Ocular Pharmacology

Pk & Pd,

and relevant considerations

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ΦΑΡΜΑΚΟΔΥΝΑΜΙΚΗ

Μια προσέγγιση με βάση τη Θεραπευτική

Overview

Πίνακας 4 **Περίληψη των φαρμάκων που χρησιμοποιούνται στην Οφθαλμολογία**

	Παραδείγματα σε συχνή χρήση	Τρόπος εφαρμογής	Δράση	Παρενέργειες
Θεραπεία γλαυκώματος (σημειώστε ότι διαφορετικοί τύποι γλαυκώματος μπορεί να απαιτούν διαφορετική θεραπευτική προσέγγιση)	Βήτα-αποκλειστές: τιμολόλη, καρτεολόλη, βεταξολόλη, λεβομπουνολόλη	Τοπική	Μειώνουν την παραγωγή υδατοειδούς υγρού αποκλείοντας τους βήτα-αδρενεργικούς υποδοχείς του ακτινωτού σώματος	Οφθαλμικές: ερεθισμός Συστηματικές: βρογχόσπασμος, βραδυκαρδία, επίταση της καρδιακής ανεπάρκειας, εφιάλτες
	Μουσκαρινικοί (παρασυμπαθητικοί) αγωνιστές: πιλοκαρπίνη	Τοπική	Αυξάνουν την αποχέτευση του υδατοειδούς υγρού διά του ηθμού μέσω σύσπασης του ακτινωτού μυός	Οφθαλμικές: μύση (ελάττωση όρασης επί παρουσίας καταρράκτη, εμποδίζει την επισκόπηση του αμφιβληστροειδούς), σπασμός προσαρμογής, μετωπιαία κεφαλαλγία Συστηματικές: εφίδρωση, βραδυκαρδία, γαστρεντερικές διαταραχές
	Άλφα 2 -αγωνιστές: βριμονιδίνη, απρακλονιδίνη	Τοπική	Μειώνουν την παραγωγή του υδατοειδούς υγρού με εκλεκτική διέγερση των άλφα 2-αδρενεργικών υποδοχέων του ακτινωτού σώματος και αυξάνουν την αποχέτευση διά της ραγοειδοσκληρικής οδού	Οφθαλμικές: αλλεργία, μυδρίαση, ανάσπαση των βλεφάρων Συστηματικές: ξηροστομία, υπόταση, αίσθημα κόπωσης, πονοκέφαλος
	Latanoprost	Τοπική	Είναι ένα ανάλογο προσταγλανδινών αυξάνει την αποχέτευση του υδατοειδούς υγρού διά της ραγοειδοσκληρικής οδού	Οφθαλμικές: αλλαγή του χρώματος της ίριδας, υπεραιμία επιπεφυκότων Συστηματικές: πικρή γεύση
	Αναστολείς της καρβονικής ανυδράσης	Συστηματική (ακεταζολαμίδη), τοπική (ντορζολαμίδη)	Μειώνουν την παραγωγή υδατοειδούς υγρού από το ακτινωτό σώμα	Οφθαλμικές (το φάρμακο): ερεθισμός, αλλεργία Συστηματικές (γενικά η συστηματική χορήγηση): κακουχία, παραισθησίες, διαταραχές ουρίας και ηλεκτρολυτών, απλαστική αναιμία
Μυδριατικά και κυκλοπληγικά (για την εξέταση του αμφιβληστροειδούς και την αντικειμενική διάθλαση (σκιασκοπία)	Αντιμουσκαρινικά: τροπικαμίδη,κυκλοπεντολάτη, ατροπίνη	Τοπική	Αποκλείουν τους μουσκαρινικούς υποδοχείς του παρασυμπαθητικού νευρικού συστήματος οπότε παραλύει ο σφιγκτήρας της κόρης και το ακτινωτό σώμα	Οφθαλμικές: θόλωση όρασης (ειδικά για κοντά), θάμπωμα, γλαύκωμα κλειστής γωνίας Συστηματικές: ταχυκαρδία, ξηροστομία, σύγχυση, τρόμος
	Άλφα-αγωνιστές: φαινυλεφρίνη	Τοπική	Διεγείρει τον διαστολέα μυ της κόρης δεν έχει κυκλοπληγική δράση	Οφθαλμικές: θόλωση όρασης, θάμβος, γλαύκωμα κλειστής γωνίας, λευκό χρώμα επιπεφυκότων Συστηματικές: υπέρταση
Εφυγραντικές ουσίες Μια ποικιλία σκευασμάτων είναι διαθέσιμα για την θεραπεία της ξηροφθαλμίας	Carbomers, hypromellose, πολυβινυλλική αλκοόλη, υγρή παραφίνη	Τοπική	Ο ακριβής μηχανισμός εξαρτάται από την ουσία	Οφθαλμικές: αλλεργία/τοξικότητα συντηρητικών, θόλωση όρασης (ιδίως οι αλοιφές)
Αντιφλεγμονώδεις παράγοντες. Τα πιο σημαντικά φάρμακα είναι αυτά της κατηγορίας των κορτικοστεροειδών μια ποικιλία άλλων παραγόντων είναι επίσης διαθέσιμα, συμπεριλαμβανομένων και των συστηματικών ανοσοκατασταλτικών	Κορτικοστεροειδή: πρεδνιζολόνη, βηταμεθαζόνη, δεξαμεθαζόνη	Τοπική, περιοφθάλμια ένεση, συστηματική	Καταστολή μιας ευρείας ομάδας φλεγμονωδών διεργασιών	Οφθαλμικές: γλαύκωμα (ιδίως κατά την τοπική χρήση) καταρράκτης (ιδίως σε παρατεταμένη συστηματική χρήση), έξαρση μερικών λοιμώξεων όπως π.χ. του απλού έρπητα Συστηματικές: Ανήμιαντες κατά την τοπική χρήση συχνές και ποικίλλουσες
	Σταθεροποιητές των μαστοκυττάρων (χρωμογλυκίνη, νεδοχρομίλη, alomide)	Τοπική	Σταθεροποιούν τα μαστοκύτταρα	Οφθαλμικές: ερεθισμός
	Αντισταμινικά	Τοπική (λεβοκαμπαστίνη), συστηματική (χλωροφενιραμίνη, τερφεναδίνη, κετιριζίνη)	Αντιϊσταμινική	Οφθαλμικό σκεύασμα: ερεθισμός Συστηματικά φάρμακα: υπνηλία
	Μη-στεροειδή αντιφλεγμονώδη φάρμακα: συστηματική βοήθεια για να ελεγχθεί ο οφθαλμικός πόνος και η φλεγμονή η τοπική τους χρήση αυξάνεται συνεχώς για την αντιμετώπιση του πόνου σε τραύμα κερατοειδούς, για την φλεγμονή μετά από εγχείρηση καταρράκτη, και για να διατηρηθεί η μυδρίαση κατά την διάρκεια της εγχείρησης καταρράκτη	Τοπική, συστηματική	Ρυθμίζουν την παραγωγή προσταγλανδινών	Συστηματικές: πεπτικό έλκος, άσθμα
Χημειοθεραπευτικά Τοπικά χορηγούμενα αντιβακτηριδιακά και αντιικά φάρμακα συνταγογραφούνται συχνά· η χρήση αντιμυκητιασικών και αντιπαρασιτικών ουσιών είναι πολύ λιγότερο συχνή	Αντιβακτηριδιακά: χλωραμφενικόλη, γενταμικίνη, σιπροφλοξασίνη, νεομυκίνη, φουκιδικό οξύ	Τοπική, ορισμένα ενδοφθάλμια, συστηματική	Ένα ολόκληρο φάσμα δράσεων και εξειδικευμένων ενεργειών	Ποικίλουν ανάλογα με την ουσία Οφθαλμικές: αλλεργία τοξικότητα ενστάλαξη Συστηματικές: συνήθως μόνο σε πολύ συστηματική χορήγηση
	Αντι-ιϊκά: ασυκλοβίρη	Τοπική, συστηματική, ενδούαλοειδική	Εμποδίζει τη σύνθεση DNA του ερπητοϊού	Οφθαλμικές: θόλωση όρασης, τοξικότητα κερατοειδούς Συστηματικές: εξάνθημα ανεπιθύμητες ενέργειες στο νεφρό, το ήπαρ και σε άλλα όργανα μπορεί να συμβούν σε συστηματική χορήγηση
Τοπικά αναισθητικά Η κύρια χρήση τους είναι να ανακουφίσουν από τον πόνο και επομένως βοηθούν στην κλινική εξέταση, και συνεπικουρούν στην χειρουργική αναισθησία	Oxybuprocaine, amethocaine, lignocaine	Τοπική, περιοφθαλμική ένεση	Αποκλείουν την μεταβίβαση ερεθισμάτων κατά μήκος των νευρικών ινών	Οφθαλμικές: ερεθισμός, τοξικότητα κερατοειδούς Συστηματικές: σε περίπτωση λανθασμένη ενδοαγγειακής ή εντός των μηνίγγων στην (εγκεφαλονωτιαίο υγρό) ένεσης κατά τη διάρκεια χειρουργικής αναισθησίας αρρυθμίες, καταστολή αναπνευστικού
Βοτουλική τοξίνη: χρησιμοποιείται στην αντιμετώπιση συγκεκριμένων διαταραχών της οφθαλμικής κινητικότητας και του βλεφαρόσπασμου, και για να προκαλέσει πτώση του άνω βλεφάρου για την προστασία του κερατοειδούς		Ένεση στην περιοχή της δράσης της	Εμποδίζει την απελευθέρωση του νευροδιαβιβαστή ακετυλοχολίνη στις νευρομυικές συνάψεις	Εξαρτάται από τη θέση της θεραπευτικής εφαρμογής: π.χ. ανεπιθύμητη πτώση του άνω βλεφάρου η διπλωπία

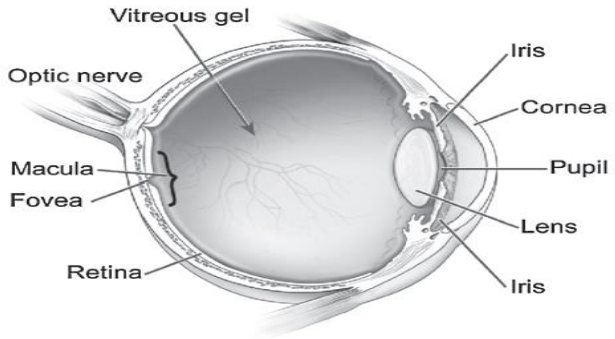


Figure 1. Anatomy of human eye.

Table 1. List of Marketed Ophthalmic Pharmaceuticals (US, Topical, Unless Specified Otherwise)

Antibacterials
- Chloramphenicol
- Aminoglycosides
  - Gentamicin
  - Tobramycin
- Macrolides
  - Azithromycin
- Fluoroquinolones
  - Ciprofloxacin
  - Gatifloxacin
  - Moxifloxacin
  - Ofloxacin
- Cephalosporins
  - Cefixime (intracameral, Europe)

Antifungals
- Natamcyin
- Propamidine (UK)

Antivirals
- Cidofovir (intravitreal)
- Fomivirsen (intravitreal)
- Ganciclovir (intravitreal implant)
- Idoxuridine
- Trifluorothymidine
- Valganciclovir (oral)

Dry Eye Disease
- Cyclosporine (Restasis® in the US, Ikervis® in the EU)
- Diquafasol (Diquas®, Japan)
- Hyaluronic acid (Hyalein®, Japan)
- Rebamipide (Mucosta®, Japan)

Glaucoma/Ocular Hypertension
- Prostaglandins
  - Bimatoprost
  - Latanoprost
  - Tafluprost
  - Travoprost
  - Unoprostone
- β-Adrenoceptor Antagonists
  - Betaxolol
  - Carteolol
  - Levobunolol
  - Metoprolol
  - Timolol (maleate and hemihydrate salts)
- Adrenergic Agonists
  - Apraclonidine
  - Brimonidine
  - Dipivefrin
  - Epinephrine
- Carbonic Anhydrase Inhibitors
  - Brinzolamide
  - Dorzolamide
- Antifibrotic Agent (During Surgery)
  - Mitomycin

Inflammation
- Corticosteroids
  - Dexamethasone (topical, intravitreal, Ozurdex®)
  - Fluocinolone acetonide (Retisert®, Ileuvin®)
  - Fluorometholone
  - Prednisolone acetate
  - Triamcinolone acetonide (Triescence®, Trivaris®)
- Nonsteroidal Anti-Inflammatory Agents
  - Bromfenac
  - Diclofenac
  - Flurbiprofen
  - Ketorolac
  - Nepafenac

Allergy
- Antihistamines
  - Alcaftadine
  - Azelastine
  - Bepotastine
  - Epinastine
  - Ketotifen
  - Olopatadine (Patanol®, Pataday®, Pazeo®—various formulations)
  - Pheniramine
- Mast cell stabilizer
  - Amlexanox
  - Cromoglycate

Surgery
- Antimuscarinics
  - Atropine
  - Tropicamide
  - Cyclopentolate
- Sympathomimetics
  - Phenylephrine
- Cholinergic agonists
  - Acetylcholine
  - Carbachol
- Ketorolac/phenylephrine

Retina—Choroidal Neovascularization due to Macular Degeneration
- Verteporfin (IV)
- VEGF inhibitors*
  - Aflibercept (intravitreal)
  - Pegaptanib (intravitreal)
  - Ranizibumab (intravitreal)

Strabismus and Blepharospasm
- Botulinum toxin (OnabotulinumtoxinA)

There are also fixed-dose combinations. These include corticosteroid-antibiotics and ocular hypotensive medications.

*Some of the VEGF inhibitors are also approved for the treatment of diabetic macular edema and diabetic retinopathy due to diabetic macular edema.

Table 1.1 Significant milestones in the development of drugs for ocular therapeutics

1831	Atropine isolated in crystalline form
1870	Physostigmine isolated
1875	Pilocarpine isolated
1885	Effect of pilocarpine on IOP recorded
1920	Nonselective sympathomimetics (epinephrine and dipivefrin)
1950	Oral carbonic anhydrase inhibitors (acetazolamide)
1970	Beta-blockers (timolol, levobunolol)
1990	Topical carbonic anhydrase inhibitors, fluoroquinolones antibacterial photodynamic therapy
2000	Intraocular antiangiogenic agents (ranibizumab, bevacizumab, pegaptanib)

Generic name	
Brand names	Common trade names
Class of drug	Therapeutic class
Indications	Common uses of the drug
Dosage form	Common forms of the drug
Dose	The amount of drug to be given or taken during therapy. The dosage is to be taken as a guideline and does not preclude other dosage regimens
Contraindications	Information pertaining to inappropriate use of the drug
Warnings	Hazardous conditions related to use of the drug and disease states or patient populations in which the drug should be used cautiously
Adverse reactions	Considerations to be taken into account
Pregnancy category	FDA categories that indicate the potential for causing birth defects
A	Controlled studies in pregnant women have failed to demonstrate a risk to the fetus in the first trimester with no evidence of risk in later trimesters. The possibility of fetal harm appears remote
B	Either animal-reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal-reproduction studies have shown an adverse effect that was not confirmed in controlled studies in women in the first trimester and there was no evidence of a risk in later trimesters
C	Either studies in animals have revealed adverse effects on the fetus (teratogenic, embryocidal effects, or other) and there are no controlled studies in women, or studies in women and animals are not available. Drugs should be given only if the potential benefits justify the potential risk to the fetus
D	There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective)

Generic name	
X	Studies in animals or humans have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience, or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant
Drug interactions	Only clinically important interactions are listed

Latanoprost

Brand Name Xalatan.

Class of Drug Glaucoma. Prostanoid-selective prostaglandin F (FP) receptor agonist.

Indications Reduction of elevated IOP in patients with OAG or ocular hypertension.

Dosage Form Topical ophthalmic solution 0.005% (50 μg/ml).

Dose 1 drop to affected eye(s) once per day in the evening; dosage should not exceed once per day since it has been shown that more frequent administration may decrease IOP-lowering effect. Reduction of IOP starts approximately 3–4 h after administration and the maximum effect is reached after 8–12 h.

Contraindications In patients with known hypersensitivity to the product or any of its components or to benzalkonium chloride.

Warnings Reported to cause changes to pigmented tissues. Most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid) and eyelashes, and growth of eyelashes; pigmentation is expected to increase as long as Xalatan is administered. After discontinuation, pigmentation of the iris is likely to be permanent while pigmentation of the periorbital tissue and eyelash changes has been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The effects of increased pigmentation beyond 5 years are not known.

May gradually increase pigmentation of the iris. The eye-color change is due to increased melanin content in the stromal melanocytes of the iris rather than to an increase in the number of melanocytes. This change may not be noticeable for several months to years Typically, the brown pigmentation around the pupil spreads concentrically toward the periphery of the iris, and the entire iris or parts of it become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly. During clinical trials, the increase in brown iris pigment has not been shown to progress further upon discontinuation of treatment, but the resultant color change may be permanent.

Eyelid skin darkening, which may be reversible, has been reported. Gradual changes to eyelashes and vellus hair around the treated eye include increased length, thickness, pigmentation, number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are usually reversible upon discontinuation of treatment.

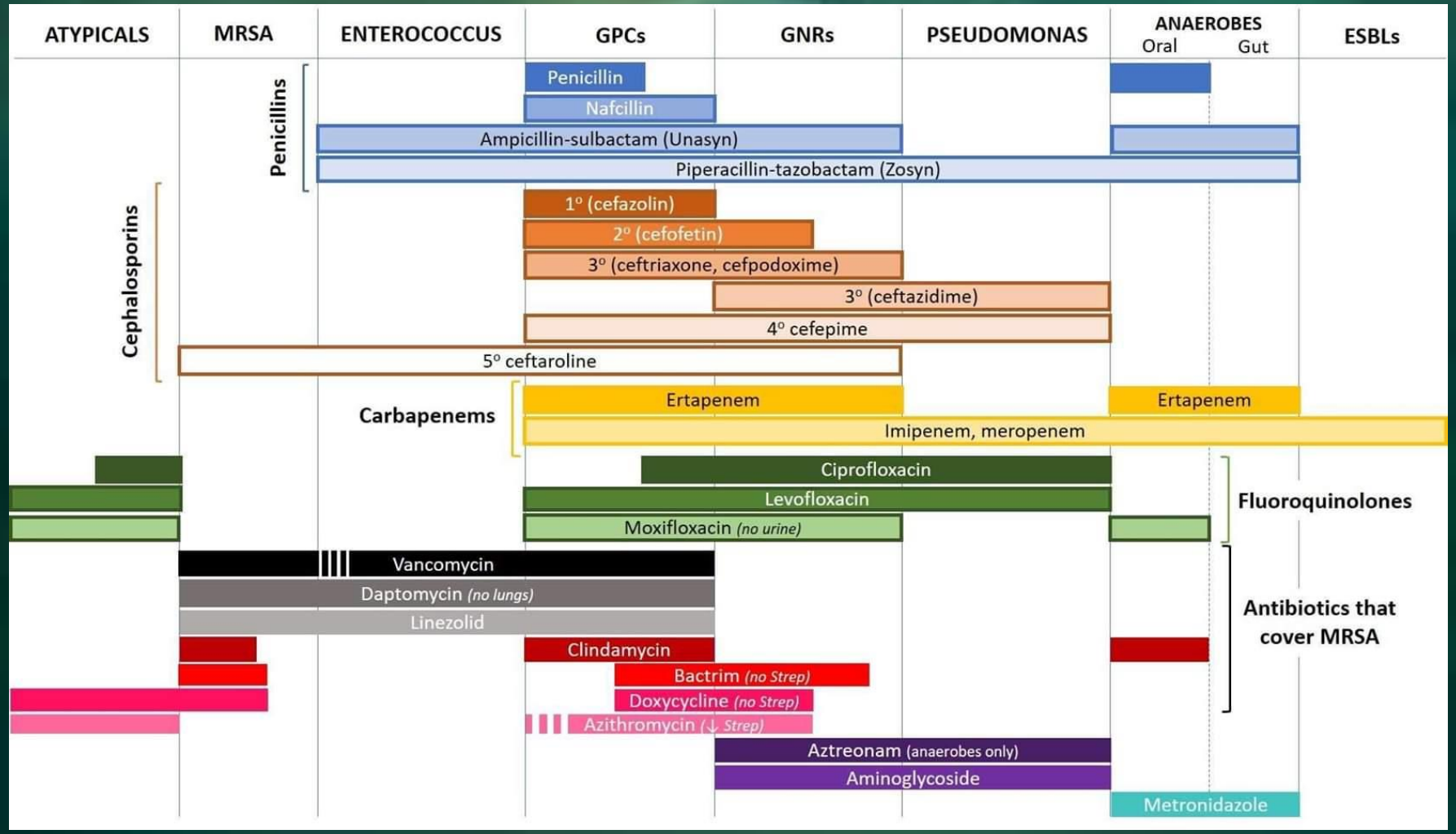
Adverse Reactions Eyelash changes (increased length, thickness, pigmentation, and number of lashes); eyelid skin darkening; intraocular inflammation (iritis/uveitis); iris pigmentation changes; and macular edema, including cystoid macular edema, which have mainly occurred in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema. Should be used with caution in patients who do not have an intact posterior capsule or who have known risk factors for macular edema and in patients with a history of intraocular inflammation (iritis/uveitis); should generally not be used in patients with active intraocular inflammation. There is limited experience in the treatment of angle closure, inflammatory, or neovascular glaucoma.

Controlled clinical trials: Symptoms reported in 5–15% of patients—blurred vision, burning and stinging, conjunctival hyperemia, foreign-body sensation, itching, increased pigmentation of the iris, and punctate epithelial keratopathy. Local conjunctival hyperemia was observed; however, less than 1% of the patients required discontinuation of therapy because of intolerance to conjunctival hyperemia. Symptoms reported in 1–4% of patients—dry eye, excessive tearing, eye pain, lid crusting, lid discomfort/pain, lid edema, lid erythema, photophobia. Symptoms reported in less than 1% of patients—conjunctivitis, diplopia, and discharge. Extremely rare reports—retinal artery embolus, retinal detachment, vitreous hemorrhage from diabetic retinopathy. Most common systemic adverse events—URTI/cold/flu, which occurred at a rate of approximately 4%. Chest pain/angina pectoris, muscle/joint/back pain, and rash/allergic skin reaction each occurred at a rate of 1–2%. *Postmarketing use in clinical practice*: asthma and exacerbation of asthma; corneal edema and erosions; dyspnea; eyelash and vellus hair changes (increased length, thickness, pigmentation, and number); eyelid skin darkening; herpes keratitis; intraocular inflammation (iritis/uveitis); keratitis; macular edema, including cystoid macular edema; misdirected eyelashes, sometimes resulting in eye irritation; toxic epidermal necrolysis.

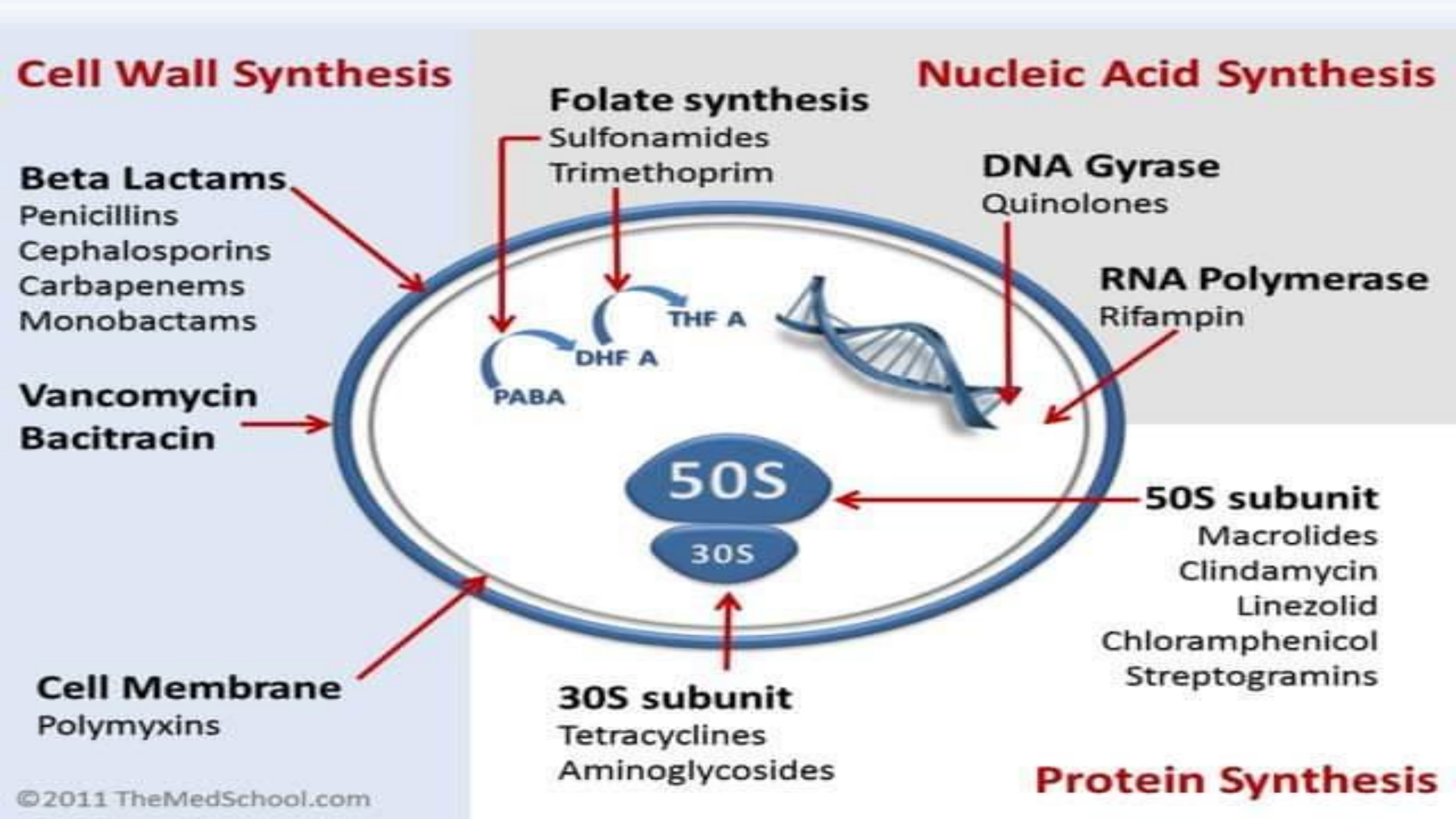
Pregnancy Category C.

Drug Interactions In vitro studies have shown that precipitation occurs when eye drops containing thimerosal are mixed with Xalatan. If such drugs are used, they should be administered at least 5 min apart.

Φάρμακα κατά των οφθαλμικών λοιμώξεων



Inhibit		Classification		Antibiotics			
Cell Wall SYNTHESIS	Beta Lactams	Penicillins	Penicillinase-Sensible				
			Natural Penicillins (Narrow Spectrum)	Penicillin G: Na, K, Procainic, Benzathine(IV, IM) Penicillin V: VO			
			Aminopenicillins (Broad Spectrum)	Ampicillin Amoxicillin			
			Penicillinase — Resistant (very narrow spectrum)				
			Nafcillin	Oxacillin	Dicloxacillin		
			Antipseudomonal (extended spectrum)				
			Carboxipenicillins	Ticarcillin- Carbenicillin			
			Ureidopenicillins	Azlocillin — Mezlocillin - Piperacillin			
		Cephalosporins	1 st Generation	Cefazolin	Cephalexine	Cephapirin	
				Cefadroxil	Cephadrine	Cephalotin	
			2 nd Generation	Cefuroxime	Cefoxitin	Cefotetan	
				Cefamandole	Cefonicid	Cefaclor	
				Cefprozil	Cefmetazole		
			3 rd Generation	Cefoperazone	Ceftriaxone	Ceftazidime	
				Cefpodoxime	Ceftizoxime	Cefotaxime	
				Cefdinir	Ceftibuten	Cefixime	
				Cefditoren			
			4 th Generation	Cefepime	Cefpirome		
			5 th Generation	Ceftaroline			
		Carbapenems		Meropenem	Ertapenem	Doripenem	Imipenem + Cylastatine
		Monobactams		Aztreonam			
		Beta-lactamase inhib.		Sulbactam	Tazobactam	Clavulinic acid	
	No lactam	Glycopeptides		Vancomycin	Bacitracin		
				Teicoplanin	Polymyxin B		
Protein Synthesis		S30	Amino-glycoside	Gentamycin	Neomycin	Streptomycin	
				Amikacin	Tobramycin		
			Tetracyclins	Doxycycline	Demeclocyclin	Minocycline	
				Tetracyclin	Tigecyclin		
		S60	Oxazolidonones	Linezolid			
			Streptogramins	Quinupristin/Dalfopristin			
			Chloramphenicol				
			Macrolides	Erythromycin	Azithromycin	Clarithromycin	
			Lincosamides	Clindamycin	Lincomycin		
DNA toboisomerases		Fluoroquinolones		Ciprofloxacin	Norfloxacin	Levofloxacin	Ofloxacin
				Sparfloxacin	Moxifloxacin	Gemifloxacin	Enofloxacin
		Quinolones		Nalidixic Acid			
Folic Acid Synthesis		Sulfonamides		Sulfamethoxazole (SMX)	Ag Sulfadiazine	Sulfasalazine	Sulfisoxazole
		DHFR inhibitors		Trimethoprim	Pirymethamine		
DNA (damage)		Metronidazole					
mRNA synthesis		Rifampin					


Cell Wall Synthesis
Nucleic Acid Synthesis
Folate synthesis
Sulfonamides
Trimethoprim
Beta Lactams
Penicillins
Cephalosporins
Carbapenems
Monobactams
DNA Gyrase
Quinolones
RNA Polymerase
Rifampin
THF A
DHF A
PABA
Vancomycin
Bacitracin
50S
30S
50S subunit
Macrolides
Clindamycin
Linezolid
Chloramphenicol
Streptogramins
Cell Membrane
Polymyxins
30S subunit
Tetracyclines
Aminoglycosides
Protein Synthesis
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- Ένδειξη: Οφθαλμικές λοιμώξεις από παθογόνους μικροοργανισμούς
  - Εμπειρικά (ευρέως φάσματος) ή βάση αντιβιογράμματος

Σταφυλόκοκκος Χρυσίζων

Κεφταρολίνη	Ε
Αμπικιλλίνη	Α
Αμπικιλλίνη/ σουλμπακτάμη	Ε
Οξακιλλίνη	Α
Κεφοξιτίνη	Α
Ιμιπενέμη	Ε
Βανκομυκίνη	Ε

FROM THE LITERATURE

NEW BENCHMARKS ON ANTIBIOTIC RESISTANCE

The five-year Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) study data was recently published in *JAMA Ophthalmology* (December 2015). This is reportedly the most robust evaluation of nationwide antibacterial susceptibility of common ocular pathogens to date. Thankfully, resistance rates have remained stable over the past five years of this study.

About half of *Staphylococcus* species are methicillin resistant, meaning they are more difficult to kill than the methicillin-sensitive bacterial pathogens. Minimal inhibitory concentration–90 (MIC_{90}) represents how effective a drug is at eradicating a bacterial species—i.e., the lowest concentration of a drug that will inhibit 90% of bacterial isolates. To interpret these results: the lower the MIC_{90}, the more effective the drug. Focusing on the most commonly prescribed drugs, the findings are as follows:

Some drugs were not tested against all pathogens, hence some blanks are present. Also, we did not list methicillin-sensitive *Staphylococcus* species because a clinician does not know the nature (i.e., methicillin sensitive vs. methicillin resistant) of the causative pathogen at clinical presentation, so we need to treat based on a "most difficult to kill" approach. If we treat a presumed *Staphylococcus* infection, and in reality it is methicillin sensitive, it will be quickly eradicated if we are assuming (and treating for) methicillin-resistant species.

Interestingly, MRSA organisms are more common among the elderly and those who reside in the southern portions of the United States. Note that the drug of choice for culture-proven *Pseudomonas* is ciprofloxacin, although the fluoroquinolones and tobramycin performed quite well.

A summary statement says: "Until rapid diagnostic methods are available to guide treatment choices, clinicians should consider these data to guide the empirical treatment of ocular infections."

Asbell PA, Sanfilippo CM, Pillar CM, et al. Antibiotic Resistance Among Ocular Pathogens in the United States: Five-Year Results From the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) Surveillance Study. JAMA Ophthalmol. 2015 Dec;133(12):1445-54.

MINIMUM INHIBITORY CONCENTRATIONS (MIC_{90}) FOR SELECTED ORGANISMS

	MRSA	MR *Staph Epi.**	*Strep. Pneumo.*	*Pseudomonas*
Ciprofloxacin	256	64	1	0.5
Gatifloxacin	16	32	0.25	2
Moxifloxacin	16	32	0.12	4
Besifloxacin	2	4	0.06	4
Azithromycin	>512	>512	>128	
Tobramycin	>256	16		1
Trimethoprim	2	>128		
Vancomycin	1	2		

* There are many organisms which are are "coagulase-negative" but *Staph. epidermidis* is by far the most numerous, and therefore we have chosen to use *Staph. epi.* as synonymous with the coagulase-negative *Staph.*

Note that besifloxacin and vancomycin share superb MIC_{90} levels, which would portend high clinical efficiacy.

Αντιβακτηριδιακά

- **Αμινογλυκοσίδες**
  - *Δραστικές:* Γενταμικίνη, Τομπραμυκίνη, Αμικασίνη, Νεομυκίνη
  - *Μηχανισμός δράσης:* Προσδένονται αναντιστρεπτά στην 30S βακτηριακή ριβοσωμική υπομονάδα, βακτηριοκτόνο
  - *Αντενδείξεις/Παρενέργειες:* νεφροτοξικότητα, ωτοτοξικότητα, νεομυκίνη → δερματίτιδα (αντίδραση τοπικής υπερευαισθησίας)
- **Κεφαλοσπορίνες και Πενικιλλίνες**
  - *Δραστικές:* Κεφιξίμη, Κεφαζολίνη, Κεφταζιδίμη, Πενικιλλίνη G, Κεφουροξίμη, Κεφτριαξόνη
  - *Μηχανισμός δράσης:* Αναστέλλουν τη σύνθεση του βακτηριακού τοιχώματος, βακτηριοκτόνα
  - *Αντενδείξεις/Παρενέργειες:* αντιδράσεις υπερευαισθησίας (3-10%), οι κεφαλοσπορίνες παρουσιάζουν διασταυρούμενη αντίδραση (αλλεργία) με τις πενικιλλίνες (10%)
- **Μακρολίδες**
  - *Δραστικές*: Αζιθρομυκίνη, Ερυθρομυκίνη
  - *Μηχανισμός δράσης:* Μη αντιστρεπτή σύνδεση στην υπομονάδα 50S του βακτηριακού ριβοσώματος
  - *Αντενδείξεις/Παρενέργειες*: (ερυθρομυκίνη) επιγαστρική δυσφορία, χολοστατικός ίκτερος, ωτοτοξικότητα (σε μεγάλες δόσεις), όχι σε ασθενείς με ηπατική δυσλειτουργία
  - *Αλληλεπιδράσεις*: ↑(θεοφυλλίνη, βαρφαρίνη, τερφεναδίνη, αστεμιζόλη, καρβαμαζεπίνης, κυκλοσπορίνη, διγοξίνη)

- **Φλουοροκινολόνες**
  - *Δραστικές*: Σιπροφλοξασίνη, Μοξιφλοξασίνη, Οφλοξασίνη, Γκατιφλοξασίνη, Λεβοφλοξασίνη, Νορφλοξασίνη
  - *Μηχανισμός δράσης*: Αναστέλλουν την βακτηριακή DNA γυράση → σύνθεση DNA, βακτηριοκτόνα
  - *Αντενδείξεις/Παρενέργειες*: ναυτία, πονοκέφαλος, αντιδράσεις υπερευαισθησίας

Clinical note

Antibiotics, notably aminoglycosides such as neomycin and gentamicin, can be toxic to the ocular surface. Signs of ocular toxicity include punctuate keratitis, injection of the inferior cul-de-sac and a weepy erythema with oedema of the eyelid tissues. Such ocular responses usually occur when the drug has been used for 1–2 weeks and are not normally serious.

Antibacterial

- **Αναστολείς της πρωτεϊνικής σύνθεσης**
  - **Χλωραμφενικόλη, Κλινδαμυκίνη**
    - *Μηχανισμός δράσης:* Σύνδεση με την υπομονάδα 50S του βακτηριακού ριβοσώματος στο στάδιο της πεπτιδυλο-τρανσφεράσης.
    - *Αντενδείξεις/Παρενέργειες:* (κλινδαμυκίνη) ψευδομεμβρανώδης κολίτιδα, δερματικά εξανθήματα
  - **Δοξυκυκλίνη, Τετρακυκλίνη**
    - *Μηχανισμός δράσης: αντιστρεπτή σύνδεση (vs αμινογλυκοσίδες) με την υπομονάδα 30S του βακτηριακού ριβοσώματος (=> βακτηριοστατικά)*
    - *Αντενδείξεις/Παρενέργειες:* γαστρικά ενοχλήματα, χρωματισμός και υποπλασία των δοντιών σε παιδιά, φωτοτοξικότητα, θανατηφόρος ηπατοτοξικότητα σε εγκύους, διαταραχές αιθουσαίας λειτουργίας, καλοήθης ενδοκράνια υπέρταση, όχι σε έγκυες γυναίκες ή γυναίκες που θηλάζουν, σε παιδιά κάτω από 8 έτη

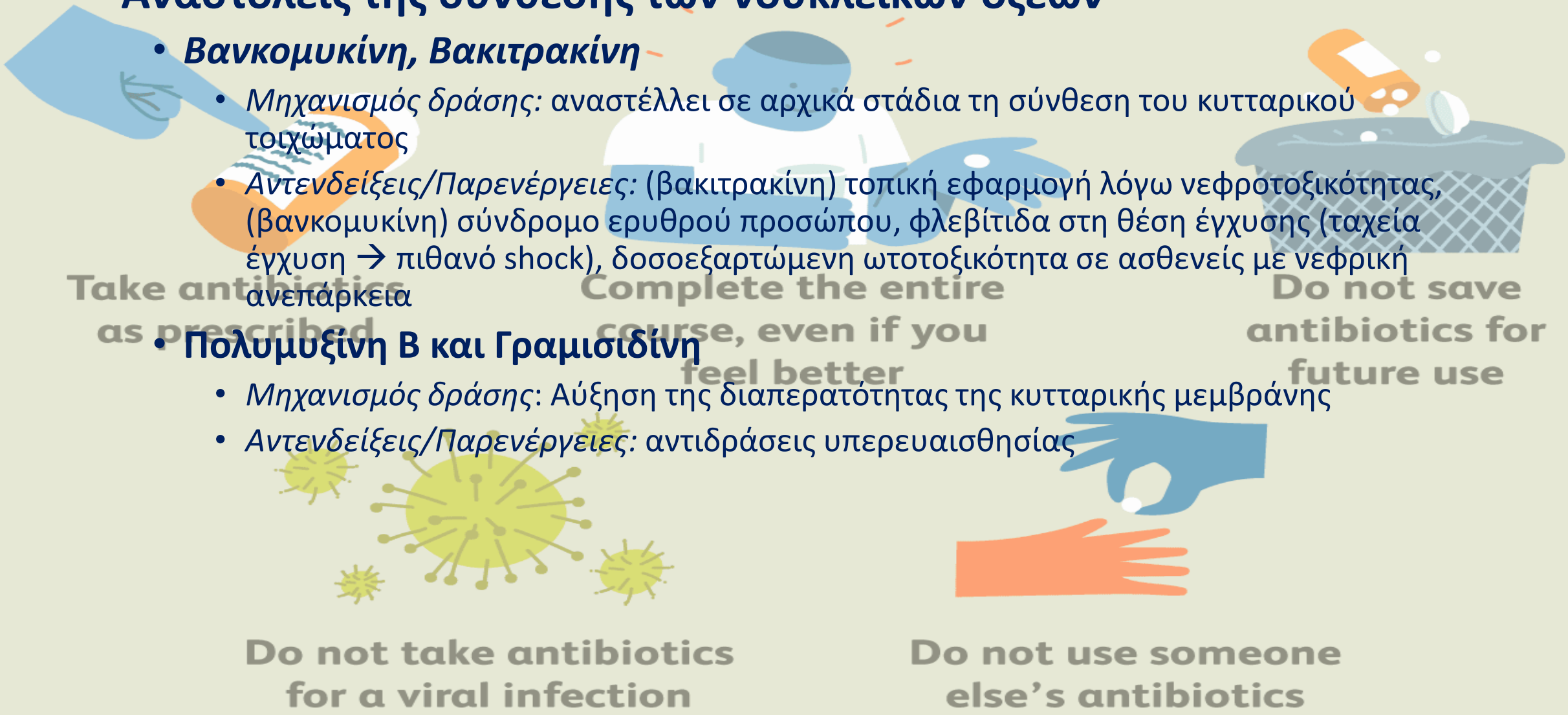
Clinical note

Chloramphenicol is considered to be the drug of choice for the treatment of superficial infections such as bacterial conjunctivitis and blepharitis.

- **Αναστολείς της σύνθεσης νουκλεϊκών οξέων**
  - **Ριφαμπικίνη**
    - *Μηχανισμός δράσης*: Αναστέλλει τη μεταγραφή μέσω πρόσδεσης στην β-υπομονάδα της βακτηριακής DNA εξαρτώμενης RNA πολυμεράσης
    - *Αντενδείξεις/Παρενέργειες*: (μεγάλες δόσεις) ίκτερος σε ασθενείς με χρόνια πάθηση του ήπατος
  - **Πυριμεθαμίνη, Τριμεθοπρίμη**
    - *Μηχανισμός δράσης*: Αναστολή της αναγωγής του φυλλικού οξέως (διϋδροφυλλικό οξύ σε τετραϋδροφυλλικό οξύ), Βακτηριοστατικό.
    - *Αντενδείξεις/Παρενέργειες*: Μπορεί να δημιουργήσει κατάσταση ανεπάρκειας φυλλικού οξέως (μεγαλοβλαστική αναιμία, λευκοπενία, ακοκκιοκυτταραιμία). => Αναστροφή με χορήγηση φολινικού οξέως.
  - **Σουλφακεταμίδη**
    - *Μηχανισμός δράσης*: Αναστέλλει τη σύνθεση του φυλλικού οξέως
    - *Αντενδείξεις/Παρενέργειες*: κρυσταλλουρία, αντιδράσεις υπερευαισθησίας (αγγειοοίδημα, σύνδρομο Stevens-Johvson), αιμολυτική αναιμία σε ασθενείς με ανεπάρκεια της γλυκοζο-6-φωσφορικής δεϋδρογενάσης, πυρηνικός ίκτερος σε νεογνά, όχι σε νεογνά και βρέφη κάτω των 2 μηνών, σε έγκυες γυναίκες προς το τέλος της κυήσεως, σε ασθενείς που λαμβάνουν μεθεναμίνη

How to Avoid Antibiotic Resistance

- **Αναστολείς της σύνθεσης των νουκλεϊκών οξέων**
  - ***Βανκομυκίνη, Βακιτρακίνη***
    - *Μηχανισμός δράσης:* αναστέλλει σε αρχικά στάδια τη σύνθεση του κυτταρικού τοιχώματος
    - *Αντενδείξεις/Παρενέργειες:* (βακιτρακίνη) τοπική εφαρμογή λόγω νεφροτοξικότητας, (βανκομυκίνη) σύνδρομο ερυθρού προσώπου, φλεβίτιδα στη θέση έγχυσης (ταχεία έγχυση → πιθανό shock), δοσοεξαρτώμενη ωτοτοξικότητα σε ασθενείς με νεφρική ανεπάρκεια
  - **Πολυμυξίνη Β και Γραμισιδίνη**
    - *Μηχανισμός δράσης*: Αύξηση της διαπερατότητας της κυτταρικής μεμβράνης
    - *Αντενδείξεις/Παρενέργειες:* αντιδράσεις υπερευαισθησίας



Clinical note

Prescribers of topical antibiotics must always aim to prevent the development of resistance to them. For example, the fluoroquinolones should be used with great caution to avoid this problem. At present, they have broad-spectrum activity with relatively little microbial resistance. It is important to use the least potent drug that can ensure the required therapeutic outcome. These preparations must *not* be used in the absence of infection.

OPHTHALMIC MYTHS: INFECTION CARE

Myth **Fourth-generation fluoroquinolones are the best, most effective medicines for ocular surface infections.**

Our Take Several recent studies have documented significant and increasing resistance to this class of medicine. Better choices would be an aminoglycoside, trimethoprim with polymyxin B, or Besivance suspension.

Myth **Pressure patching abrasions is now obsolete.**

Our Take Patients with large, painful abrasions may be best treated with therapeutic cycloplegia and a well-placed pressure patch over an antibiotic ointment, such as Polysporin (bacitracin with polymyxin B), at least initially. Most abrasions are treated with a bandage/therapeutic soft contact lens with topical trimethoprim/polymyxin B (Polytrim) eye drops used four times a day until the abrasion is healed. The generic Polytrim is used because it is minimally toxic to the ocular surface, highly effective and affordable.

Myth **Don't touch the dropper tip to the eye, as it could cause an infection.**

Our Take We all know many patients do this routinely, and we have never seen an eye infection from such a behavior. No doubt this has happened to some unlucky soul, but such a complication would be exceedingly rare. The greater risk is the potential for corneal abrasion.

Myth **Ointments retard re-epithelialization in the setting of corneal abrasion.**

Our Take This has long been proven to be false.

KEEP IN MIND

THE EFFICIENT RED EYE EVALUATION

Each of these procedures generally takes about two to three minutes in most cases.

- Assess visual acuity (pinhole if indicated)
- Note the degree of conjunctival injection
  - Mild: dry eyes, allergy, chlamydia, mild bacterial infections
  - Marked: acute viral or non-specific bacterial infection, acute iritis
- Note the degree of conjunctival injection pattern
  - Sector injection: corneal infiltrate, episcleritis, phlyctenule, inflamed pinguecula
  - Global injection: uniform—bacterial or viral infection, or uveitis
  - More pronounced in fornices: bacterial infection
  - More pronounced paralimbally: uveitis
- Quality and quantity of discharge if any
  - Watery: viral
  - Mucoid: dry eyes, allergy, chlamydia
  - Mucopurulent: bacteria
- Preauricular lymphadenopathy (not grossly visible)
  - Most commonly, adenoviral
  - Less commonly, chlamydial
  - Rarely, hyperacute conjunctivitis
  - If grossly visible: Parinaud's oculoglandular syndrome (cat-scratch disease)
- Follicles vs. papillae: clinically virtually meaningless
  - Exception: Giant follicles in the inferior forniceal conjunctiva are highly indicative of chlamydial infection
- Character of cornea: Examine without, then with, fluorescein dye to rule out herpes keratitis, subtle abrasions, ulceration, through-and-through perforation (Seidel's sign)
- Measure the IOP if no contraindications exist
- Evert the eyelid to rule out conjunctival foreign material or pathology
- Examine the anterior chamber for cells/flare
- Quick ophthalmoscopy to rule out concurrent intraocular disease

Ενισχυμένα αντιβιοτικά

- Fortification means to intensify or strengthen the medication, to achieve adequate drug concentration. Fortified antimicrobials are not commercially available, thus should be, prepared of optimal constitution in a sterile pharmaceutical dispensary.
- Most of our available ophthalmic antibiotic preparations are in 0.3% concentration, which is not sufficient to attain minimum inhibitory concentration to halt the progression of certain pathologies.
- Fortified antimicrobials are not commercially available, thus should be prepared of optimal constitution in a sterile pharmaceutical dispensary. For preparation of fortified antibiotics, a standard parenteral or lyophilized antibiotic preparation is combined with a compatible vehicle such that the antibiotic does not precipitate.

Table 1: Drugs and their coverage[1,9]

Bacteria type	First-line option
Gram-positive Cocci (*Staphylococcus, Streptococcus*)	Cefazolin - 50 mg/ml Vancomycin - 25 or 50 mg/ml Bacitracin - 10,000 IU Fluoroquinolones
Gram-negative Cocci (*Neisseria meningitidis, Neisseria meningitidis, and Moraxella catarrhalis*)	Fortified ceftazidime: 50 mg/mL (5%) Fortified ceftriaxone: 50 mg/mL
Gram-negative rods (*Pseudomonas* and *Klebsiella pneumoniae*)	Fortified gentamicin: 14 mg/mL (1.4%) Fortified tobramycin: 14 mg/mL (1.4%) Fortified ceftazidime: 50 mg/mL (5%)
Nontuberculous mycobacteria	Fortified amikacin eyedrops: 40mg/ml Clarithromycin: 10 mg/mL Azithromycin: 10 mg/mL Fluoroquinolones
Methicillin-resistant *Staphylococcus aureus*	Topical vancomycin eyedrops: 50 mg/ml (5%) Topical linezolid: 2 mg/ml (0.2%)
Nocardia	Fortified amikacin eyedrops: 40 mg/ml Co-trimoxazole (trimethoprim 16 mg/ml + sulfamethoxazole 80 mg/ml)

General guidelines

- Selection of fortified antimicrobials must be adapted to the type of bacteria suspected for safe and effective treatment
- Fortified drops should be prepared by a doctor or a pharmacist inside a laminar air hood/operation room under aseptic precautions
- Disposable syringe should be used
- Date of preparation and date of expiry should be mentioned in prepared drops
- Frequency of application with storage instructions should be explained to the patient
- Short shelf-life (preservative free)
- Since there is a risk for contamination and also it is preservative free, it should be refrigerated and can be kept up to 7 days at 4°C
- Shake well before instillation.

Topical vancomycin eyedrops: 15 mg/ml, 25 mg/ml, or 50 mg/ml (5%)

- Method: To a 500 mg vial of vancomycin:[1,5]

a) Add 33 ml of 0.9% sodium chloride for injection USP (no preservatives) or artificial tears to produce a solution of 15 mg/ml.

b) Add 20 ml of 0.9% sodium chloride for injection USP (no preservatives) or artificial tears to produce a solution of 25 mg/ml.

c) Add 10 ml of 0.9% sodium chloride for injection USP (no preservatives) or artificial tears to produce a solution of 50 mg/ml.

- Storage: Refrigerate and shake well before instillation.

DRAWBACKS OF FORTIFIED PREPARATIONS

The main drawback of fortified antimicrobial preparations is epithelial toxicity as epithelial-healing rate is retarded by aminoglycosides and vancomycin. When large epithelial defect or conjunctival ulcers are seen, the frequency of drug therapy must be reduced or to be thought of as an alternative drug regimen.[1,2]

Nixon HK. Preparation of fortified antimicrobial eye drops. Kerala J Ophthalmol 2018;30:152-4

Συνδυασμοί αντιβιοτικού και κορτιζόνης

- ‘’Μικτά Κολλύρια’’
- Τι σας έρχεται στο μυαλό? →

- Tobradex (Τομπραμυκίνη + Δεξαμεθαζόνη)

Εμπορικές ονομασίες ομάδας

Κ	Εμπορική ονομασία	Ενεργά συστατικά	Υπεύθυνος κυκλοφορίας
⚠	AFACORT	Δεξαμεθαζόνη - Νεομυκίνη	Anfarm Hellas A.E.
✓	ANTILERG-F	Δεξαμεθαζόνη - Νεομυκίνη	Demo A.B.E.E.
✓	CHLORAPRED	Χλωραμφαινικόλη - Δεξαμεθαζόνη	Demo A.B.E.E.
⚠	CORTIPHENOL	Κορτιζόλη - Χλωραμφαινικόλη	
◈	DECADRON	Δεξαμεθαζόνη	
✓	DEXACHLOR	Χλωραμφαινικόλη - Δεξαμεθαζόνη	
⚠	DEXAMYCIN	Τομπραμυκίνη - Δεξαμεθαζόνη	
✓	DEXAMYTREX	Γενταμικίνη - Δεξαμεθαζόνη	
✓	DISPERSADRON-C	Χλωραμφαινικόλη - Δεξαμεθαζόνη	
⚠	FML-NEO	Φθοριομεθολόνη - Νεομυκίνη	
✓	GENTADEX	Γενταμικίνη - Δεξαμεθαζόνη	
✓	LOFOTO	Τομπραμυκίνη - Δεξαμεθαζόνη	
✓	NEZEFIB	Χλωραμφαινικόλη - Δεξαμεθαζόνη	
✓	O-BIOTIC	Τομπραμυκίνη - Δεξαμεθαζόνη	
✓	SAOCIN-D	Dexamethasone sodium phosphate - Νεομυ	
⚠	THILOMICIN-DEX	Τομπραμυκίνη - Δεξαμεθαζόνη	Pharmex S.A.
✓	TOBRADEX	Δεξαμεθαζόνη - Τομπραμυκίνη	Novartis Hellas A.B.E.E.
⚠	TOBRAFEN	Τομπραμυκίνη - Δικλοφαινάκη	Zwitter Pharmaceuticals E.Π.E.

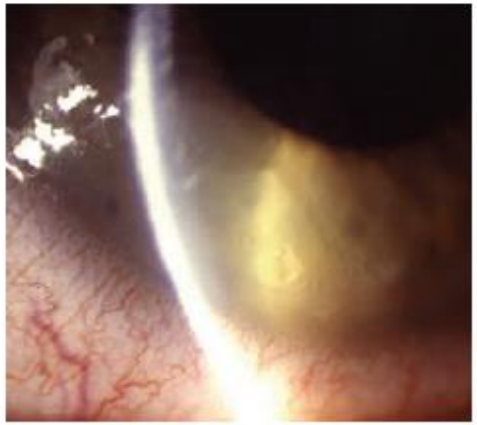
Antibacterial and Corticosteroid Combinations

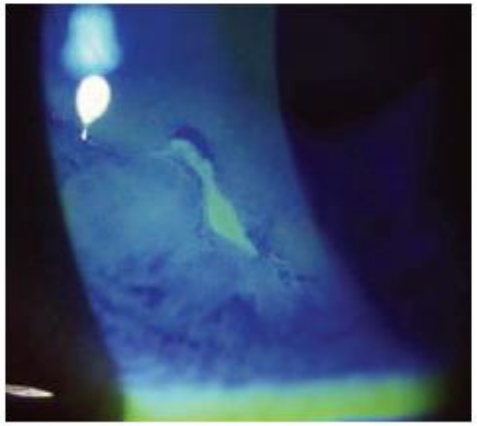
CORTISPORIN (neomycin + polymyxin + hydrocortisone 1%) 1 drop or ½ inch ribbon of ointment every 3 to 4 hours.

MAXITROL (dexamethasone + neomycin + polymyxin) 1 drop every 1 to 8 hours or ½–1 inch ribbon of ointment qd–qid.

TOBRADEX (tobramycin + dexamethasone) 1 drop every 2 to 6 hours or ½ inch ribbon of ointment bid–qid.

Χορήγηση κορτιζόνης: αντενδείξεις?





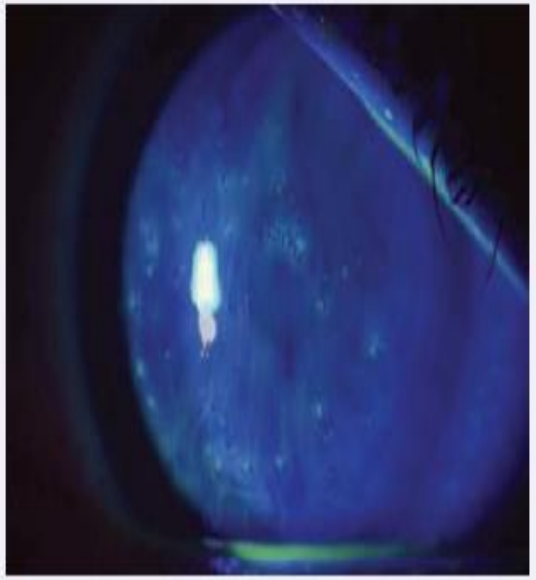
LEFT: There is a large epithelial defect inferiorly. Note that the anterior two thirds of the cornea is heavily infiltrated, which nicely explains why the overlying epithelium is secondarily compromised. This is a non-infectious epithelial defect, most likely as a result of epithelial demise secondary to staphylococcal exotoxins. This defect is near the limbus, which is very fertile soil for inflammatory events. The limbal area has an abundance of blood vessels that carry immune weaponry of both humeral immunity (antibodies) and cellular immunity (leukocytes). This explains why most all events at or near the limbus are inflammatory in nature, and therefore why corticosteroid suppression is so essential to hasten resolution of tissue compromise.

RIGHT: After just two days of an antibiotic/steroid combination, the epithelial defect is healing rapidly. The antibiotic is for the benefit of the doctor; the steroid is for the benefit of the patient! It is vital to know *why* there is epithelial compromise. If such is a result of anterior stromal inflammation (as evidenced by the rather profound anterior corneal infiltration as seen in optic section), then a steroid is the drug best suited to help restore these tissues.

OPHTHALMIC MYTHS: STEROIDS

Myth **Never use a steroid (even combined with an antibiotic) on a cornea with a staining epithelial defect.**

Our Take We have encountered numerous epithelial defects over the years that were non-healing until we added a steroid that quelled the corneal inflammation preventing re-epithelialization. The nature and cause of the epithelial defect must be understood in order to properly select therapeutic intervention. If the epithelial defect is present as a result of subepithelial inflammation, as evidenced by leukocytic anterior stromal disease, then adding a steroid to suppress the underlying inflammatory process can promote re-epithelialization. We know that inflammation and superficial punctate keratitis commonly coexist in dry eye disease, yet the proper application of a steroid can help restore and enhance the integrity of the epithelial tissues.



A mild steroid will suffice for Thygeson's superficial punctate keratopathy.

Συνδυασμοί αντιβιοτικών

- Νεομυκίνη + Βακιτρακίνη + Πολυμυξίνη Β
- Πολυμυξίνη Β + Βακιτρακίνη
- Πολυμυξίνη Β + τριμεθοπρίμη
- Πολυμυξίνη + Νεομυκίνη + Γραμισιδίνη

Φάρμακα που περιέχουν τη δραστική σε συνδυασμό με άλλες δραστικές

Κ	Εμπορική ονομασία	Ενεργά συστατικά	Υπεύθυνος κυκλοφορίας
✓	PAROTICIN	Φθοριοϋδροκορτιζόνη - Πολυμυξίνη Β - Λιδοκαΐνη	Adelco Χρωματουργεία Αθηνών Α.Ε.
✓	SYNALAR OTIC	Ακετονίδιο της φθοριοκινολόνης - Νεομυκίνη - Πολυμυξίνη Β	Minerva Pharmaceuticals Α.Ε.
✓	TEAM-BIOTIC	Νεομυκίνη - Βακιτρακίνη - Πολυμυξίνη Β	Nassington Ltd
⚠	TERRAMYCIN+POLYMYXIN	Oxytetracycline hydrochloride - Polymyxin B sulfate	Pfizer Hellas A.E.

Οδοί χορήγησης – Συγκεντρώσεις / Δοσολογίες

Table 2.4 Compounding of major antibiotics for the treatment of ocular infections

	Route of administration			
Drug name[a]	Topical	Subconjunctival	Intravitreal	Intravenous[b]
Amikacin sulfate	10 mg/mL	25 mg	400 µgm	15 mg/kg daily in 2–3 doses
Ampicillin sodium	50 mg/mL	50–150 mg	5 mg	4–12 g daily in 4 doses
Bacitracin zinc	10,000 units/mL	5,000 units	–	–
Cefazolin sodium	50 mg/mL	100 mg	2,250 µgm	2–4 g daily in 3–4 doses
Ceftazidime	50 mg/mL	100 mg	2,000 µgm	1 g daily in 2–3 doses
Ceftriaxone	50 mg/mL	–	–	1–4 g daily in 1–2 doses
Clindamycin	50 mg/mL	15–50 mg	1,000 µgm	900–1,800 mg daily in 2–3 doses
Colistimethate sodium	10 mg/mL	15–25 mg	100 µgm	2.5–5 mg/kg daily in 2–4 doses
Erythromycin	50 mg/ml	100 mg	500 µgm	–
Gentamicin sulfate	8–15 mg/ml	10–20 mg	100–200 µgm	3–5 mg/kg daily in 2–3 doses
Imipenem/cilastatin sodium	5 mg/ml	–	–	2 g daily in 3–4 doses
Kanamycin sulfate	30–50 mg/ml	30 mg	500 mg	–
Neomycin sulfate	5–8 mg/ml	125–250 mg	–	–
Penicillin G	100,000 units/mL	0.5–1.0 million units	300 units	12–24 million units daily in 4–6 doses
Piperacillin	12.5 mg/mL	100 mg	–	–
Polymyxin B sulfate	10,000 units/mL	100,000 units	–	–
Ticarcillin disodium	6 mg/mL	100 mg	–	200–300 mg/kg daily 3 × in 4–6 doses
Tobramycin sulfate	8–15 mg/mL	10–20 mg	100–200 µgm	3–5 mg/kg daily in 2–3 doses
Vancomycin hydrochloride[c]	20–25 mg/mL	25 mg	1,000 µgm	15–30 mg/kg daily in 1–2 doses

[a]Most penicillins and cephalosporins are physically incompatible when combined in the same bottle with aminoglycosides such as amikacin, gentamicin, or tobramycin
[b]Adult doses
[c]Usage discouraged by CDC because of increased resistant organisms

Αντιμυκητιακά

- Μηχανισμός δράσης →→→
- Αντενδείξεις/Παρενέργειες: Τοπική Υπερευαισθησία, νεφρική βλάβη

Generic (trade) name	Route	Dosage
Amphotericin B (Fungizone®)	Topical	0.1–0.5 % solution (most commonly 0.15 %); dilute with water for injection or dextrose 5 % in water
	Subconj.	0.8–1.0 mg
	Intravitreal	5 mcg
Liposomal amphotericin B	Intravenous	
Fluconazole (Diflucan®)	Oral	200 mg on day 1, then 100 mg daily in divided doses
		400 mg on day 1, then 200 mg daily in divided doses
Intravenous	IV	200–400 mg
Flucytosine (Ancobon®)	Oral	50–150 mg/kg daily 4 divided doses
Itraconazole (Sporanox®)	Oral	200–400 mg/kg daily
	Intravenous	200 mg IV twice a day for 4 doses, then 200 mg IV daily for 14 days
Ketoconazole (Nizoral®)	Oral	200–400 mg daily
Natamycin (Natacyn®)	Topical	5 % suspension
Voriconazole (Vfend®)	Oral	200 mg twice a day
	Intravenous	3–6 mg/kg every 12 h
	Intracorneal	25 µgm
	Topical	1 % eyedrops

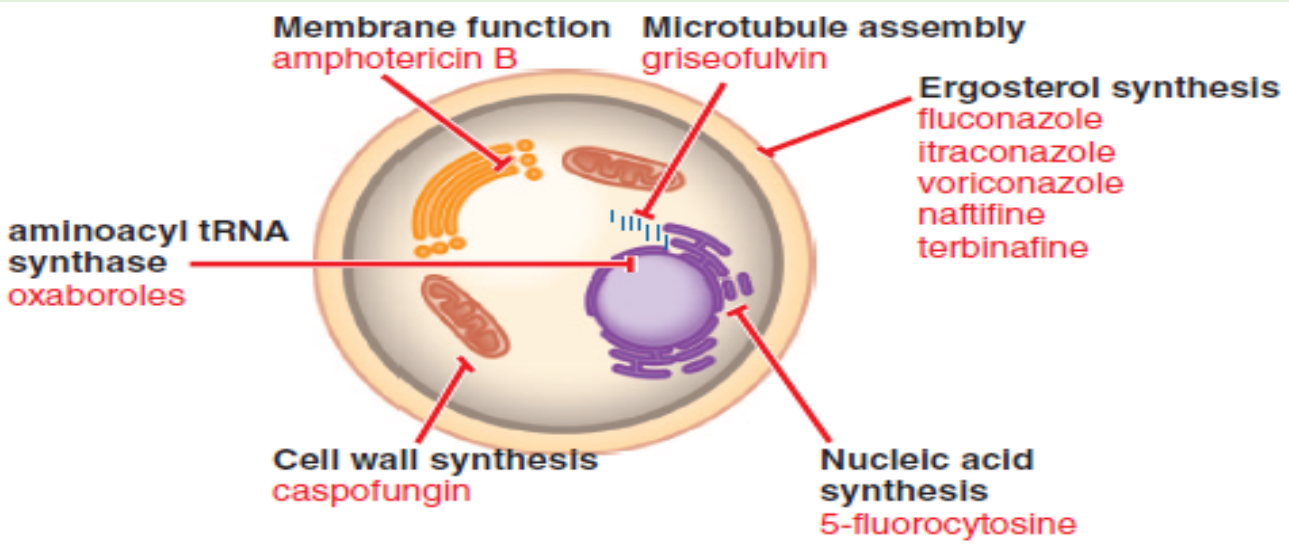


Figure 61–1 *Sites of action of antifungal agents.* Many antifungal agents act at sites involving cell wall and cell membrane function. Amphotericin B and other polyenes (e.g., nystatin) bind to ergosterol in fungal cell membranes and increase membrane permeability. The imidazoles and triazoles (itraconazole, etc.) inhibit 14-α-sterol demethylase, prevent ergosterol synthesis, and lead to the accumulation of toxic 14-α-methylsterols. The allylamines (e.g., naftifine and terbinafine) inhibit squalene epoxidase and prevent ergosterol synthesis. The echinocandins (e.g., caspofungin) inhibit the formation of glucans in the fungal cell wall. Metabolites of 5-fluorocytosine can disrupt fungal RNA and DNA synthesis. Griseofulvin inhibits microtubule assembly, thereby blocking fungal mitosis. Oxaboroles inhibit fungal aminoacyly tRNA synthase, thereby inhibiting fungal protein synthesis.

Αντιπαρασιτικά

--->Αντιπρωτοζωικά<---

- Συνδυασμός φαρμακευτικών παραγόντων ανάλογα με το εκάστοτε παθογόνο (*Πρωτόζωα*: ακανθαμοιβάδα, τοξόπλασμα, λεϊσμάνιες, Giardia lamblia, Plasmodium, μικροσπορίδια (Encephalitozoon hellem, Nosema corneum), Pneumocystis carinii, *Έλμινθες*: Onchocerca volvulus, Loa loa, Taenia solium, Toxocara canis)
- Συνηθέστερες η κερατίτιδα από ακανθαμοιβάδα και η αμφιβληστροχοριοειδίτιδα τοξοπλάσμωση.

Table 2.12 Antimicrobial therapy for ocular toxoplasmosis

Treatment regimen (adult)
Pyrimethamine 200 mg orally on day 1, followed by 50 mg orally daily for 4 weeks
Sulfadiazine 2 g orally as a loading dose followed by 1 g orally 4 times daily for 4 weeks
Folinic acid 15 mg orally every other day twice a week
Force fluids and give sodium bicarbonate
Alternate regimen (adult)
Azithromycin, 500 mg orally twice daily for 4 weeks, or clindamycin 300–450 mg orally q 6 h for 4 weeks
Trimethoprim, 160 mg/sulfamethoxazole 800 mg twice daily for 4 weeks
Vision-threatening lesions
Corticosteroids to be used only when vision is threatened: prednisone, 1 mg to 1.5 mg/kg/day, gradually tapered over a period of 4 weeks, or periocular injection of triamcinolone acetonide 40 mg once
Give corticosteroids 3 days after initiation of antimicrobial agents
Congenital toxoplasmosis
Pyrimethamine, 1 mg/kg/day orally once every 3 days, and sulfadiazine, 50 mg to 100 mg/kg/day orally in two divided doses for 3 weeks
Corticosteroids for vision-threatening lesions: 1 mg/kg/day orally in two divided doses. The dosage should be tapered progressively and later discontinued
Folinic acid, 3 mg twice weekly during treatment with pyrimethamine

Adapted and modified from [1, 68]

Table 26-7
Medications Currently Used in the Treatment of *Acanthamoeba* Keratitis

Medication	Effective Against
Chlorhexidine diglucotate 0.02% (mainstay treatment)	Trophozoite and cystic stage
PHMB 0.02% (mainstay treatment)	Trophozoite and cystic stage
Propamidine 0.1% (Brolene®) (additive therapy)	Trophozoite with some cystic activity
Hexamidine isethionate 0.1% (Vivier®) (additive therapy)	Trophozoite with some cystic activity
Flurbiprofen (oral)	Adjunctive therapy providing anti-inflammatory and analgesic properties
Topical steroids	Can be used in late stages after the amoebae have been killed to control inflammation
Imidazoles 1% (e.g., ketoconazole)	Effective against trophozoites but not cysts; never used as primary therapy but may be used concurrently

Figure 36.1
Summary of antiprotozoal agents.

Αντιικά

ACYCLOVIR (Zovirax) For HSV, use 200–400 mg PO 5x/day for 7 to 10 days, or HZV 600–800 mg 5x/day for 10 days; use IV if immunosuppressed. All current antivirals are virostatic.

- Synthetic guanosine analogue that is tri-phosphorylated by thymidine kinase (TK) to acyclovir triphosphate. The triphosphate accumulates in infected cells and competes with doxyguanosine triphosphate for viral DNA polymerase and terminates replication after incorporated into DNA.
- 200× greater affinity for viral thymidine kinase (TK) than mammalian cell TK, thus low toxicity. Activity greatest for HSV-1 > HSV-2 > HZV > EBV > CMV.
- Most viral resistance is from alteration of TK gene.

CIDOFOVIR Nucleotide analogue inhibits viral DNA polymerase, used for CMV infection; does not require viral activation; long intracellular half-life. May cause profound hypotony (CB destruction) and severe uveitis (14% of intravitreal usage).

FAMICICLOVIR (Famvir) 500 mg PO every 8 hours to treat HZV and genital herpes, typically treated for 7 days.

FOMIVIRSEN (Vitravene) Exonuclease used as intravitreal injection for CMV retinitis.

FOSCARNET Inhibits CMV DNA and RNA polymerase, demonstrates improved AIDS survival; use limited by nephrotoxicity.

IDOXURIDINE (IDU) First topical antiviral, pyrimidine nucleoside, similar to thymidine and incorporated into DNA; very toxic.

GANCYCLOVIR May be delivered PO, IV, or intravitreal. Structurally similar to acyclovir, as it is phophorylated to gancyclovir triphosphate; blocks DNA polymerase and is incorporated into DNA instead of doxyguanosine. Is 10–20x more active than acyclovir against CMV, equally active against HSV and EBV, and has 10x greated affinity among virus-infected cells.

PROTEASE INHIBITORS HAART has demonstrated increased CD4 count, decreased HIV load, improves CMV retinitis, and may cause increased CME (overall a good sign, in that the body is responding with inflammation).

TRIFLURIDINE (Viroptic) For HSV, 1 gtt every 2 to 4 hours for 7 to 14 days, maximum 9 drops/day (solution 1%). Structural analogue of thymidine and is thus incorporated into viral DNA; also directly inhibits thymidylate synthase.

VALACYCLOVIR (Valtrex) 1 g PO tid; begin at earliest signs of HZV or genital herpes, typically for 7 days, and adjust dosage for renal insufficiency. Prodrug that is converted to acyclovir in small intestine and liver; increased concentration with concurrent cimetidine; effective for HZV.

VIDARABINE (Vira-A) ½ inch ribbon of ointment bid up to 5 times daily for 5 to 7 days (ointment 3%).

Generic (trade) name	Topical conc.	Intravit. dose	Systemic dosage
Trifluridine (Viroptic®)	1.0 %	–	–
Acyclovir sodium	–	24,000 µgm	Oral – *herpes simplex* keratitis: 200 mg 5 times daily for 7–10 days Oral – *herpes zoster ophthalmicus*: 600–800 mg 5 times daily for 10 days; IV therapy
Cidofovir (Vistide®)	–	–	IV – induction: 5 mg/kg constant infusion over 1 h administered once weekly for 2 consecutive weeks Maintenance: 5 mg/kg constant infusion over 1 h administered once every 2 weeks
Generic (trade) name	Topical conc.	Intravit. dose	Systemic dosage
Famciclovir (Famvir®)	–	–	Oral – *herpes zoster ophthalmicus* 500 mg 3 times daily for 7 days
Fomivirsen (Vitravene®)	–	330 µgm	Every other week for 4 doses, then every 4 weeks. Contains 6.6 mg/mL, in a 0.25-ml vial
Foscarnet sodium (Foscavir®)	–	1 mg	IV – by controlled infusion only, either by central vein or by peripheral vein induction: 60 mg/kg (adjusted for renal function) given over 1 h every 8 h for 14–21 days Maintenance: 90–120 mg/kg given over 2 h once daily
Ganciclovir (gel) (Zirgan®, Virgan)	0.15 %		
Ganciclovir sodium (Cytovene®)	–	0.2 mg	IV – induction: 5 mg/kg every 12 h for 14–21 days Maintenance: 5 mg/kg daily for 7 days or 6 mg once daily for 5 days/week Oral – after IV induction: 1,000 mg 3 times daily with food or 500 mg 6 times daily every 3 h
Ganciclovir sodium (Vitrasert®)[a]	–	4.5 mg	
Valacyclovir (Valtrex®)	–	–	Oral – *herpes zoster ophthalmicus*: 1 g 3 times daily for 7 days Herpes simplex virus (types 1 & II): 1 g 2 times daily

[a]Sterile intravitreal insert designed to release the drug over a 5–8-month period

Θεραπευτική: At a glance

GENERIC NAME	FORMULATION[a]	TOXICITY	INDICATIONS FOR USE
Azithromycin	1% solution	H	Conjunctivitis
Bacitracin	500 units/g ointment	H	Conjunctivitis, blepharitis, keratitis, keratoconjunctivitis, corneal ulcers, blepharoconjunctivitis, meibomianitis, dacryocystitis
Besifloxacin	0.6% suspension		Conjunctivitis
Chloramphenicol	1% ointment	H, BD	Conjunctivitis, keratitis
Ciprofloxacin hydrochloride	0.3% solution; 0.3% ointment	H, D-RCD	Conjunctivitis, keratitis, keratoconjunctivitis, corneal ulcers, blepharitis, blepharoconjunctivitis, meibomianitis, dacryocystitis
Erythromycin	0.5% ointment	H	Superficial ocular infections involving the conjunctiva or cornea; prophylaxis of ophthalmia neonatorum
Gatifloxacin	0.3% solution	H	Conjunctivitis
Gentamicin sulfate	0.3% solution; 0.3% ointment	H	Conjunctivitis, blepharitis, keratitis, keratoconjunctivitis, corneal ulcers, blepharoconjunctivitis, meibomianitis, dacryocystitis
Levofloxacin	0.5% solution	H	Conjunctivitis
	1.5% solution	H	Corneal ulcers
Moxifloxacin	0.5% solution	H	Conjunctivitis
Ofloxacin	0.3% solution	H	Conjunctivitis, corneal ulcers
Sulfacetamide sodium	1, 10, 15, 30% solutions; 10% ointment	H, BD	Conjunctivitis, other superficial ocular infections
Polymyxin B combinations[b]	Various solutions and ointments		Conjunctivitis, blepharitis, keratitis
Tobramycin sulfate[c]	0.3% solution; 0.3% ointment	H	External infections of the eye and its adnexa

H, hypersensitivity; BD, blood dyscrasia; D-RCD, drug-related corneal deposits.

[a]For specific information on dosing, formulation, and trade names, refer to the Physicians' Desk Reference for Ophthalmic Medicines, which is published annually.

[b]Polymyxin B is formulated for delivery to the eye in combination with bacitracin, neomycin, gramicidin, oxytetracycline, or trimethoprim. See Chapters 52–55 for further discussion of these antibacterial agents.

[c]Tobramycin is formulated for delivery to the eye in combination with dexamethasone or loteprednol etabonate.

Antiviral Agents for Ophthalmic Use

GENERIC NAME	ROUTE OF ADMINISTRATION	OCULAR TOXICITY	INDICATIONS FOR USE
Trifluridine	Topical (1% solution)	PK, H	Herpes simplex keratitis and keratoconjunctivitis
Acyclovir	Oral, intravenous (200-mg capsules, 400- and 800-mg tablets)		Herpes zoster ophthalmicus[a] Herpes simplex iridocyclitis
Valacyclovir	Oral (500- and 1000-mg tablets)		Herpes simplex keratitis[a] Herpes zoster ophthalmicus[a]
Famciclovir	Oral (125-, 250-, and 500-mg tablets)		Herpes simplex keratitis[a] Herpes zoster ophthalmicus[a]
Foscarnet	Intravenous Intravitreal[a]		Cytomegalovirus retinitis
Ganciclovir	Intravenous, oral, intravitreal implant		Cytomegalovirus retinitis
Valganciclovir	Oral		Cytomegalovirus retinitis
Cidofovir	Intravenous		Cytomegalovirus retinitis

PK, punctate keratopathy; H, hypersensitivity.
[a]Off-label use. For additional details, see Chapter 58.

Antifungal Agents for Ophthalmic Use

DRUG CLASS/ AGENT	METHOD OF ADMINISTRATION	INDICATIONS FOR USE
Polyenes		
Amphotericin B[a]	0.1-0.5% (typically 0.15%) topical solution	Yeast and fungal keratitis and endophthalmitis
	0.8-1 mg subconjunctival	Yeast and fungal endophthalmitis
	5-µg intravitreal injection	Yeast and fungal endophthalmitis
	Intravenous	Yeast and fungal endophthalmitis
Natamycin	5% topical suspension	Yeast and fungal blepharitis, conjunctivitis, keratitis
Imidazoles		
Fluconazole[a]	Oral, intravenous	Yeast keratitis and endophthalmitis
Itraconazole[a]	Oral	Yeast and fungal keratitis and endophthalmitis
Ketoconazole[a]	Oral	Yeast keratitis and endophthalmitis
Miconazole[a]	1% topical solution	Yeast and fungal keratitis
	5-10 mg subconjunctival	Yeast and fungal endophthalmitis
	10-µg intravitreal injection	Yeast and fungal endophthalmitis

[a]Off-label use. Only natamycin (NATACYN) is commercially available and labeled for ophthalmic use. All other antifungal drugs are not labeled for ophthalmic use and must be formulated for the given method of administration. For further dosing information, refer to the Physicians' Desk Reference for Ophthalmic Medicines. *For additional discussion of these antifungal agents, see Chapter 57.*

Αντιγλαυκωματικά

LESSONS LEARNED FROM A LIFE IN THE CLINIC

- https://www.aao.org/basic-skills/animation-of-aqueous-flow
- Προσταγλανδίνες
- Β-αποκλειστές
- Παρασυμπαθητικομιμητικά
- Αδρενεργικοί αγωνιστές
- Αναστολείς καρβονικής ανυδράσης

Glaucoma: Prostaglandin Analogues

LATANOPROST (Xalatan) 1 gtt qhs (solution 0.005%]. Onset 2 to 3 hours and works by enhancing uveoscleral outflow (thus, theoretically not useful in acute increased IOP or ACG, although it may help). Prodrug that is changed by corneal esterases into acidic form that acts at the ciliary body to mimic prostaglandin F2-alpha (from arachidonic acid). This increases matrix metalloproteinase (MMP) enzyme release, causing degradation of extracellular matrix collagen and thus increased uveoscleral outflow. Up to 25 to 35% decreased IOP (approximately equivalent to timolol bid). May cause a permanent increased brown iris pigmentation or heterochromia, exuberant eyelash growth, and may increase postoperative CME or inflammation. Dose before pilocarpine, as it decreases latanoprost's access to uveosceral outflow.

BIMATOPROST (Lumigan) 1 gtt qhs (solution 0.03%). A prostamide analogue that works like latanoprost, except a higher concentration is needed because the corneal esterases do not cleave it. Causes conjunctival hyperemia.

TRAVAPROST (Travatan) 1 gtt qhs (solution 0.004%). Similar to latanoprost.

UNOPROSTONE (Rescula) 1 gtt bid (solution 0.15%). Prostanoid (docosanoid) with action similar to latanoprost.

Η Λατανοπρόστη στη Φαρμακοθεραπεία του Γλαυκώματος

Το μεγαλύτερο βήμα:

- Χορήγηση μία φορά την ημέρα → βελτίωση συμμόρφωσης
- Υψηλά ποσοστά μείωσης της ΕΟΠ
- Πολύ καλό προφίλ ασφαλείας συγκριτικά με τα υπόλοιπα αντιγλαυκωματικά, είτε συστηματικά είτε τοπικά

➢ Πρωτότυπο Λατανοπρόστης

-1996 ΗΠΑ

-1997 Ευρώπη

➢ Γενόσημα Λατανοπρόστης

-2011 ΗΠΑ και Ελλάδα

Λόγω μεγάλης εμπορικής επιτυχίας → παραγωγή πολλών γενοσήμων

Glaucoma: Beta-Blockers

PROPERTIES Decreases cAMP in ciliary epithelium, which causes decreased active secretion and thus decreased aqueous production. Peak 2 hours, some effect up to 4 weeks; 10 to 20% of patients do not respond. Additive effect to most drops (especially miotics), except epinephrine/dipivefrin. See Table 10–1 for side effects and precautions.

BETAXOLOL (Betoptic, Betopic-S) 1 drop bid (suspension 0.25%, solution 0.5%). Beta-1 cardioselective (safer to use in mild, intermittent asthma, but generally should not be used in CHF). Less IOP control than nonselectives; possibly increased ON blood flow (may be better in NTG); more additive effect with Propine.

TABLE 10–1
Beta-Blocker Precautions

Side Effects		Contraindications
Bronchospasm	Confusion or depression	Asthma
Bradycardia	Impotence	Obstructive pulmonary disease
Arrhythmia	Masked diabetic hypoglycemic symptoms	Heart block
Hypotension	Exacerbated myasthenia gravis	Congestive heart failure
Syncope	Punctate keratitis	Cardiogenic shock
Decreased HDL cholesterol	Corneal anesthesia	Hypersensitivity

CARTEOLOL (Ocupress) 1 gtt bid (solution 1%). Nonselective with intrinsic sympathomimetic activity (decreased systemic effects), better lipid profile, less ocular irritation.

LEVOBUNOLOL (Betagan) 1 drop qid–bid (solution 0.25, 0.5%). Nonselective.

METIPRANOLOL (Optipranolol) 1 gtt bid (solution 0.3%). Nonselective; inexpensive. May cause rare granulomatous uveitis.

TIMOLOL (Timoptic, Betimol) 1 gtt bid (solution 0.25, 0.5%). Timoptic XE: 1 gtt qam (solution 0.25, 0.5%). Nonselective; decreases IOP up to 30%. Substantial systemic levels may be obtained with topical usage; thus, decreased effectiveness if on systemic beta-blocker.

Glaucoma: Carbonic Anhydrase Inhibitors

PROPERTIES First discovered in the ciliary epithelium, carbonic anhydrase (CA) is a zinc metalloenzyme that catalyzes the reversible hydration of CO_2 to bicarbonate. Carbonic anhydrase inhibitors have free sulfonamide ($-SO_2NH_2$) linked to aromatic ring that competes with bicarbonate binding to CA in its acidic form → decreased bicarbonate synthesis → decreased Na+ and water influx → decreased aqueous production by up to 30%. See Table 10–2 for side effects and precautions.

ACETAZOLAMIDE (Diamox) 250 mg PO up to qid (immediate release) or 500 mg PO up to bid (Diamox Sequels or timed-release) (tablets 125, 250, extended release capsules 500 mg). In addition to lowered IOP, resultant

TABLE 10–2

Carbonic Anhydrase Inhibitor Precautions

Side Effects		Contraindications
Paresthesias	Hemolysis	Sulfa allergy
Dizziness	Aplastic anemia (sulfa)	Kidney or liver disease
Confusion	Gastrointestinal upset	Na^+/K^+ depletion
Tinnitus	Polyuria	Hyper-Cl acidosis
Anorexia	Kidney stones	Chronic obstructive lung disease
Metallic taste	Stevens-Johnson syndrome	

metabolic acidosis may increase ON perfusion and increase visual function. May cause hypokalemia when used with K^+-depleting diuretics such as Lasix and HCTZ. Not metabolized but excreted in urine. Diamox Sequels are better tolerated but have limited immediate effect.

BRINZOLAMIDE (Azopt) 1 gtt tid (suspension 1%). Less acidic, less stinging, but blurs vision more than dorzolamide. Can be dosed bid with a beta-blocker.

DICHLORPHENAMIDE (Daranide) 50 mg PO qd–tid. Many side effects, thus not commonly used in humans (veterinarians often use it).

DORZOLAMIDE (Trusopt) 1 gtt tid (solution 2%). Most common adverse effect is superficial punctate keratitis and local allergy. Can be dosed bid with a beta-blocker.

COSOPT (dorzolamide 2% + timolol 0.5%) 1 gtt bid.

METHAZOLAMIDE (Neptazane) 25–50 mg bid–tid. Has longer half-life than Diamox, is better tolerated and metabolized in the liver, not primarily excreted by the kidneys; thus, there are fewer stones and less metabolic acidosis (also less potent).

Glaucoma: Miotics/Cholinergic, Direct Acting

PROPERTIES Parasympathetic agents that mimic the effect of acetylcholine on muscarinic nerve endings. Used to lower IOP by stimulation of the longitudinal ciliary muscle to pull open and increase outflow through the TM (also closes intramuscular spaces and thus causes decreased uveoscleral outflow). In addition, may be used in the control of accommodative esotropia. Miotics cause accommodation and miosis and thus may have decreased patient compliance.

ACETYLCHOLINE (Miochol) Up to 3 mL intraocular; short acting.

CARBACHOL (Isopto Carbachol, Miostat intraocular) 1 drop tid (solution 0.75–3%), or intraocular injection 0.5 mL. Dual action as a direct muscarinic cholinergic agonist and also indirect-acting agent. Longer acting than Miochol.

PILOCARPINE (Pilocar, Isopto Carpine, Ocusert P-20 and P-40) 1 drop tid–qid or ½ inch ribbon of gel at bedtime (solution 0.25, 0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 8.0, 10%, gel 4.0%). Solution effect peaks in 2 hours, and half-life is 6 hours. Gel decreases IOP for 18 to 24 hours. Ocusert is left in place for 5 to 7 days and releases 20 µg (equivalent to 1% drop qid) or 40 µg (equivalent to 2% qid). Works as a direct muscarinic agonist. Used for glaucoma control, prior to LPI, and 0.125% solution confirms an Adie's tonic pupil from supersensitive denervated smooth muscle. Binds to melanin; thus, increased dose is needed in darker irides.

- Cautions: RD potential from longitudinal ciliary muscle traction on the vitreous base. Young myopes may have increased myopia with miotics from increased convexity of lens and forward lens movement. Miosis causes nyctalopia and is especially troublesome in older patients with cataracts. May increase relative pupillary block; thus, 4% is contraindicated in acute and chronic angle closure, as there is increased anterior movement of the lens–iris diaphragm. Avoid in patients with uveitis who may have increased inflamation and pain; with chamber shallowing, may have posterior synechiae and may progress to pupillary block.

- Pilocarpine used with phospholine iodide (PI) actually causes slight pupillary dilation because acetylcholine (potentiated by PI) binds stronger than pilocarpine, which acts to displace acetylcholine from its receptor.
- Mnemonic: "4-3-2" rule: pilocarpine maximum concentration is 4% and is used qid, carbachol maximum is 3% and is dosed tid, and echothiophate maximum is 0.25% and is used bid.

Glaucoma: Miotics/Cholinergic, Indirect Irreversible

PROPERTIES Acetylcholinesterase is a ubiquitous enzyme in all cell membranes that hydrolyzes acetylcholine to inactive choline + acetic acid. Acetylcholinesterase inhibitors allow individual acetylcholine molecules to repeat their effect at muscarinic receptors (miosis, accommodation, longitudinal ciliary muscle) and with some agents at nicotinic receptors (as with edrophonium). Used in glaucoma to stimulate the longitudinal ciliary muscle that pulls open the TM. See Table 10–3 for side effects and precautions.

DEMECARIUM BROMIDE (Bromide) Indirect-acting cholinesterase inhibitor that irreversibly carbamylates acetylcholinesterase. Most carbamylating agents are shorter acting (physostigmine, enostigmine, pyridostigmine) and not used for glaucoma, except demercarium, which is longer acting.

DIISOPROPYL PHOSPHOROFLUORIDATE (DFP) Similar to phospholine iodide, irreversibly phosphorylates acetylcholinesterase.

TABLE 10–3
Cholinergic Precautions

Side Effects		Contraindications
Salivation	Myopia	Concurrent MAOI use
Lacrimation	Cataract	Anterior uveitis
Urination	Miosis	RRD risks (relative contraindications in young, high myopes)
Diarrhea	AV heart block	
Gastrointestinal upset	Bronchoconstriction	
Excessive sweating	Confusion, ataxia	
Pupil cysts	Hypotension	
Brow ache	Bradycardia	

AV, atrioventricular; MAOI, monoamine oxidase inhibitor.
Mnemonic: SLUDGE describes the common side effects.

ECHOTHIOPHATE IODIDE (phospholine iodide) 1 gtt bid (solution 0.03, 0.06, 0.125, 0.25%). Needs to be fresh and refrigerated. Indirect-acting cholinesterase inhibitor; longer duration and more potent than direct-acting agents. Used to lower IOP and decrease AC/A ratio in accommodative ET; also, is an insecticide that could be used topically for lice infestation of the eyelashes. Use only in pseudophakes or aphakes, as miosis is poorly tolerated in phakic patients.

- Irreversible phosphorylates not only acetylcholinesterase of the synaptic cleft and also pseudocholinesterase in the plasma that may cause prolonged succinylcholine paralysis and potentiate ester-type local anesthetics (like tetracaine, not lidocaine).
- Systemic side effects are uncommon, but there are many local effects: orbicularis or ciliary muscle spasm, intense miosis, cataractogenic (primarily in adults), iris pigment epithelium cysts (usually in children; may be prevented by coadministration with phenylephrine to constrict the dilator muscle), disruption of blood–aqueous barrier, anterior subcapsular cataract, punctal stenosis, and pseudopemphigoid.
- Treat overdose of phosphorylating cholinesterase inhibitors acutely with pralidoxime (2-PAM) that also treats organophosphate poisoning (e.g., insecticides).

Glaucoma: Sympathomimetics

APRACLONIDINE (Iopidine) 1 drop tid (solution 0.5, 1.0%]. Mainly used perioperatively for anterior segment laser treatment.

- Action: relatively selective alpha$_2$-adrenergic agonist that inhibits norepinephrine release from sympathetic nerves that are destined for beta-receptors in the ciliary epithelium (thus, it is an indirect beta-blocker). This leads to decreased aqueous humor formation and may increase uveoscleral outflow.
- Side effects: may cause follicular conjunctivitis and vasovagal response; up to 33% of patients develop tachyphylaxis. Some alpha$_1$ effect seen that causes pupil dilation, lid retraction, and does not cause systemic hypotension like clonidine.

BRIMONIDINE (Alphagan) 1 gtt bid–tid (solution 0.2%) now released as Alphagan P (0.15%) with a different preservative and less side effects.

- Action: highly selective alpha$_2$-adrenergic agonist (same mechanism as Iopidine) that decreases aqueous formation by up to 20%. Also increases uveoscleral outflow, and theoretically may be neuroprotective.
- Side effects: dry mouth, headache, fatigue, conjunctival blanching, lid edema, depression, syncope; in children, has been reported to cause respiratory distress or arrhythmias. Contraindicated with MAOI, use and use caution with concomitant beta-blockers or other antihypertensives, cardiac glycosides, and tricyclic antidepressants.

DIPIVEFRIN (Propine) 1 gtt every 12 hours (solution 0.1%).

- Action: nonselective prodrug of epinephrine that penetrates cornea better because it is more lipophilic. It is transformed by corneal esterases into active epinephrine; thus, it allows a 0.1% strength to be dosed rather than epinephrine (0.5%, 1.0%, 2.0%) and causes fewer systemic side effects than epinephrine.
- Side effects: often causes toxic follicular conjunctivitis or contact dermatitis.

EPINEPHRINE (Epifrin, Glaucon, Epinal, Eppy/N, Epitrate) 1 gtt qd–bid.

- Action: nonselective alpha and beta agonist that decreases aqueous formation acutely (may also have a paradoxical increased IOP) and increases uveoscleral and TM outflow by beta$_2$ stimulation. This leads to increased cAMP and decreased outflow resistance and thus decreased IOP by up to 20%.
- Side effects: mydriasis may precipitate ACG in narrow angles, may cause adrenochrome deposits, rebound hyperemia, hypertension, headache, and CME in aphakes and pseudophakes. See Table 10–4 for sympathomimetic precautions.

TABLE 10–4
Sympathomimetic or Adrenergic Agonist Precautions

Side Effects	Contraindications	
Hypertension	Cardiovascular disease	Narrow angles
Tachycardia	Hypertension	Aphakia
Arrhythmia		

Clinical note

Guidelines published by the Royal College of Ophthalmologists in 2004 indicate that the drugs of first choice in the treatment of primary open-angle glaucoma are prostaglandin analogues or beta-blockers, with carbonic anhydrase inhibitors and alpha agonists representing second choice. Combination drops are becoming increasingly popular (if for no other reason than saving patients prescription charges!)

Σκευάσματα Συνδυασμού Παραγόντων

- **Cosopt®**: timolol and dorzolamide, administered twice daily.
- **Xalacom®**: timolol and latanoprost once daily.
- **TimPilo®**: timolol and pilocarpine twice daily.
- **Combigan®**: timolol and brimonidine twice daily.
- **DuoTrav®**: timolol and travoprost once daily.
- **Ganfort®**: timolol and bimatoprost once daily.
- **Azarga®**: timolol and brinzolamide twice daily.
- **Simbrinza®**: brimonidine and brinzolamide; a new combination – the only one that does not contain the beta-blocker timolol; administered twice daily.

Taptiqom: Tafluprost and Timolol once daily

Θεραπευτική: At a glance

DRUG CLASS	FORMULATION	INDICATIONS	SIDE EFFECTS
α Adrenergic agonists			
Dipivefrin	0.1% solution	Glaucoma	Photosensitivity, conjunctival, hyperemia hypersensitivity
Phenylephrine	0.12%, 2.5%, and 10% solution	Mydriasis, vasoconstriction, decongestion	Same as for dipivefrin
Apraclonidine	0.5% and 1% solution	Ocular hypertension	
Brimonidine	0.1%, 0.15%, and 0.2% solution	Glaucoma, ocular hypertension	
Naphazoline	0.012%, 0.03%, and 0.1% solution	Decongestant	
Tetrahydrozoline	0.05% solution	Decongestant	
β Adrenergic antagonists			
Betaxolol (β_1-selective)	0.25% and 0.5% suspension	Glaucoma, ocular hypertension	
Carteolol (β)	1% solution		
Levobunolol (β)	0.25% and 0.5% solution		
Metipranolol (β)	0.3% solution		
Timolol (β)	0.25% and 0.5% solution and gel		

[a]Off-label use. Refer to Physicians' Desk Reference for Ophthalmic Medicines for specific indications and dosing.
[b]Mydriasis and cycloplegia, or paralysis of accommodation, of the human eye occurs after one drop of atropine 1%, scopolamine 0.5%, homatropine 1%, cyclopentolate 0.5% or 1%, and tropicamide 0.5% or 1%. Recovery of mydriasis is defined by return to baseline pupil size to within 1 mm. Recovery of cycloplegia is defined by return to within 2 diopters of baseline accommodative power. The maximal mydriatic effect of homatropine is achieved with a 5% solution, but cycloplegia may be incomplete. Maximal cycloplegia with tropicamide may be achieved with a 1% solution. Times to development of maximal mydriasis and to recovery, respectively, are: for atropine, 30-40 min and 7-10 d; for scopolamine, 20-130 min and 3-7 d; for homatropine, 40-60 min and 1-3 d; for cyclopentolate, 30-60 min and 1 d; for tropicamide, 20-40 min and 6 h. Times to development of maximal cycloplegia and to recovery, respectively, are: for atropine, 60-180 min and 6-12 d; for scopolamine, 30-60 min and 3-7 d; for homatropine, 30-60 min and 1-3 d; for cyclopentolate, 25-75 min and 6 h to 1 d; for tropicamide, 30 min and 6 h.

Μέγιστο Υποτονικό Αποτέλεσμα: Πότε?

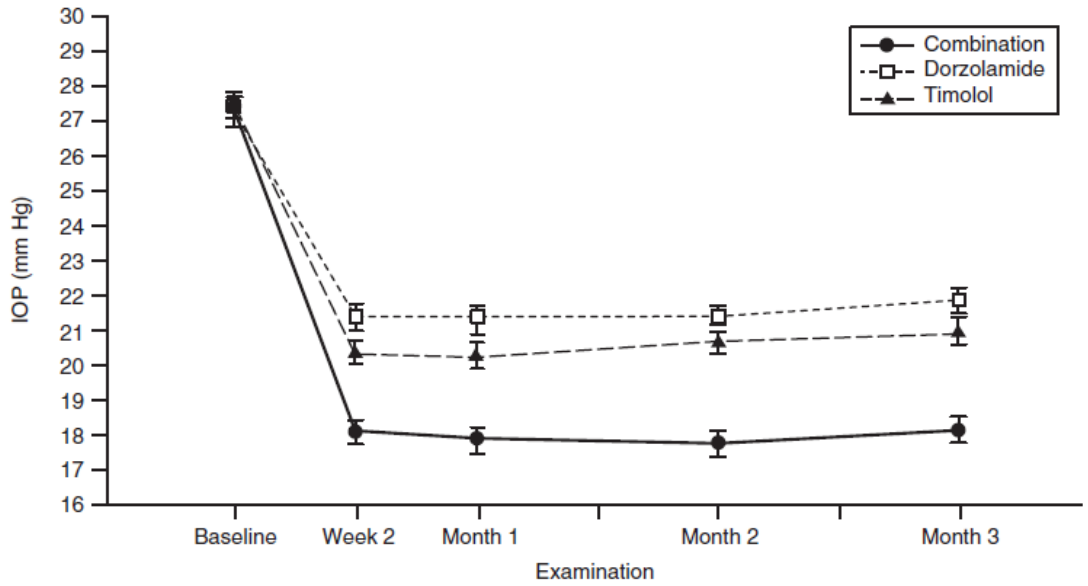


Figure 10-16 Mean intraocular pressure (IOP) at hour 2 (morning peak) for dorzolamide, timolol, and the combination product (Cosopt). The combination provided a greater decrease in IOP at all time points than did either single product. (Adapted from Boyle JE, Ghosh K, Gieser DK, et al. A randomized trial comparing the dorzolamide-timolol combination given twice daily to monotherapy with timolol and dorzolamide. Ophthalmology 1998;105:1945–1951.)

- Συστημικά

Glaucoma: Hyperosmotics

GLYCERIN (Osmoglyn) 1.0–1.5 g/kg PO (50%). Nauseating; give with cracked ice.

ISOSORBIDE (Ismotic) 1.5 g/kg PO (45%). Preferred in diabetic patients, as it is a nonmetabolized sugar.

Ακεταζολαμίδη PO
Ανεπ. Ενέργεια: Υπερχλωραιμική μεταβ. οξέωση με υποκαλιαιμία

MANNITOL (Osmitrol) 0.5–2.0 g/kg IV (5–20%). Because solutes are freely filtered by the glomerulus, serum osmolarity is increased and vitreous volume is decreased by 3 to 4%, resulting in decreased IOP. More potent than urea.

Αν. ενέργεια: επί καρδιακή ανεπάρκειας,προκαλει πνευμονικό οίδημα.

UREA (Ureaphil) 0.5–2.0 g/kg IV (30%).

- Αντιμεταβολίτες

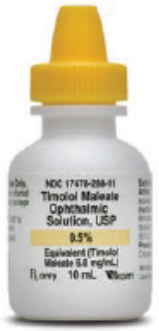
5-FLUOROURACIL (5FU): 50 mg/mL, 0.1 mL in 5–10 subconjunctival injections post-trabeculectomy, or 50 mg/mL on sponge for 3 to 5 minutes intraoperative. Pyrimidine analogue, inhibits thymidylate synthesis and DNA synthesis, incorporated during and aborts S phase, inhibits fibroblast proliferation; application effective for about 3 weeks. Epithelial toxic. Also used in breast, gastrointestinal, and skin CA.

MITOMYCIN C (MMC) 0.2–0.5 mg/mL, 2 mL administered intraoperatively. Alkylating agent that cross-links DNA, not cell cycle specific; dose is effective for about 5 hours. Has 100× > potency than 5FU. May cause avascular blebs, wound leak, hypotony, and intraocular toxicity.

HOW TO SAVE MONEY ON GENERIC LATANOPROST AND OTHER DRUGS

TIMOLOL EYE DROPS FOR MIGRAINE HEADACHE?

Acute migraine headaches may be reduced in intensity or stopped altogether with beta blocker eye drops. While the daily use of beta blocker pills has proved effective in preventing chronic migraine headaches, they have been unsuccessful in treating acute, sudden-onset migraines. Beta-blocker eye drops, however, are absorbed more quickly than pills by tear duct drainage onto the nasal mucosa, achieving therapeutic plasma levels "within minutes."



Migliazzo CV, Hagan JC. Beta-blocker eyedrops for treatment of acute migraine. Missouri Medicine. 2014; 111(4):283-8.

Myth **Never use a topical beta-blocker in a patient with asthma.**

Our Take With written consultation with the patient's asthma doctor, we have successfully used topical beta-blockers with several patients having asthma. Obviously, it is absolutely essential that you have the full, written consent of the patient's asthma physician before you prescribe a beta-blocker.

KEEP IN MIND

FINGERNAIL GROWTH, HEADACHE AND PROSTAGLANDIN EYE DROPS?

According to general correspondence from the American Glaucoma Society, it appears that prostaglandins, particularly bimatoprost, may cause fingernails to grow a bit faster than normal. This effect might be enhanced with direct application of a prostaglandin to the lunula (the crescent) up to the finger. Further, some patients have noticed an attenuation of their migraine headaches.

We have no idea of the widespread clinical validity of these anecdotal musings, but wanted to lay them out there for general clinical contemplation. It certainly appears that patients taking timolol and a prostaglandin could have improvement with their migraine headaches.

FROM THE LITERATURE

NEW PERSPECTIVES ON TARGET IOP

- "Meta-analysis shows mean IOP reduction with prostaglandin analogues ranges from 28-33%. Slightly smaller IOP reduction is typically achieved with beta-blockers whereas alpha-agonists and carbonic anhydrase inhibitors will usually reduce IOP by 15-20%."

Clement CI, Bhartiya S, Shaarawy T. New perspectives on target intraocular pressure. Surv Ophthalmol. 2014 Nov-Dec;59(6):615-26.

Αντιφλεγμονώδεις παράγοντες

- Κορτικοστεροειδή
  - Δραστικές: Δεξαμεθαζόνη, Κορτιζόνη, Φλουοκινολόνη, Φθοριομεθολόνη, Πρεδνιζολόνη, Τριαμσινολόνη, Μεθυλπρεδνιζολόνη, Υδροκορτιζόνη, Βηταμεθαζόνη
  - Αντενδείξεις/Παρενέργειες: Αύξηση ΕΟΠ – Δευτεροπαθές Γλαύκωμα Ανοικτής Γωνίας, Καταρρακτογένεση

UNLEASH THE POWER OF CORTICOSTEROIDS

Short acting
Hydrocortisone, cortisone, prednisolone

Intermediate acting
Triamcinolone, Fluprednisolone

Long acting
Dexamethasone ,betamethasone

Potency

Relative potencies of steroids

Steroid	Relative potency
Hydrocortisone	1 (the standard)
Cortisone	0.8
Triamcinolone	4
Prednisone	4
Prednisolone	5
Dexamethasone	25–30
Betamethasone	25–30
Fluorometholone	40–50
Fluocinolone	240

Anti-Inflammatory Effect of Different Dosage Schedules for Topical Administration of Prednisolone Acetate 1%

Treatment Regimen	Total No. of Doses Delivered	Decrease of Corneal Inflammation (%)
One drop every 4 hr	6	11
One drop every 2 hr	10	30
One drop every hr	18	51
One drop every 30 min	34	61
One drop every 15 min	66	68
One drop each min for 5 min every hr	90	72

Reprinted with permission from Leibowitz HM, Kupferman A. Anti-inflammatory medications. Int Ophthalmol Clin 1980;20: 117–134.

Scheme of relative potencies of steroids

Scheme	Steroid	Relative potency
Hide	Hydrocortisone	1
This	Triamcinolon	4
powerful	Prednisone	4
	Prednisolone	5
drug	Dexamethason	25-30
bees	Betamethason	25-30
fly	Flurometholone	40-50
	Flucinolone	240

Μηχανισμός Δράσης

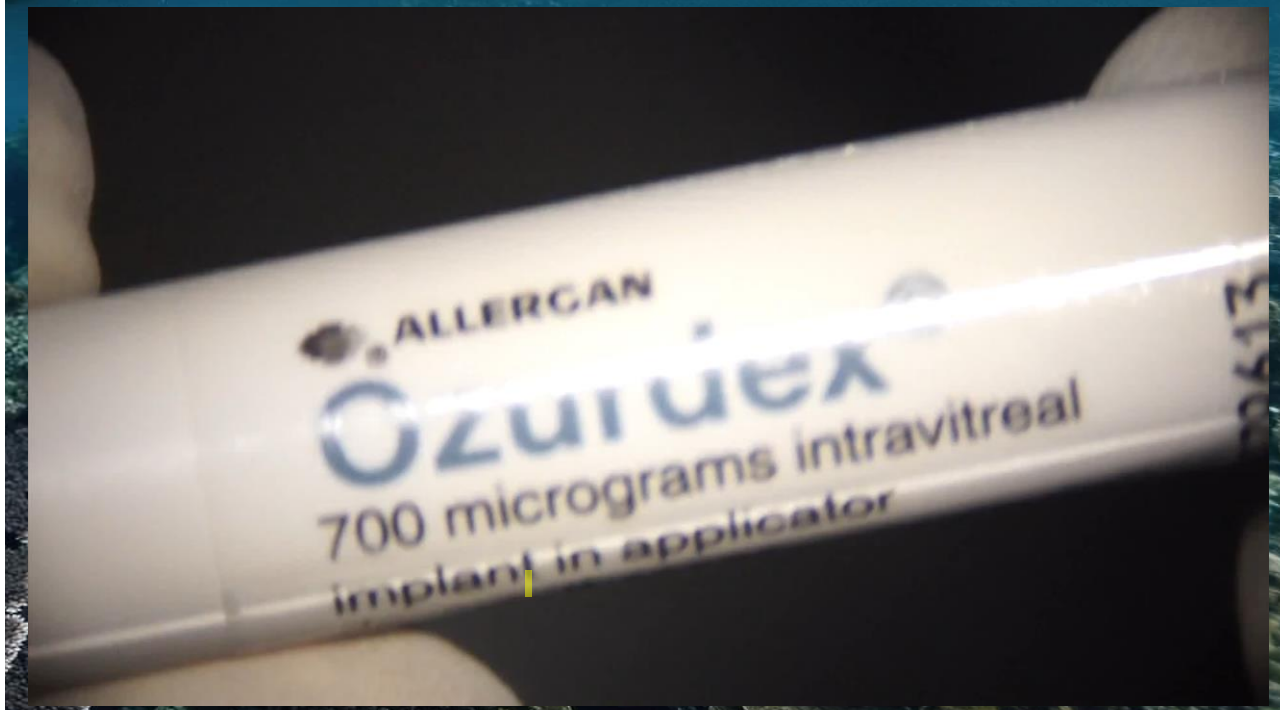
Anti-inflammatory: Corticosteroids

PROPERTIES Binds to cytoplasmic glucocorticoid receptor that binds to DNA to increase or decrease gene transcription (over 100 steroid-responsive genes). Clinical effects include decreased capillary permeability, chemotaxis inhibition, and suppression of fibrin deposition.

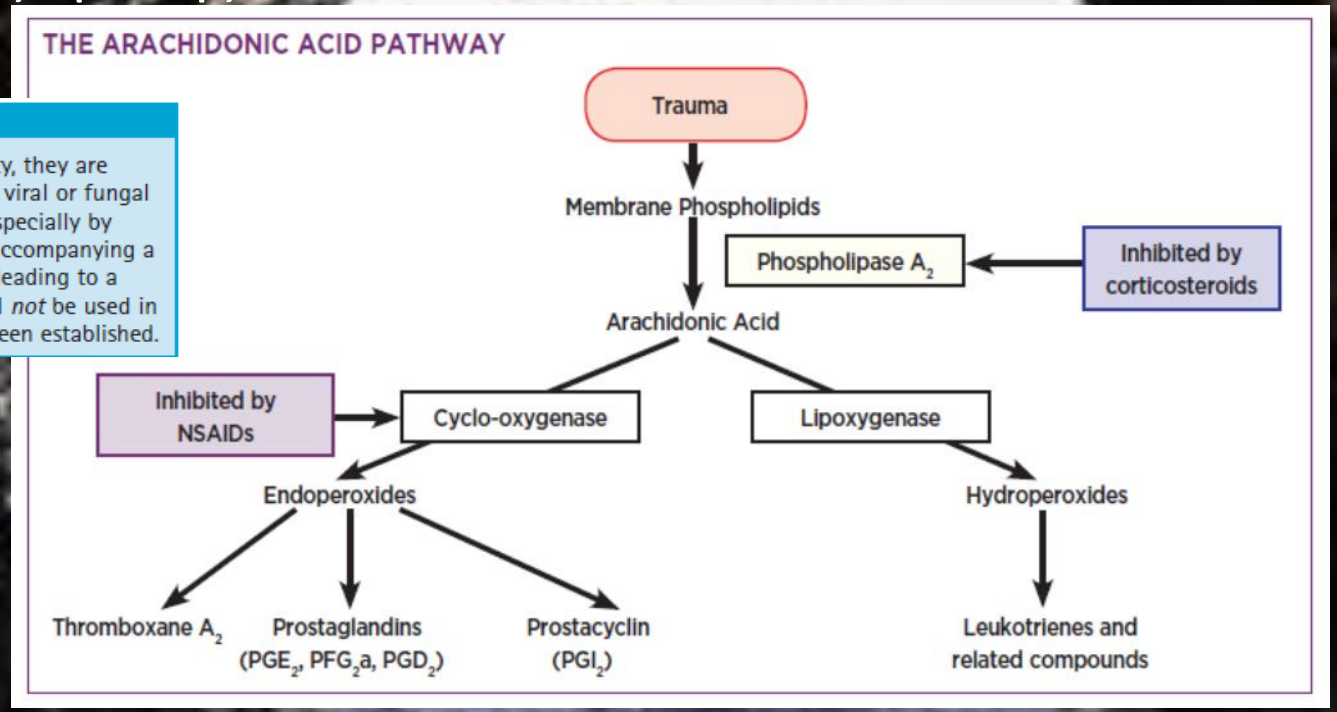
- Also decreases eicosanoids (lipids derived from arachidonic acid in the cell membrane phospholipids):
  - Inhibits cyclooxygenase-created prostaglandins: vasodilation, increased permeability of blood–ocular barrier, corneal neovascularization, decreased IOP via prostaglandin E2, prostaglandin D2, and prostaglandin F2-alpha.
  - Inhibits lipoxygenase-created leukotrienes: chemotactic for PMNs and eosinophils, conjunctival and uveal edema, immune modulation.
- Also decreases platelet-activating factor, cytokines, tumor necrosis factor, nitrous oxide, and adhesion molecules. Downregulates ICAM-1, which is responsible for white blood cell (WBC) migration, and decreases growth factors and beta-adrenergic receptors.
- May suppress endogenous steroids from adrenal cortex; created from cholesterol into corticosteroids (21 carbons) or androgens (19 carbons).

Ενδοϋαλοειδικά εμφυτεύματα Δεξαμεθαζόνης

- Παρατεταμένη Χορήγηση (Εξάμηνη)
- Χρόνιες Παθήσεις Οπισθίου Ημιμορίου



- Μη Στεροειδή Αντιφλεγμονώδη
  - Δραστικές: Δικλοφενάκη, Κετορολάκη, Νεπαφενάκη, Φλουρμπιπροφένη, Βρωμφενάκη
  - Μηχανισμός δράσης:



Clinical note

Because topical corticosteroids reduce local tissue immunity, they are capable of aggravating an eye infection, particularly if it is viral or fungal in origin. They can also facilitate opportunistic infection, especially by bacteria. If a steroid were used to treat the inflammation accompanying a herpes simplex ulcer, viral replication would be encourage leading to a much larger area of ulceration. Accordingly, steroids should *not* be used in the treatment of a 'red eye' if the exact aetiology has not been established.

Clinical note

Aspirin (acetylsalicylic acid) is a well-known example of a NSAID. The use of NSAIDs is generally considered to be contraindicated in patients with a history of sensitivity to, or adverse reactions from, aspirin.

- Αντενδείξεις/Παρενέργειες: ενδέχεται να οδηγήσουν σε κερατίτιδα ή έλκος κερατοειδούς

Αντιαλλεργικά

- Αντιισταμινικά (ανταγωνιστές των υποδοχέων H_1)
  - Δραστικές: Κετοτιφαίνη, Φενιραμίνη, Ανταζολίνη
  - Μηχανισμός δράσης: Αναστολή της απελευθέρωσης ισταμίνης
- Σταθεροποιητές των μαστοκυττάρων
  - Δραστικές: Χρωμογλυκικό, Αμλεξανόξη
  - Μηχανισμός δράσης: Αναστολή της απελευθέρωσης της ισταμίνης και διαφόρων μεσολαβητών της φλεγμονής από τα μαστοκύτταρα
- Αντιισταμινικά και Αναστολείς των μαστοκυττάρων
  - H_1 ανταγωνιστές και Αναστολείς των Μαστοκυττάρων: Ολοπαταδίνη, Αζελαστίνη, Βεποταστίνη
  - H_1 και H_2 ανταγωνιστές και Αναστολείς των Μαστοκυττάρων: Επιναστίνη

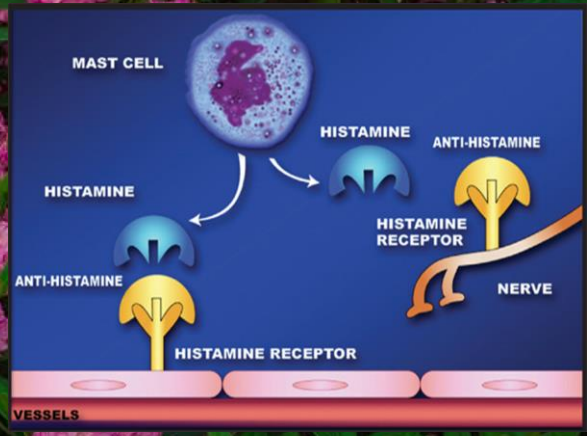


Table 16.1

Drug category	Precaution
Anti-bacterials	Must be used with caution in pregnancy, lactating mothers and infants under the age of 1 year.
Anti-virals	These agents are relatively toxic and may lead to a punctate keratopathy.
Anti-fungals	These are toxic to the corneal epithelium and lead to superficial punctate keratopathy. If used together, polyenes and imadazoles may antagonize each other and reduce effectiveness.
Corticosteroids	**Contraindicated** in acute superficial herpes simplex keratitis and fungal keratitis. Corticosteroids may potentiate herpes simples virus replication and their long-term use may increase intraocular pressure and induce cataract.
Non-steroidal anti-imflammatory	Occasionally implicated in the development of sterile corneal infiltrates and sterile keratolysis.
Vasoconstrictors	Excessive systemic absorption may cause hypertension and long-term use can cause an acute or chronic inflammatory conjunctivitis due to the preservative.
Mydriatics and cycloplegics	Will cause photophobia. Adults should not drive or operate machinery while the pupils are significantly dilated. Mydriatics have the potential to induce angle-closure glaucoma in patients with shallow anterior chamber angles.

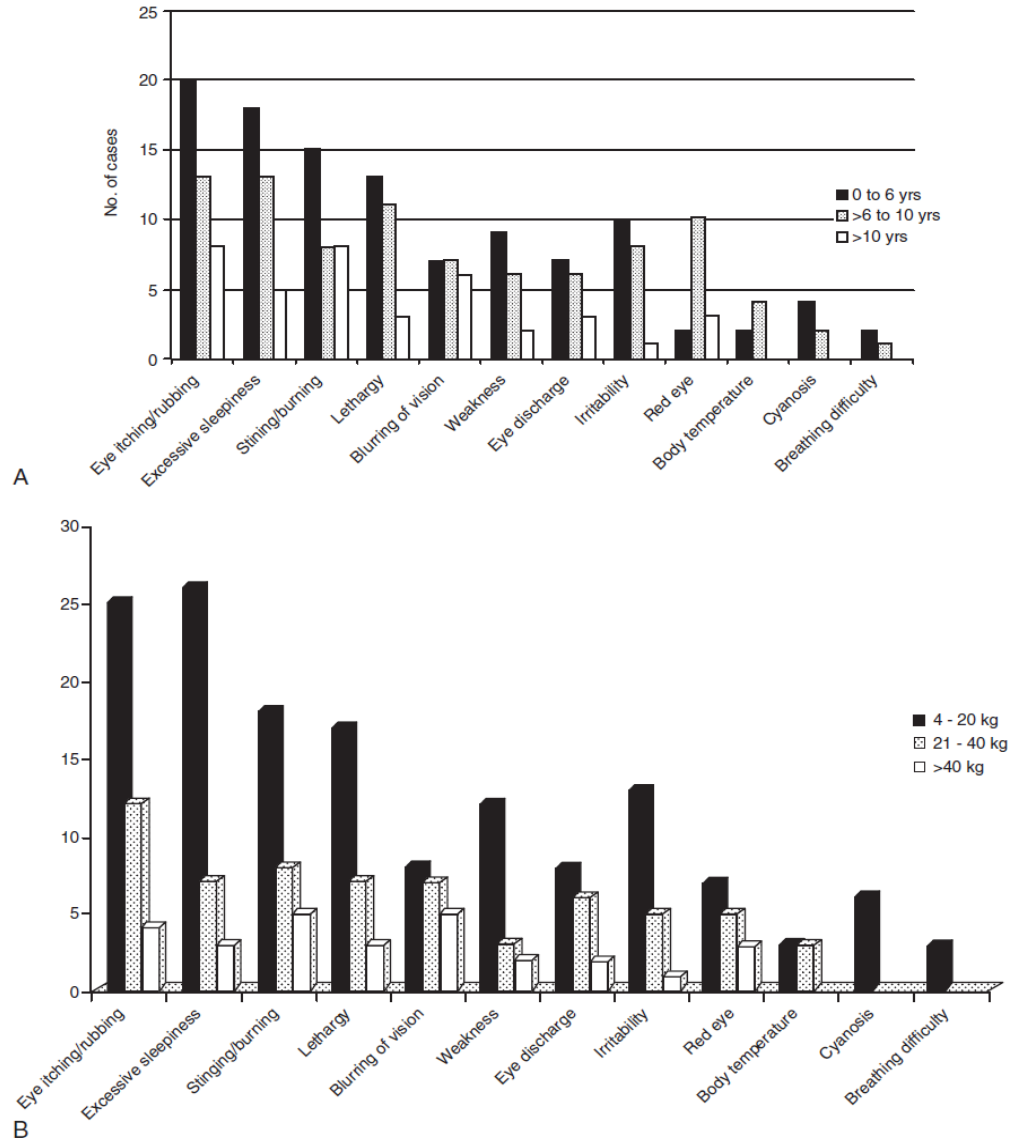


Figure 10-13 *(A)* Bar graph showing an overview of brimonidine side effects by age. Note that most side effects were reported in patients younger than 10 years of age. *(B)* Bar graph showing an overview of brimonidine side effects by weight. Note that most side effects were reported in patients less than 20 kg. (Adapted from Al-Shahwan S, Al-Torbak AA, Turkmani S, et al. Ophthalmology 2005;112:2143–2148.)

***Ένθετο**: Από που ενημερώνομαι για τα εμπορικά σκευάσματα?*

Είσοδος χρήστη | Ανανέωση συνθηματικού | Δωρεάν εγγραφή

Γαληνός
Οδηγός φαρμάκων

Εμπορική, δραστική, barcode, νόσος, κ.α. Αναζήτηση

Περιεχόμενα | Φαρμακευτικός οδηγός | Κωδικοποιήσεις | Εργαλεία | Περί Γαληνού

Γαληνός Mobile

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Φάρμακα | Δραστικές | Συμπληρώματα | Συγχορήγηση | Νόσοι ICD-10 | Ομάδες ATC

Καλώς ήλθατε στον Γαληνό

Τα δημοφιλέστερα φαρμακευτικά σκευάσματα τις τελευταίες 30 ημέρες

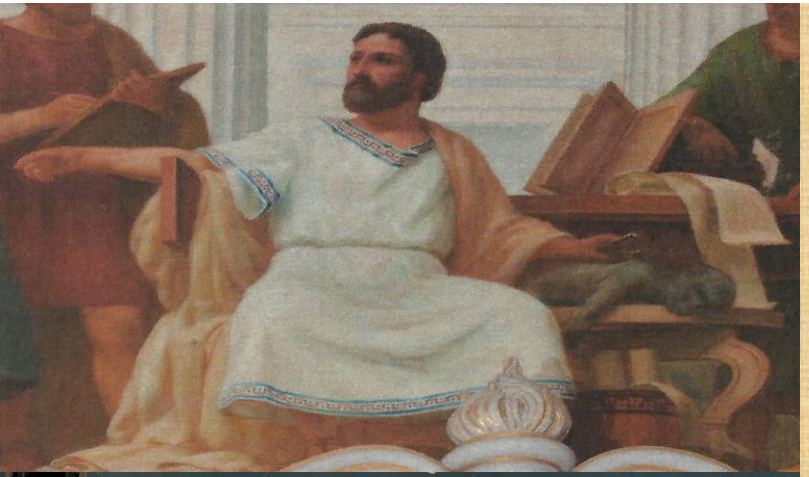
VAXIGRIP TETRA INJ.SU.PFS (15+15+15+15)MCG/0.5ML PF.S...	Sanofi Pasteur MSD
VIBRAMYCIN DISP.TAB 100MG/TAB BTX8 (BLIST.1X8)	Pfizer Hellas A.E.
FOSFOCIN GRA.OR.SOL 3G/SACHET BTx2SACHETSx3g	Vocate A.E.
VERTIGO-VOMEX MOD.R.CA.H (120+75+30)MG/CAP BTx20	Galenica A.E.
CIPROXIN F.C.TAB 500MG/TAB BTX10	Bayer Hellas A.B.E.E.
PREVENAR-13 INJ.SUSP 0,5ML/PF.SYR BTx1PF.SYR με χωριστ...	Pfizer Europe MA EEIG
ZINADOL F.C.TAB 500MG/TAB BTX14(BLIST2X7)	GlaxoSmithKline A.B.E.E.
FLAGYL CAPS 500MG/CAP BTX30 (BLIST.3X10)	Sanofi-Aventis A.E.B.E.
DALACIN C CAPS 300MG/CAP BTx16(BLIST 2x8)	Pfizer Hellas A.E.
NORGESIC TAB (450+35)MG/TAB BTx30	Meda Pharmaceuticals S.A.

Οι δημοφιλέστερες δραστικές ουσίες τις τελευταίες 30 ημέρες

Δεξαμεθαζόνη	Η δεξαμεθαζόνη (dexamethasone) είναι ένα συνθετικό γλυκοκορτικοειδές με επταπλάσια αντιφλεγμονώδη δράση από την πρεδνιζολόνη. Όπως άλλα γλυκοκορτικοειδή, η δεξαμεθαζόνη έχει επίσης αντιαλλεργικές, αντιτοξικές, αντιπυρετικές και ανοσοκατασταλτικές ιδιότητες.
Αμοξυκιλλίνη	Η αμοξυκιλλίνη (amoxycillin) είναι μία ημισυνθετική πενικιλλίνη (αντιβιοτικό βήτα-λακτάμης) η οποία αναστέλλει ένα ή περισσότερα ένζυμα (αναφέρονται συνήθως ως πενικιλλινοδεσμευτικές πρωτεΐνες, PBP) στην οδό βιοσύνθεσης της βακτηριακής πεπτιδογλυκάνης, ενός βασικού δομικού συστατικού του τοιχώματος του βακτηριακού κυττάρου. Η αναστολή της πεπτιδογλυκάνης οδηγεί σε εξασθένηση του κυτταρικού τοιχώματος, της οποίας συνήθως έπεται η λύση και ο θάνατος του κυττάρου.

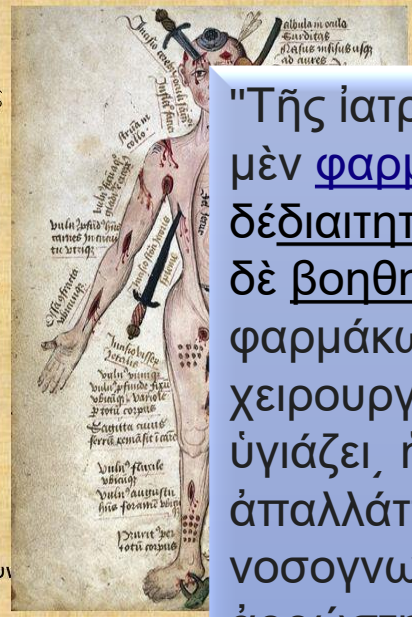
ZANIDIP
Λερκανιδιπίνη

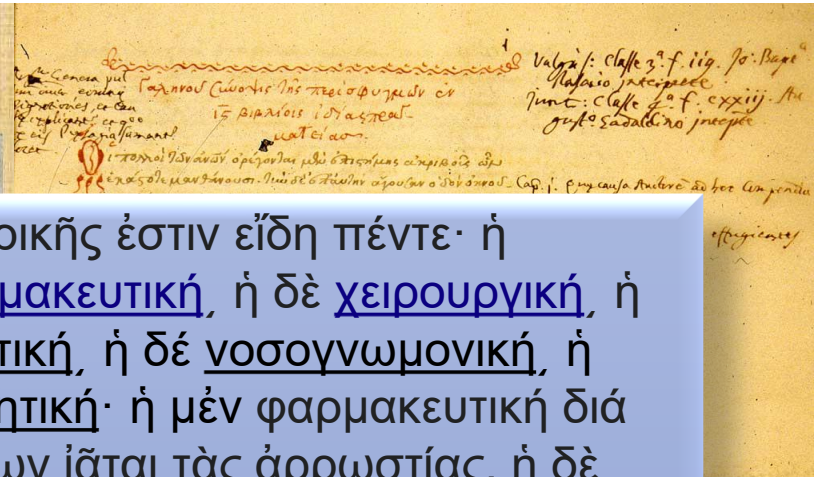
https://www.galinos.gr/



Γαληνός

- Στην **ελληνορωμαϊκή περίοδο** εμφανίζεται **ο Γαληνός** (Πέργαμος 129μ.Χ. – Ρώμη 199μ.Χ.). **Ήταν ο δεύτερος σπουδαιότερος Έλληνας ιατρός** της Αρχαιότητας μετά τον Ιπποκράτη και **ο τελευταίος** χρονικά από όλους τους σημαντικούς ιατρούς του ελληνορωμαϊκού κόσμου.
- Ασχολήθηκε με **την ανατομία, τη φυσιολογία, τη χειρουργική, την οφθαλμολογία, τη μαιευτική, την παθολογία, τη θεραπευτική, την υγιεινή και τη φαρμακολογία.**
- Ήταν ο πρώτος γιατρός στον οποίο επιτράπηκε να κάνει ανατομία σε άνθρωπο και οι παρατηρήσεις του στο **νευρικό, καρδιαγγειακό και αναπνευστικό σύστημα** ισχύουν ως σήμερα.
- Οι ανατομικές, βοτανολογικές, φαρμακευτικές και θεραπευτικές του μελέτες αποτέλεσαν την βάση της δυτικής ιατρικής για τα επόμενα 1500 χρόνια.
- Σε αντίθεση με τους συναδέλφους του, **τα φάρμακα τα παρασκεύαζε ο ίδιος**. Τα πολυσύνθετα φαρμακευτικά σκευάσματά του είναι γνωστά ως **«γαληνικά».** Έτσι, ονομάζονται και τα **σκευάσματα που σήμερα, φτιάχνουν οι φαρμακοποιοί στα φαρμακεία** → γαληνικά.





"Τῆς ἰατρικῆς ἐστιν εἴδη πέντε· ἡ μὲν φαρμακευτική, ἡ δὲ χειρουργική, ἡ δέδιαιτητική, ἡ δέ νοσογνωμονική, ἡ δὲ βοηθητική· ἡ μέν φαρμακευτική διά φαρμάκων ἰᾶται τὰς ἀρρωστίας, ἡ δὲ χειρουργικὴ διά τοῦ τέμνειν καὶ καίειν ὑγιάζει, ἡ δὲ διαιτητικὴ διά τοῦ διαιτᾶν ἀπαλλάττει τῆς ἀρρωστίας, ἡ δὲ νοσογνωμονική διὰ τοῦ γνῶναι τὸ ἀρρώστημα, ἡ δὲ βοηθητική διά τοῦ βοηθῆσαι εἰς τὸ παραχρῆμα ἀπαλλάττει τῆς ἀλγηδόνος."
Αριστοτέλης, Περί διαιρέσεων (De divisiones).

Τα πολυσύνθετα φαρμακευτικά σκε
γνωστά στη βιβλιογραφία ως «γαλ
ονομάζεται «γαληνική φαρμακευτικ
προώθησαν σημαντικά την ιατρική
«γαληνισμός», επεκράτησε στην ευρωπαϊκή ιατρική επί δεκατέσσερις αιώνες (κατά τον Μεσαίωνα και στον αραβικό κόσμο). η βαθμονόμηση της δραστικότητας των φαρμάκων απολάμβανε καθολική αποδοχή για περισσότερο από 1600 χρόνια και μόλις στα μέσα του 19ου η φαρμακολογία εγκατέλειψε το σύστημα των ποιοτήτων και των βαθμών έντασης των φαρμάκων που εισήγαγε.

Σας Ευχαριστώ για την
Προσοχή σας!
Καλά Χριστούγεννα!
Και
Ευτυχισμένο το Νέο Έτος!