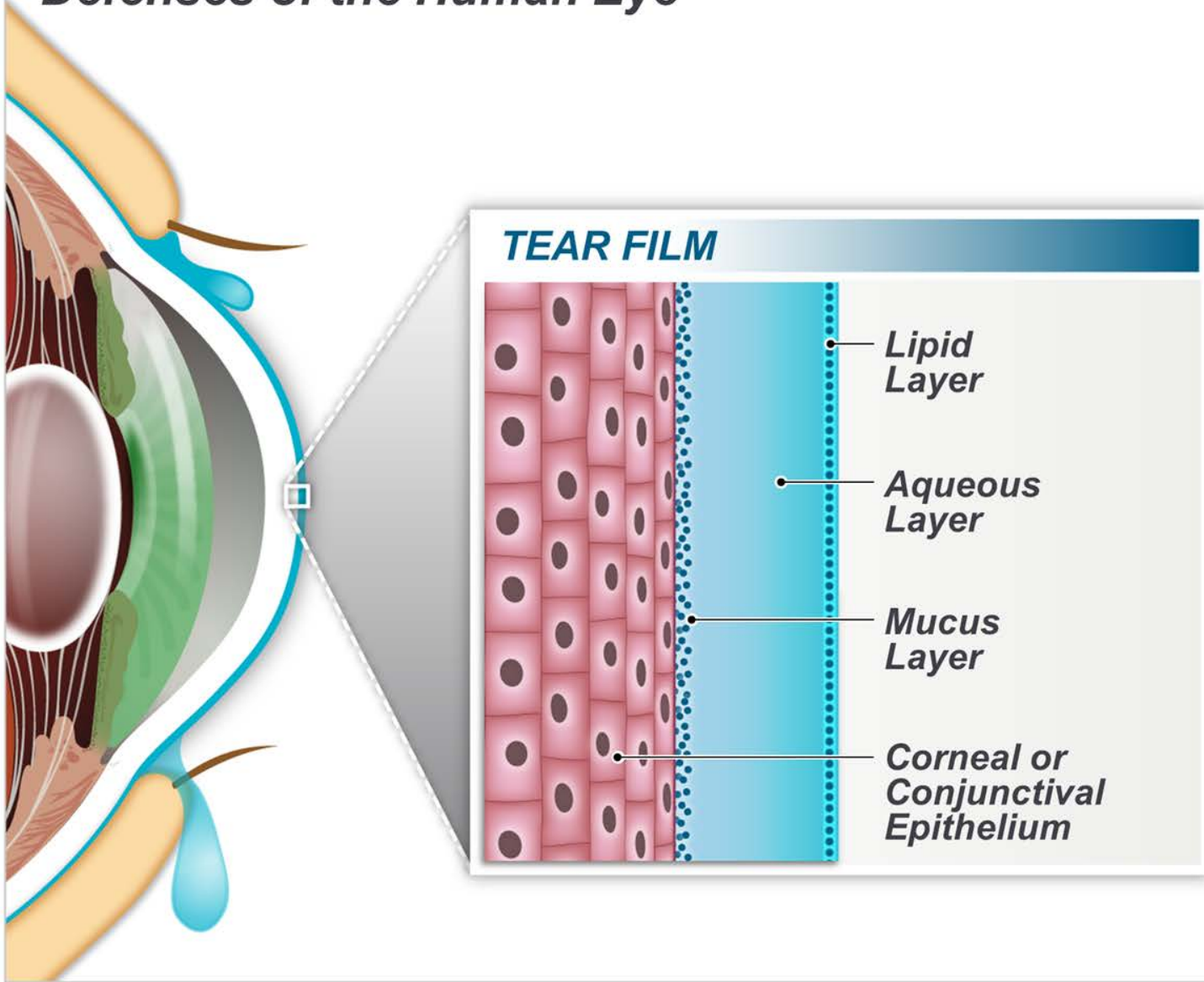
5 Conjunctiva:
Conjunctivitis

6 Posterior Segment:
Endophthalmitis

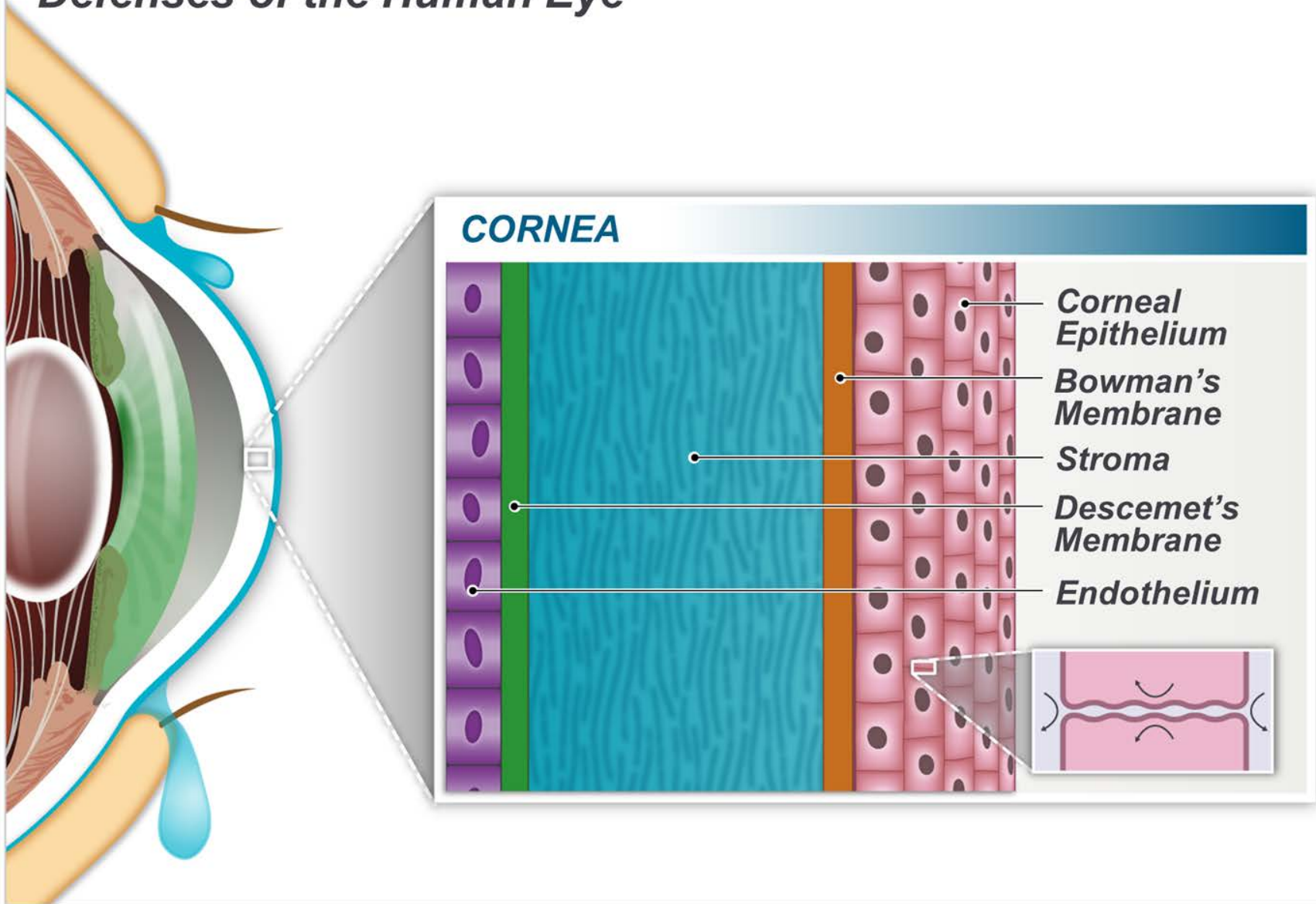
Anatomical Layers and Defenses of the Eye



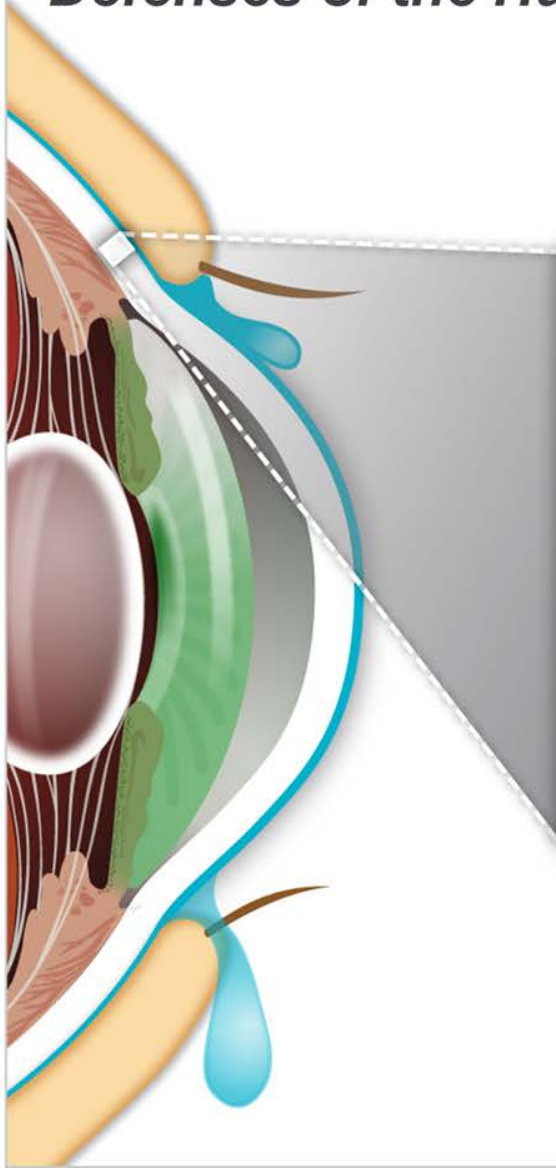
Defenses of the Human Eye



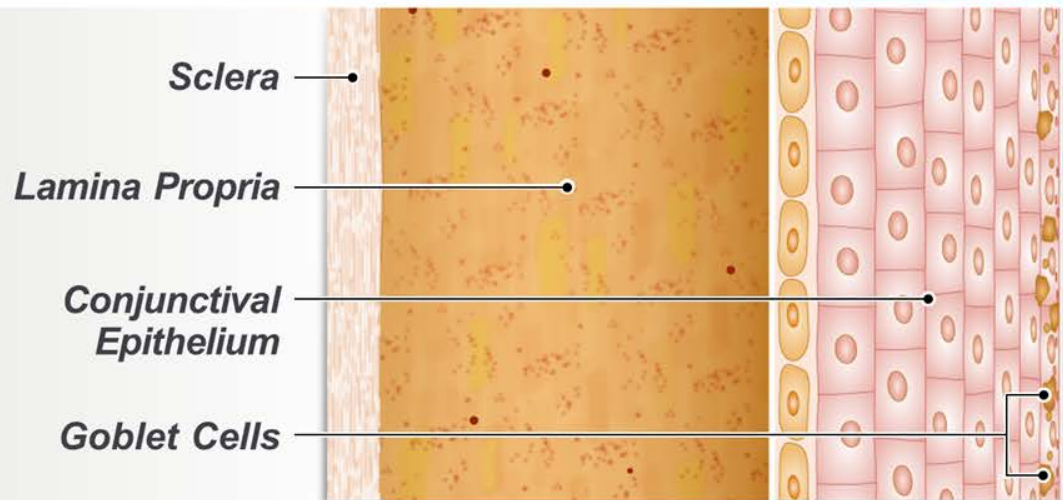
Defenses of the Human Eye



Defenses of the Human Eye



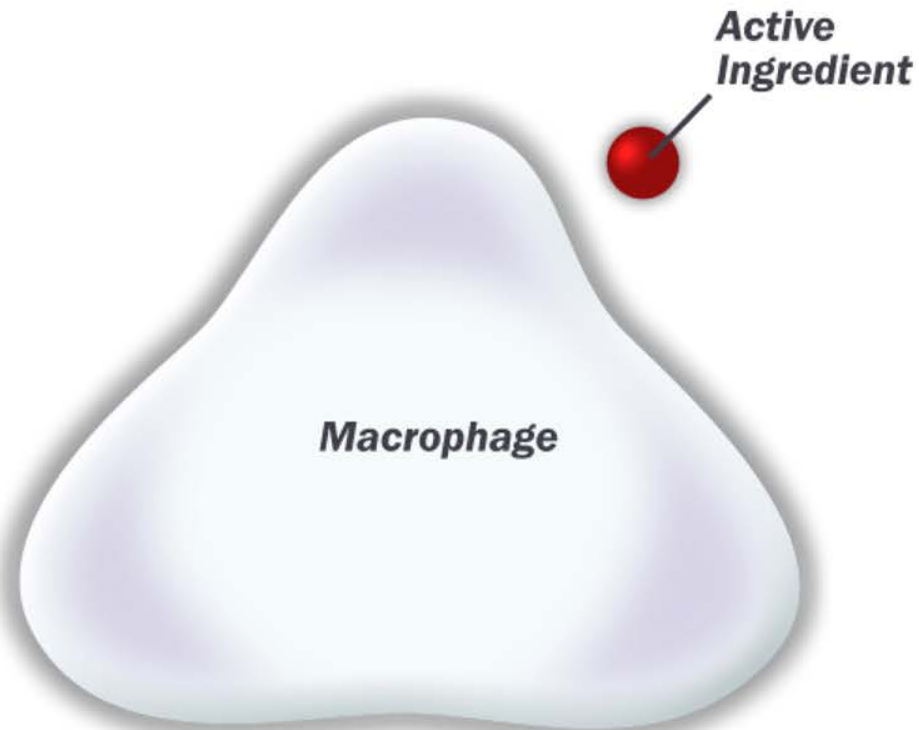
CONJUNCTIVA



Phagocytosis Can Affect Drug Concentration with Oral Administration

PHAGOCYTOSIS

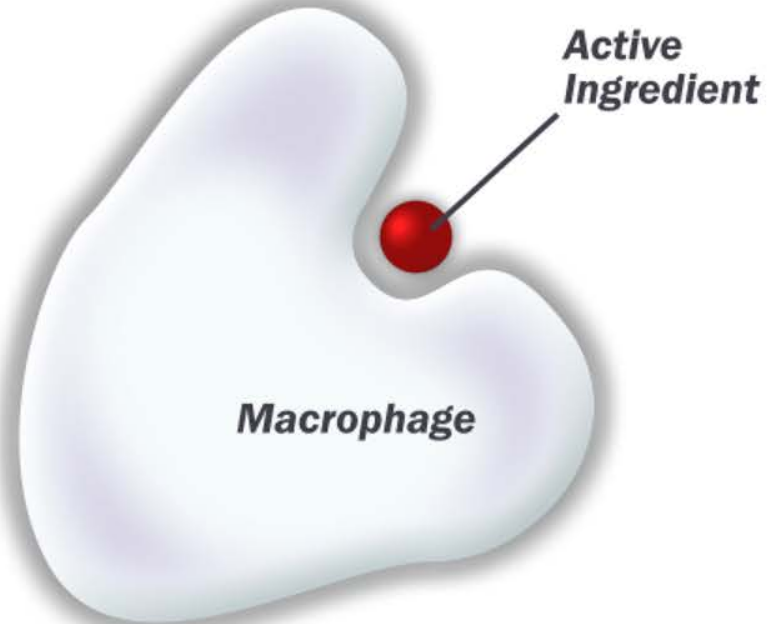
Special blood cells can take up the drug and carry it to the site of infection following oral drug administration.



Phagocytosis Can Affect Drug Concentration with Oral Administration

PHAGOCYTOSIS

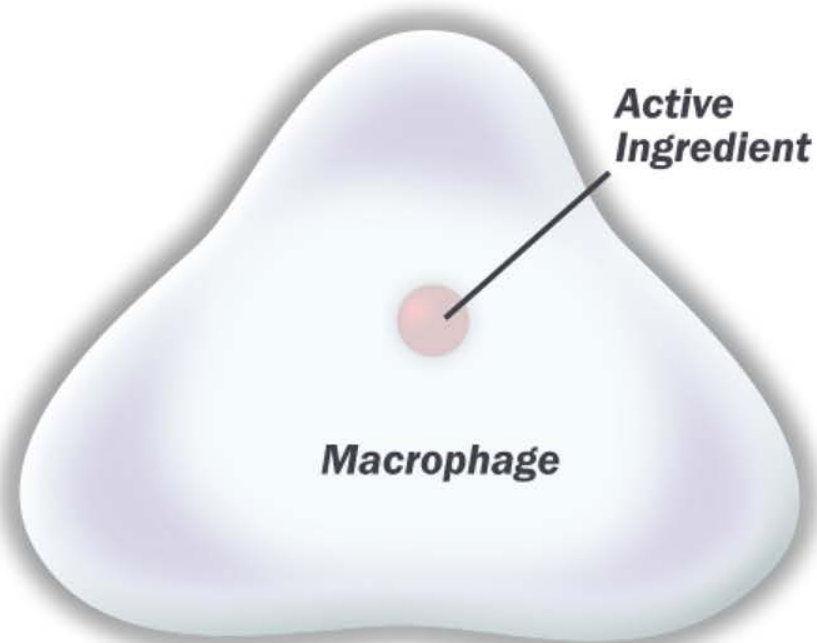
Special blood cells can take up the drug and carry it to the site of infection following oral drug administration.



Phagocytosis Can Affect Drug Concentration with Oral Administration

PHAGOCYTOSIS

Special blood cells can take up the drug and carry it to the site of infection following oral drug administration.



Viscosity Is the Measure of How Thick a Liquid Is or How Hard It Is for the Fluid to Flow

VISCOSITY



↑ Viscosity = ↑ Residence Time

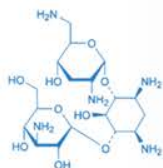
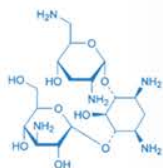
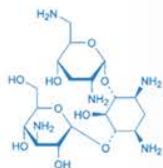
↑ Viscosity = ↓ Comfort

FDA Approval Process

TREATMENT OPTIONS

Active Ingredient?

- **Penetration?**
- **Duration?**
- **Safety?**



IN-VITRO TESTING



PRE-CLINICAL ANIMAL TESTING

FORMULATION DEVELOPMENT

- **Penetration?**
- **Duration?**
- **Safety?**
- **Dosing?**



IN-VITRO TESTING



PRE-CLINICAL ANIMAL TESTING



CLINICAL TRIALS IN HUMANS



TREATING PHYSICIAN

