

Site of Action / Mechanism / Effect	Options	Clinical Use	Ocular Side Effects	Systemic Side Effects	Prescribing Considerations	Contraindications Drug Interactions
<p>→ mimic phys. effects of glucocort., mineralocort., androgens</p> <p><u>mediated by nuclear receptors to:</u></p> <p>-alter transcription, protein synthesis @ nuclear level -induce lipocortin-1, cAMP-dep. Kinases -repress AP-1, NF-kB -block phospholipase A2 -inhibit COX2, iNOS (affects NO), collagenase (inflamm.) synthesis -inhibit all eicosanoid synthesis</p> <p><u>affects these mediators:</u></p> <p>-eicosanoids (release PG to get pupil miosis, vasodilation, inc. vasc. Perm., disruption of BR/BA barriers, altered IOP) -cytokines -complement -NO -IgG</p> <p><u>→ effect::</u></p> <p>-inhibit inflamm. cell migration -interfere w/ lymphocyte act. -inhibit fibroblast proliferation &amp; activity -decrease collagen &amp; GAG synthesis -decrease mediator synthesis -reduce capillary permeability/proliferation -free radical scavenging</p>	<p><u>Topical ocular</u></p> <p>-monocular Tx, ant. seg. Disease, get epithelial keratopathy, alternate day therapy to get Gcort synthesis)</p> <p><u>Periocular</u></p> <p>-for greater anti-inflamm effect, noncompliant patients, monocular... but uncomfortable</p> <p><u>Systemic</u></p> <p>-posterior segment, optic nerve and orbit, to treat both eyes</p> <p><u>systemic/ophthalmic:</u></p> <p><b>1. prednisolone</b> -suspension/solution -prodrug is prednisone -ant. seg.. inflammation (pred acetate)</p> <p><b>2. dexamethasone</b> -suspension/solution/oint. -most potent! -long acting</p> <p><u>ophthalmic:</u></p> <p><b>3. fluormetholone</b> -suspension/ointment -allergies -ant. seg.. inflammation</p> <p><b>4. rimexolone</b> -suspension -allergies -ant. seg.. inflammation</p> <p><b>5. loteprednol</b> -suspension -soft drug→ broken down quickly; good for GLC -allergies</p> <p><b>6. medrysone</b> -suspension -least potent! -poor corneal penetration -superficial inflammation</p> <p>(Also methyprednosolone, tramcinolone, fluticasone, bethamethasone, budesonide)</p>	<p><b>1. suppress all inflammatory responses</b> -in unresponsive/severe allergies -primary/secondary inflammation</p> <p><b>2. anti-inflammatory agent</b> -palliative therapy -degenerative conditions refractory to steroid therapy -autoimmune disorders, cancer, transplant rejection</p>	<p>With <u>periocular administration:</u></p> <p>-local ulceration/subconj adhesions, RD, papilloedema, orbital infections, allergy</p> <p><b>-posterior subcapsular cataract (PSC)</b> [via less protein binding, inhibit Na/K ATPase, incr. gluconeogenesis, inhibit RNA synthesis, unresolving; esp in children, DB, Hispanics; greater risk oral/inhaled]</p> <p><b>-elevated IOP/GLC</b> [topical therapy, esp with dexamethasone, prednisolone]</p> <p><b>-retardation of corneal epithelial healing</b></p> <p><b>-lowered resistance to infections</b> [can increase super-infection risk, mask/reactivate underlying disease, prolong HS infections, fungal infections]</p> <p><b>-steroid uveitis</b></p> <p><b>-mydriasis &amp; ptosis</b></p> <p><b>-transient ocular discomfort</b></p> <p><b>-refractive changes</b></p> <p><b>-blurred vision</b></p> <p><b>-increased corneal thickness</b></p> <p><b>-dry eye syndrome</b></p>	<p><b>metabolism</b> -osteoporosis/growth retardation -muscle/skin wastage -increase blood glucose -increase blood glucose/exacerbation diabetes -obesity, acne</p> <p><b>immune</b> -increase susceptibility to infection</p> <p><b>altered salt/water balance</b> -hypertension -edema -hypokalaemia -hypernatraemia</p> <p><b>hoarse voice</b></p> <p><b>depression / psychoses</b></p> <p><b>adrenal suppression</b></p> <p><b>hirsutism</b></p>	<p>-penetration ability -location</p> <p>-potency: acetate&gt; alcohol&gt; phosphate</p> <p>-ointments reach higher conc. In ant. Seg. Except dexamethasone</p> <p>-Use minimal effective dose for shortest period because of SE</p> <p>-Necessary to taper off of long-term, high-dose therapy because of feedback control of CORTs to prevent relapse and death</p> <p>-Don't use for: -degenerative cond. -infections</p> <p>-alternate day therapy for shorter acting steroids</p>	<p><b>CONTRAINDICATION</b> -infections. Need to use with drug that directly targets the organism</p> <p>-Glaucoma</p> <p>-Also, diabetes, heart conditions, renal disease, osteoporosis, sever psychosis</p> <p><b>DRUG INTERACTION</b> -barbituates, phenytoin lower efficacy of anti-coagulants</p>

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<p><b>1. inhibit cyclooxygenase</b> (PG synthesis)</p> <p>2. minimal effect on leukotriene synthesis at low doses -except diclofenac— indirect partial</p> <p>3. free radical scavengers</p> <p><u>actions:</u></p> <ol style="list-style-type: none"> <li>anti-inflammatory</li> <li>analgesic -PG related -or Direct on nerves</li> <li>antipyretic</li> </ol>	<p><u>ophthalmic:</u></p> <ol style="list-style-type: none"> <li><b>diclofenac (0.1%)</b></li> <li><b>flurbiprofen (0.03%)</b></li> <li><b>suprofen (1%)</b></li> <li><b>ketorolac (0.5%)</b></li> </ol> <p><u>systemic OTC's</u></p> <ol style="list-style-type: none"> <li><b>aspirin &amp; salicylate der</b> -methy/copper salicylate, diflunisal (no anti-pyretic activity, good anti-inflamm. -low dose analgesic -high doses anti-inflamm.</li> <li><b>propionic acid der.</b> -ibuprofen, naproxen, ketoprofen, flurbiprofen</li> <li><b>indoleacetic acid der.</b> -indomethacin, etodolac, sulindac</li> <li><b>fenamates</b> -diclofenac, meclofenamate</li> <li><b>oxicams</b> -pairoxicam</li> <li><b>ketorolac</b></li> <li><b>COX2 Inhibitors</b> -celecoxib, rofecoxib</li> <li><b>pyrazolones</b> -phenylbutazone</li> <li><b>acetaminophen</b> -paracetamol -weak inflammatory action -good antipyretic/analgesic</li> </ol>	<p><i>* off label</i></p> <p>- block intraoperative miosis from PG release (e.g. CAT surgery; effect small when used alone and effect greater in light irides) -<i>*post-op inflammation</i> -<i>*allergies</i> -<i>*pain control post-RK, PRL</i></p> <p>-block intraoperative miosis -post-op inflammation -uveitis</p> <p>-intraoperative miosis -contact lens GPC</p> <p>-post-op inflammation -allergies -<i>*pain control</i> -<i>*cystoid macular edema</i></p> <p>-more generalized effect; adjunct to ophthalmic therapy</p> <p>NSAIDS: -also corns, muscle sprains (salicylates), auto immune diseases, ulcerative colitis (sulfasalazine), colon cancer prophylaxis and CV uses (aspirin), gout</p>	<p>-NO rebound inflamm. or risk of GLC!</p> <p>-delayed wound healing, corneal melts -transient ocular irritation</p> <p>-delayed wound healing, corneal melts</p> <p>-delayed wound healing, corneal melts -transient ocular irritation</p> <p>-delayed wound healing, corneal melts -transient ocular irritation</p> <p><u>Long term, high systemic doses:</u> -blurred vision, -retinopathy</p> <p>In general, -allergies -interactions with viruses? -photosensitivity -corneal deposits -optic neuritis -pseudomotor cerebri</p>	<p>-GI distress/bleeding</p> <p>- prolongation bleeding</p> <p>-hypersensitivity (15% with <i>aspirin</i>, also cross-sensitization)</p> <p>-Reye's syndrome (<i>aspirin/salicylates</i>)</p> <p>-toxic doses (<i>salicylism</i>) can be deadly</p> <p>-<i>idoleacetic acids</i> generally high tolerance</p> <p>-less GI effects with propionic acid der. Cf. aspirin</p> <p>-<i>phenylbutazone</i> SEs life-threatening</p> <p>-<i>acetaminophen</i> hepatotoxicity</p> <p>-CNS effects</p>	<p>-Good alternative to corticosteroids because no risk of glaucoma.</p> <p>-Don't need to taper like corticosteroids</p> <p>-drugs vary in duration of action</p> <p><b>Condition specific:</b></p> <p><u>Short term analgesia</u> -acetaminophen -ibuprofen -aspirin?</p> <p><u>Fever</u> -acetaminophen -aspirin</p> <p><u>external applications</u> (corns, muscle sprains) -aspirin/salicylates</p> <p><u>chronic pain/inflamm.</u> -sulfasalazine (RA) -naproxen -piroxicam -diflunisal -celecoxib -rofecoxib</p> <p><u>aspirin special app</u> -colon cancer prophylaxis</p> <p><u>COX2 new role</u> -stomach cancer</p>	<p><u>Precaution:</u> -soft contact lenses</p> <p>-older eyes + intraocular surgery</p> <p>-children? Pregnant?</p> <p><u>Drug Interactions:</u> -bromonidine, carbachol will decrease their efficacies b/c of decrease in PG</p> <p>-possible cross reaction with aspirin</p>

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Slow Acting Anti-Rheumatic Drugs / Disease Modifying Anti-Rheumatic Drugs	<p><b>1. inhibits phagocytosis</b> -gold salts</p> <p><b>2. lysosome stabilization</b> (gold salts, chloroquines)</p> <p><b>3. traps free radicals</b> -chloroquines</p> <p><b>4. inhibits nucleic acid synthesis</b> -chloroquines, lefunomide</p> <p><b>5. T cell inhibition</b> -cyclosporin</p> <p><b>6. neutralize TNF-alpha</b> -monoclonal Ab, infliximab, receptor fusion protein, etanercept</p> <p><b>7. MMP inhibition</b> -galardin, tetracyclines</p> <p><b>8. chelation</b> -D-penicillanime</p>	<p><b>1. methotrexate</b> -first choice for RA</p> <p><b>2. chloroquine derivatives</b> -e.g. hydroxychloroquine -autoimmune -lysosome stabilization -traps free radicals -inhibit nucleic acid syn.</p> <p><b>3. gold salts</b> -e.g. aurothioglucose -for RA -inhibits phagocytosis -lysosome stabilization</p> <p><b>4. D-penicillamine</b> -chelation</p> <p><b>5. leflunomide</b> -inhibits nucleic acid syn.</p> <p><b>6. infliximab</b> -usu needs to be injected -neutralize TNF-alpha</p> <p><b>7. etanercept</b> -neutralize TNF-alpha</p> <p><b>8. cyclosporine</b> -dry eye -T cell inhibition</p>	<p>1. slow disease process and/or cause remissions</p> <p><u>D-penicillamine special app:</u> -heavy metal poisoning -Wilson's disease and copper accumulation</p> <p><u>Infliximab special app:</u> -Crohn's disease -inflammatory bowel disease [watch out for GI perforation if above 2 are long term!] -psoriasis</p>	<p><u>methotrexate</u> one of least problematic</p> <p><u>chloroquine:</u> -retinopathy -corneal whorls</p> <p><u>gold salts:</u> -corneal/lens deposits</p>	<p>SEs are often serious, high incidence due to cytotoxicity...</p> <p>-skin &amp; mucus membrane problems (can be ulcerations in mouth)</p> <p>-blood dyscrasias</p> <p>-renal &amp; liver damage</p> <p>-neuropathies (inc. hearing)</p> <p>-myopathies</p> <p>-infections</p>	<p>Slow onset (months) except for methotrexate</p>	
Gout	<p><b>1. inhibition of uric acid reabsorption</b></p> <p><b>2. inhibition of uric acid formation</b> -inhibit xanthine oxidase</p> <p><b>3. inhibition of uric acid phagocytosis</b> -colchicine</p> <p><b>4. reduce inflammatory response</b> -NSAIDs, colchicine</p>	<p><b>1. uricosuric agents</b> -probenacid -sulfapyrazone</p> <p><b>2. metabolic inhibitors</b> -allopurinol -for prophylaxis</p> <p><b>3. others (acute)</b> -colchicine -NSAIDs -steroids for severe</p>	<p>-for the excessive accumulation of uric acid in joints and kidney stones in gout</p>	<p>-photosensitivity</p>	<p>-GI (nausea, vomiting)</p> <p>-allergies (skin rashes, aplastic anemia)</p>		

Immunosuppressants	Site of Action / Mechanism / Effect	Options	Clinical Use	Ocular Side Effects	Systemic Side Effects	Prescribing Considerations	Contraindications Drug Interactions
	<p><u>Cytotoxic agents</u>  <b>1. prevent lymphocyte proliferation</b></p> <p><u>Immune modulators</u>  <b>1. block lymphokine synthesis</b>  <b>2. block inflammatory response</b></p>	<p><u>Cytotoxic agents</u>  <b>1. cyclophosphamide</b>  <b>2. chlorambucil</b>  <b>3. methotrexate</b>            -RA  <b>4. azathiaprine</b>  <b>5. colchicines</b>            -gout</p> <p><u>Immune modulators</u>  <b>1. cyclosporine A</b>            -dry eye  <b>2. dapsone</b>  <b>3. bromocriptine</b>  <b>4. tetracyclines</b>            -dry eye            a) decrease bacterial lipase activity            b) decrease expression &amp; activation of MMP to prevent collagen destruction in inflamm.</p>	<p>-catractal pemphigoid, Sjogren's syndrome</p> <p>-Bechet's disease</p> <p>-Mooren's &amp; other sterile corneal ulcers</p> <p>-ocular manifestations of rheumatoid arthritis</p> <p>-corneal grafts</p> <p>-sever atopic/vernal keratoconjunctivitis</p> <p>-uveitis</p> <p>-sympathetic ophthalmia</p>	<p>-nausea/vomiting            -headaches            -fatigue            -anorexia            -pneumonitis            -gingival hyperplasia            -hypertension            -hyperglycemia            -nephrotoxicity            -cirrhosis</p> <p><u>most serious:</u>            -bone marrow depression            Oleukopenia            -thrombocytopenia            -hemolytic anemia            -infertility            -mutogenicity            -teratogenicity            -cancer</p>			