

Case Based Management with Systemic Medications in Treating Adults and Special Populations

**Bruce E. Onofrey, OD, RPh, FAAO
Professor, University of Houston
University Eye Institute**

QUESTIONS? CALL ME



- **E:MAIL**

- **EYEDOC3@AOL.COM**

bonofrey@optometry.uh.edu

What is a special population?

- **Pregnant**
- **Reduced renal function**
 - **Diabetes**
 - **Drugs**
 - **Age**
- **Reduced hepatic function**
 - **Age**
 - **Drugs**
 - **Disease**
- **Pediatric**

Know your drug class for the pregnant patient

- **A = absolutely safe in pregnancy**
- **B = Probably safe**
- **C = questionable safety**
- **D = Probably NOT safe**
- **X = Absolutely NOT safe**

Reduced renal function

- **Be familiar with creatinin clearance formula – age related risk**

– Cockcroft Gault equation

(IBW in kg) x (140-age)

----- x (0.85 for females)

72 x (Scr in mg/dL)

- **Drug risk ie NSAIDS**
- **Disease risk ie Diabetes**

Reduced hepatic function

- **Main site of metabolism**
 - Phase 1
 - Phase 2
- **Under 16 yrs**
- **Alcohol consumption**
- **Acetaminophen use**
- **Hepatitis**
- **1st pass effect**
- **Abnormal bleeding hx**

Special dosing formulas for special patients

- **Age**
- **Weight**
- **Body Surface Area**

Young's Rule

- **Based on age**
- **$\frac{\text{Age (yrs)}}{\text{Age} + 12} \times \text{Adult dose} = \text{Pediatric dose}$**
- **Example: 6 y/o gets acetaminophen q 4h.
Adult dosage = 650mg q 4h**
- **$\frac{6}{6 + 12} \times 650\text{mg} = 216 \text{ mg}$**

Webster's Rule (Modified Young's)

- **Based on age (modified- Kids are fatter now)**
- $\frac{\text{Age} + 1 \text{ (yrs)}}{\text{Age} + 7} \times \text{adult dose} = \text{Pediatric dose}$
- **Example:**
- $\frac{6 + 1}{6 + 7} \times 650 = 350\text{mg}$

Clark's Rule

- **Based on weight**
- **More realistic and individualized**
- **Kids are larger today/greater obesity**
- **$\frac{\text{Wt (Lbs)}}{150} \times \text{adult dose} = \text{Pediatric dosage}$**
- **Example: 50/60/70 lb 6 Y/O's/
acetaminophen at adult dose of 650mg q
4h**
- **$\frac{50/60/70}{150} \times 650\text{mg} = 216/260/303\text{mg}$**

BSA example

- 3ft 3in tall child weighting 44 lbs has a BSA of:

- $$\frac{39 \text{ in} \times 44 \text{ lbs}}{3131} = 0.548\text{-sq rt} = 0.74 \text{ sq meters}$$

- $$\frac{100 \text{ cm} \times 20 \text{ kg}}{3600} = 0.555\text{-sq rt} = 0.75 \text{ sq meters}$$

- Quick BSA dose calculation =

Adult BSA = 1.73 sq M/adult dose acetaminophen
= 650mg q 6h

- Child's dose =
$$\frac{0.74 \text{ sq.M}}{1.73 \text{ sq. M}} \times 650\text{mg} = 282\text{mg}$$

Simple weight/dose calculations

- **PDR/package insert/facts and comparisons lists dose by weight**
- **Weight is almost always in Kg**
- **Dose is the full 24 hour dose**
- **Must know the frequency of dosing/D**
- **Must know the concentration of liquid dosage forms**
- **Must know the strengths of all solid dosage forms**

**If the standard pediatric
DAILY dosage of prednisolone
is 1mg/kg in divided dosage**

**Prescribe a standard dose for
a 33 lb child to be administered**

TID

**NOTE pediaped syrup contain
5mg/5ml prednisolone**

PEDIATRIC DOSAGE CALCULATION

- **CONVERT WEIGHT TO KILOS LBS/2.2
= KILO 33/2.2 = 15 KILOS**
- **DOSE OF 1MG/K X 15 K = 15MG
TOTAL DAILY DOSE**
- **DIVIDE DAILY DOSE BY NUMBER OF
DAILY DOSAGES 15MG/3 = 5MG
PER DOSE**
- **CONC = 5MG/5CC ADMINISTER 5 CC
TID PO**

Reference Material



Facts and Comparisons

PATIENT TO EYE DOCTOR:

**WHY DO YOU WANT TO
KNOW ABOUT MY LIVER?**

- **KIDNEYS?**
- **HEART?**
- **CREDIT REPORT?**

KNOW THY PATIENT

- Individuals ARE different
- HISTORY, HISTORY HISTORY @@@
- Medical
- Eye
- Allergy
- Medications
- Family
- Social
- Demographics

Pharmacologically: What is different about the elderly?

Greater incidence of pre-existing conditions= **contraindications**

Greater risk of drug interactions via autonomic effects

Greater incidence of interactions via altered pharmacokinetics –**Absorption distribution, metabolism and excretion**

Greater use of systemic meds with greater potential for **drug interactions**

ABSORPTION ISSUES

- **INCREASED** pH
- **DECREASED** GI motility
- **DECREASED** GI Empty time
- **DECREASED** Lipase
- **DECREASED** Bile acids
- **DECREASED** Gastric blood flow

- **END RESULT: DECREASED
ABSORPTION**

DISTRIBUTION ISSUES

- **DECREASED** Albumin 10-20%
- **DECREASED** TBW (water) now 50%
- **INCREASED** Body Fat

- **END RESULT: INCREASED FREE DRUG**
- **INCREASED TOXICITY POSSIBLE**



HEPATIC METABOLISM ISSUES

- **40-45% DECREASED** Renal blood flow
@ 65 y/o
- **DECREASED** Phase I
–OX/Red/hydrolysis/hydroxylation
- **SLTLY DECREASED** Phase II
–Synthetic RX's

**END RESULT: REDUCED
METABOLISM**

Plasma Half-Lives in Young and Old

Drug	Young (20-30)	Elderly (65-80)
Penicillin G	20.7 min	39.1 min
Tetracycline	3.5 hr	4.5 hr
Digoxin	51 hr	73 hr
Diazepam	20 hr	80 hr
Lidocaine	80.6 hr	139.6 hr
Chlordiazepoxide	8.9 hr	16.7 hr
Phenobarbital	71 hr	107 hr
Warfarin	37 hr	44 hr

RENAL EXCRETION ISSUES

- 20% **DECREASED** KIDNEY SIZE @ 80
- 12% GLOMERULAR SCLEROSIS
- **DECREASED** GFR
- **DECREASED** Creatinine Clear. 30-40% @80
- $(140 - \text{AGE}) \times \text{WT (kg)} / 72 \times \text{serum creatinine} = \text{Creatinine Clearance MEN}$
- **Woman X 0.85- less muscle mass**

CR Clearance and dosage

- **PEDIATRIC ACYCLOVIR**
- **> 50** **100% Q 8H**
- **25-50** **100% Q 12H**
- **10-25** **100% Q 24H**
- **0-10** **50% Q 24H**

BEWARE of Cardio- Pulmonary Disease patients

- **Most common condition in the elderly**
- **Patients take multiple meds**
- **Dosages very carefully titrated**
- **Very fine line between risk and benefit with meds**
- **High risk of Drug-Drug and Drug-patient interactions**

Pediatric Patients

- ◆ **Higher proportion of water**
- ◆ **Lower plasma protein levels**
 - More available drug
- ◆ **Immature liver/kidneys**
 - Liver often metabolizes more slowly
 - Kidneys may excrete more slowly

Conclusions

- ◆ **Children are not little adults**
- ◆ **Dosages must be based on actual pharmacokinetics factors**
- ◆ **Pediatric dosage formulas can only estimate a proper dose**
- ◆ **Pedes are always at greater risk for drug induced toxicity**
- ◆ **Go low and go slow**
- ◆ **Consult with pediatrician**

Augmentin

Indications/Dosage forms

- **Indications:**
- **Preseptal cellulitis**
- **Dacryocystitis**
- **Pediatric Hemophilus**
- **Amoxicillin + Clavulanate**
- **Dosage forms:**
- **500 or 875mg tablets BID**
- **125 or 250mg/5cc pediatric suspension**

Augmentin

Amoxicillin/Clavulanate

- **Broad spectrum penicillin (Staph, Strep, Hemophilus)**
- **Effective against penicillinase producers-
clavulanate blocks penicillinase@@@**
- **High therapeutic index**
- **Bacteriocidal**
- **Low GI side-effects**
- **Safe in pregnancy**
- **Watch out for allergy**
- **Cheap*****

Augmentin Dosing: Bacterial infections

Dose: 30 mg/kg/day PO div q12h; Info: use 125 mg/5 mL susp; dose based on amoxicillin component; give w/ food or milk

[>3 mo, <40 kg]

Dose: 25-45 mg/kg/day PO div q12h, use 200 or 400 mg forms; Alt: 20-40 mg/kg/day PO div q8h, use 125 or 250 mg forms; Info: dose based on amoxicillin component; give w/ food or milk

[>40 kg]

see Adult Dosing

Zithromax Azithromycin

- **Broad spectrum activity**
- **64 hour 1/2 life**
- **DOC in penicillin sensitive patients**
- **Effective in pediatric Hemophilus**
- **Mild-medium GI side effects**
- **Excellent compliance (5 day TX) (1 day for chlamydia)**
- **Moderate cost**
- **Drug Interactions??**

Azithromycin

Indications/Dosage forms

- **Indications:**
- **Drug of choice for Chlamydia**
- **Pediatric Hemophilus**
- **Penicillin substitute**
- **Dosage forms:**
- **250mg Z-Pak (6 capsules)**
- **1 gm packet**
- **100 and 200mg/5ml ped. suspension**

New Zithromax Tripak

- **Three 500mg tablets**
- **For adults**

Pediatric dosing-azithromycin

- ***3 day: 10mg/kg daily**
- **1 day: 30mg/kg**

Management Treatment of Impetigo

- **Cause: S. aureus/Strep sp**
- **Hypochlorous acid**
- **Oral Macrolide**
- **Bactroban (Mupirocin)**
- **Topical macrolide**
- **Can be mistaken for H. simplex**

Keflex

Cephalexin

- **Broad spectrum cephalosporin (1st generation)**
- **Bacteriocidal**
- **Moderately effective against penicillinase**
- **Relatively inexpensive**
- **Option for penicillin allergic patient******
- **Low GI side-effects**

The Second Generation Cephalosporins are Good for “HENPEK” Gram Negatives

- **H: Hemophilus**
- **E: E. coli**
- **N: Neisseria**
- **P: Proteus**
- **E: Enterococci**
- **K: Klebsiella**

Marginal Blepharitis and the “STAR TREK PARADOX”

- **IN THE 25TH CENTURY YOU CAN.....**
- **TRAVEL FASTER THAN THE SPEED OF LIGHT.....**
- **TRANSPORT INSTANTLY 1000'S OF MILES.....**
- **CURE ANY DISEASE, BUT UNFORTUNATELY.....**

JON LUC PICARD IS STILL BALD

- **BOTH BALDNESS AND MARGINAL BLEPHARITIS ARE INCURABLE**
- **IF YOU DON'T KNOW IT, YOUR PATIENT WILL EXPECT A CURE.....**
- **THAT WILL NEVER COME**

DOXYCYCLINE

- **Long acting/potent tetracycline**
- **Resistant to absorption problems**
- **Medium GI upset**
- **Good compliance (1-2 X/D dosing)**
- **No activity in acute bacterial eye disease**
- **Inexpensive**
- **Contraindicated in kids and pregnant patients**

Doxycycline

Indications/Dosage forms

- **Indications:**
- **Back-up drug for Chlamydia**
- **Acne rosaceae/chronic Staph blepharitis**
- **Dosage forms:**
- **50 and 100mg tablets/capsules**
- **25mg/5ml suspension**

A NEW USE FOR DOXYCYCLINE?

Doxycycline inhibition of interleukin-1 in the corneal epithelium.

Solomon A, Rosenblatt M, Li DQ, Liu Z, Monroy D, Ji Z, Lokeshwar BL, Pflugfelder SC

Ocular Surface and Tear Center, Bascom Palmer Eye Institute, Department of Ophthalmology, University of Miami School of Medicine, Florida 33136, USA.

PURPOSE: To evaluate the effect of doxycycline on the regulation of interleukin (IL)-1 expression and activity in human cultured corneal epithelium. MP.

RESULTS: Doxycycline significantly decreased IL-1beta bioactivity in the supernatants from LPS-treated corneal epithelial cultures. These effects were comparable to those induced by the corticosteroid,

CONCLUSIONS: Doxycycline can suppress the steady state amounts of mRNA and protein of IL-beta and decrease the bioactivity of this major inflammatory cytokine. These data may partially explain the clinically observed anti-inflammatory properties of doxycycline. The observation that doxycycline was equally potent as a corticosteroid, combined with the relative absence of adverse effects, makes it a potent drug for a wide spectrum of ocular surface inflammatory diseases.

BLEPHAROKERATOCONJUNCTIVITIS

**Most common in pedes and a different kind
of animal**



The Forgotten Antibiotics



Sulfa

- **Limited coverage**
- **Allergy**
- **No pregnancy**
- **No sickle-cell**
- **Only use with trimethoprim**

The Forgotten Antibiotics



The Fluoroquinolones

- **Only if allergic to all else**
- **No pregnant**
- **No Kids under 16**

Famvir

Famcyclovir

- **Third generation anti-viral medication**
- **Pro-drug**
- **Selective toxicity**
- **Excellent anti-herpetic activity**
- **Expensive, but cost-effective**

Famvir

Indications/Dosage forms

- **Indications:**
- **Resistant ocular simplex or Type II simplex**
- **125-250mg BID**
- **Hepes zoster 500mg TID**
- **Dosage forms:**
- **125/250/500mg tablets**

The Bridesmaids



- **Less potent**
- **More frequent dosing required**
- **longer TX period**
- **Not as proven in prevention of post-herpetic neuralgia**

Anti-viral dosages

- **SIMPLEX/ZOSTER**
- **Acyclovir: 400mg 5X/D @@@@/ 800 5X/D**
- **Valacyclovir: 500mg TID/ 1000mg TID**
- **Famcyclovir: 125mg BID/250mg TID/ 500mg TID**

Salagen Pilocarpine

- **Oral parasympathomimetic agent**
- **Stimulates exocrine gland secretion**
- **Monitor for GI upset**
- **Don't use in asthmatics**
- **Expensive**

Salagen

Indications/Dosage forms

- **Indications:**
- **Advanced, non-responsive Sjogrens@@@**
- **5mg QID**
- **Dosage form:**
- **5mg tablets**

Evoxac: New and improved pilocarpine



- **Parasympathomimetic**
- **Better tolerated**
- **30mg TID**
- **No titration necessary**
- **NEVER in asthmatics**

Vicodin

Hydrocodone/acetaminophen

- **Effective opiate analgesic agent**
- **Schedule III drug**
- **Good ratio of opiate to acetaminophen**
- **excellent synergism with ingredients**
- **Watch out for opiate (codeine) allergy-
ALLERGIC TO ONE OPIATE,
ALLERGIC TO ALL OPIATES@@@**
- **Watch out for alcohol and drowsiness**
- **Constipation/GI upset**

Vicodin

Indications/dosage form

- **Indications:**
- **Moderate to severe pain**
- **Corneal injuries/burns**
- **Procedures:**
- **Cryo therapy/PRK/PTK/micropuncture**
- **Dosage forms:**
- **Fixed ratio of 5mg/325mg**
Hydrocodone/acetaminophen

A better choice of narcotic anagesic:HOW ABOUT ULTRAM?

- **A synthetic opiate with slightly reduced opiate side-effects**
- **NOT for opiate allergics**
- **Not for addicts-Induce withdrawal**
- **Has produced addiction**
- **50-100mg QID prn-max 400mg/D**
- **>65, then 300mg/D max**
- **Ultracet, like Tylenol #3**

Ibuprofen/acetaminophen

- **Incredible synergism**
- **Non-narcotic drugs**
- **Non RX drugs**
- **Inexpensive**
- **Monitor for sensitivity to either drug**
- **No motrin in pregnancy/with blood thinners/GI problems/renal disease/CHF**

Ibuprofen/Acetaminophen Indication/contraindications

- **Indications:**
- **Mild to severe pain**
- **Dosage forms**
- **400-600mg motrin with 500-1000mg acetaminophen
(Do not exceed 4 gms acetaminophen/day)**
- **No acetaminophen for persons that regularly consume
daily alcohol**
- **Remember that acetaminophen does not inhibit
platelets and has no anti-inflammatory effect like
ibuprofen**
- **Acetaminophen OK in hyphema/ibuprofen-
NOT@@@**

Acetaminophen is a Safe Drug?



Drug of Choice (DOC) in:

- **Children**
- **Viral induced fever**
- **Pregnancy@@@@**
- **Nursing mothers**
- **No GI distress**
- **No Increase in Bleeding?**

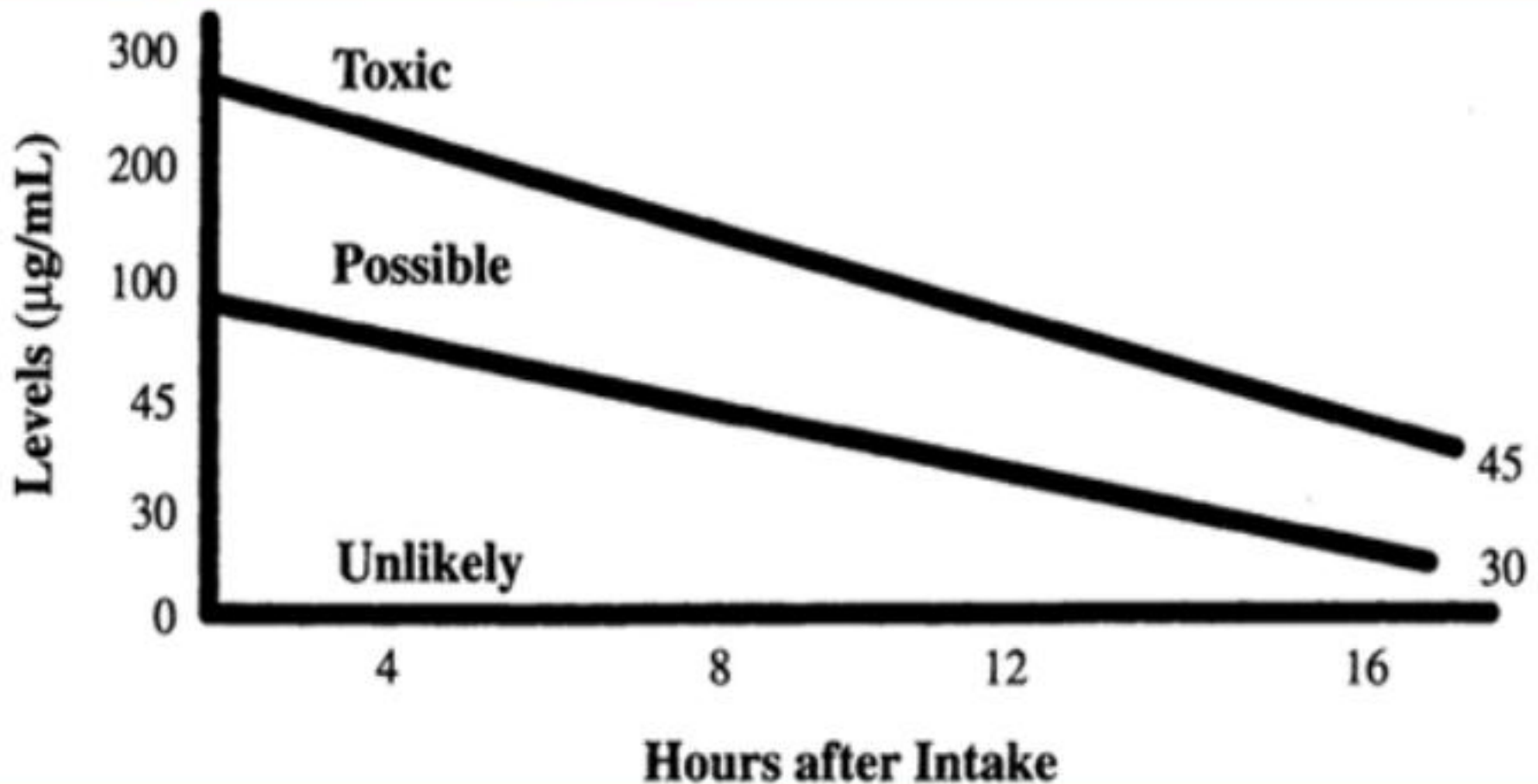
If They Like to Drink, Think Twice About Acetaminophen

- **Acetaminophen associated with liver failure in alcoholics (>3 drinks/d)**
- **Liver failure = decreased drug metabolism = overdose**
- **Reduced vitamin K clotting factors = increased bleeding**
- **Max adult dose = 4gm/D = 8 extra-strength Tylenol per 24 hours (2.6gms?)**
- **5% of metabolites hepatotoxic**

Acetaminophen toxicity

Medscape®

www.medscape.com



Medicines for Fever or Pain Relief

Acetaminophen Dosing Chart

Acetaminophen (Tylenol) is available without a prescription. Determine the correct dosage by finding your child's weight in the top row of the table. You may repeat the dosage every 4 to 6 hours as needed. Do not give acetaminophen more than 5 times a day. Do not use acetaminophen in children under 3 months of age. *If your infant has a fever during the first 12 weeks of life, see your child's health care provider.*

Weight	7-13 lbs	14-20 lbs	21-27 lbs	28-41 lbs	42-55 lbs	56-83 lbs	84-111 lbs	112+ lbs
Milligram dosage	40 mg	80 mg	120 mg	160 mg	240 mg	325 mg	480 mg	650 mg
Infant drops 80 mg/0.8 ml 1 dropper=0.8 ml	0.4 ml	0.8 ml	1.2 ml	1.6 ml	2.4 ml			
Children's liquid 160 mg/5 ml (1 tsp)	½ tsp (1.25 ml)	½ tsp (2.5 ml)	¾ tsp (3.75 ml)	1 tsp (5 ml)	1 ½ tsp (7.5 ml)			
Chewable Tablets 80 mg each			1 ½ tablets	2 tablets	3 tablets	4 tablets	6 tablets	8 tablets
Junior strength Tablets 160 mg each				1 tablet	1 ½ tablet	2 tablets	3 tablets	4 tablets
Adult Strength Tablets 325 mg each						1 tablet	1 ½ tablets	2 tablets

Abbreviations: mg = milligrams ml = milliliter tsp = teaspoon

Suppositories: Acetaminophen is also available as a rectal suppository in 120-mg, 325-mg, and 650-mg dosages. Suppositories are useful if a child with a fever is vomiting often or having seizures caused by the fever. Use the same dose as listed above for the suppository. Most suppositories can be cut (for example, cut in half) to supply the right dose for your child's age

NSAID Fact Sheet

- **Block cyclooxygenase**
- **All NSAID's have equivalent efficacy in equal dosages and dose frequency** ie 800mg motrin QID = 20mg of Feldene
- **Allergic to one allergic to all**
- **Never give to diabetics**

NSAIDS OF COURSE THEY'RE SAFER?

- **Only anti-inflammatory in high doses**
- **Think RK good for -11.00 myope or LASIK**
- **GI ulceration**
- **Renal failure**
- **Congestive heart failure**
- **All diabetics/No No No**
- **POOR anti-inflammatory effect**

Steroids Are Safer?

You must be kidding

- **Extremely effective anti-inflammatory effect**
- **Safe for short term use if.....**
- **No GI ulcer**
- **No psychotic**
- **No high BP**
- **No diabetes**

Medrol Dospak

Methyl prednisolone

- **High potency oral corticosteroid**
- **Good anti-inflammatory activity (glucocorticoid)**
- **Low mineralocorticoid activity**
- **Convenient**
- **inexpensive**
- **Safe*****

Medrol Dose-pak

Indications/dosage forms

- **Indications:**
- **Anterior uveitis/scleritis/Type I allergy**
- **Dosage form:**
- **Pre-labeled with descending dosage
(automatic daily taper over 6 days of TX)**
- **Always take with food/avoid in
diabetics/GI bleeders/blood
thinners/NSAIDS/hypertension/psychosis**

The 3 TOP REASONS FOR STEROIDS IN EYE DISEASE ARE:

@@@@@@@@

1. TEMPORAL ARTERITIS
2. CRANIAL ARTERITIS
3. ARTERITIC ISCHEMIC OPTIC
NEUROPATHY

No, you probably won't Tx it here, but
you'd better not miss it

80-100mg prednisone daily

The End



**Thanks for your time and
interest**