One View of STEROIDS
Who is this?

Infections With Possible Steroid Rx
- EBV
- TB
- Meningitis
- Septic Arthritis

EBV/Mono
Who painted this young woman with mono?
Steroids for her?
## Steroids for Acute Mononucleosis

<table>
<thead>
<tr>
<th>Rx</th>
<th>Assessment</th>
<th>T</th>
<th>Sx</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>IM, 5days</td>
<td>Daily</td>
<td>&lt;.001</td>
<td>ND</td>
<td>-</td>
</tr>
<tr>
<td>PO, 5days</td>
<td>Day 2</td>
<td>-</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>PO, variable</td>
<td>Daily</td>
<td>.01</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PO, 6days</td>
<td>Variable</td>
<td>.001</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>PO, 9days</td>
<td>12 hours</td>
<td>ND</td>
<td>.01</td>
<td>ND</td>
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<tr>
<td></td>
<td>60 hours</td>
<td>ND</td>
<td>-</td>
<td>ND</td>
</tr>
<tr>
<td>PO, 6days</td>
<td>1 week</td>
<td>ND</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>4 weeks</td>
<td>ND</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

## Use of Steroids for Complications

- Hemolytic Anemia / ITP
- Myocarditis
- Impending Airway Obstruction**

##何人得了TB？
**TB: Indications for Steroids**

- Pericarditis
- Meningitis
- Endo-bronchial disease in children
Meningitis
Yes To Steroids

Animal Data
- Post antibiotics- increase is TNF, interleukin 1, WBC in CSF
- Aborted by steroids with antibiotics
- Not aborted by antibiotics followed by steroids
- Inflammation correlated with poor prognostic features

Human Trial: Hearing Loss

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td># Evaluated</td>
<td>Study 1</td>
<td>Study 2</td>
</tr>
<tr>
<td></td>
<td>38</td>
<td>43</td>
</tr>
<tr>
<td>Any loss (%)</td>
<td>Study 1</td>
<td>Study 2</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>14</td>
</tr>
<tr>
<td>Severe bilat</td>
<td>Study 1</td>
<td>Study 2</td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>5</td>
</tr>
<tr>
<td>Hearing aids</td>
<td>Study 1</td>
<td>Study 2</td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>2</td>
</tr>
</tbody>
</table>

Lebel, MH. NEJM 1988; 319:964-71. Dexamethasone Therapy for Bacterial Meningitis: Results of Two Double-Blind, Placebo-Controlled Trials

Hearing Loss by Pathogen

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Placebo</th>
<th>Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>H.Flu</td>
<td>Study 1</td>
<td>Study 2</td>
</tr>
<tr>
<td></td>
<td>7/29</td>
<td>4/35</td>
</tr>
<tr>
<td>S.pneumo</td>
<td>Study 1</td>
<td>Study 2</td>
</tr>
<tr>
<td></td>
<td>1/6</td>
<td>1/3</td>
</tr>
</tbody>
</table>

Lebel, MH. NEJM 1988; 319:964-71. Dexamethasone Therapy for Bacterial Meningitis: Results of Two Double-Blind, Placebo-Controlled Trials

*P< 0.01
Human Trial: Neurologic Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Dex</th>
<th>p</th>
<th>RR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td># Eval</td>
<td>48</td>
<td>51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuro seq</td>
<td>15 (31)</td>
<td>5 (10)</td>
<td>0.008*</td>
<td>4.2 (1.3-14.8)</td>
</tr>
<tr>
<td>Exclude sz</td>
<td>12 (25)</td>
<td>4 (8)</td>
<td>0.020*</td>
<td>3.9 (1.1-15.9)</td>
</tr>
<tr>
<td>Severe HL</td>
<td>7 (16)</td>
<td>3 (6)</td>
<td>0.18</td>
<td>1.6 (1.0-2.5)</td>
</tr>
<tr>
<td>Hearing aid</td>
<td>3 (7)</td>
<td>0</td>
<td>0.10</td>
<td>2.2 (1.8-2.8)</td>
</tr>
</tbody>
</table>

This study also showed decreases in TNF, platelet activating factor in the steroids treated group: correlates with in vitro data.


Studies that Show Steroids Don’t Work?

- Arditi
  - retrospective non-randomized surveillance study
  - Dex given before or within 1 hr
- Wald
  - Dex given within 4 hrs after first antibx

“Reasons” Steroids Not Given

- Studies involved *H flu > S pneumo*
- Sent to scanner first so antibx given
- Concern re: antibiotic penetration with steroids on board

“Pus”iness of Meningitis

- High WBC
  - Pneumococcus
  - H.influenza
  - Meningococcus

- Low WBC
  - Meningococcus
Management algorithm for infants and children with suspected bacterial meningitis. “Stat” indicates that the intervention should be done emergently.

Corticosteroids for Bacterial Meningitis

By organism
- \textit{S. pneumoniae} mortality RR 0.59 (CI 0.45-0.77)
- \textit{H. influenzae} hearing loss RR 0.37 (CI 0.20-0.68)
- \textit{N. meningitidis} no difference

Corticosteroids for Bacterial Meningitis

Separated by country’s SES
- High income
  - Retained Mortality, short term sequelae and severe pediatric hearing loss
  - Positive ‘trends’ only for overall pediatric hearing loss, short term neurologic sequelae
- Low income
  - No benefit

Corticosteroids for Bacterial Meningitis

Cochrane Review
- 2,750 pts
- Mortality RR 0.83 (CI 0.71 - 0.99)
- Severe hearing loss RR 0.65 (CI 0.47 – 0.91)
- Peds hearing loss RR 0.61 (0.44 – 0.86)
No Steroids
- Infants less than 6 wk-2 months
- After antibx started
- N. meningitidis in adults or non-bacterial

Septic Arthritis: Dexamethasone
- Why Try This?
  - Residual joint dysfunction in 10-25% of children with SA
  - Cytokine levels in joints correlate with severity of inflammation
  - Animal data with rabbits and mice show decreased inflammation/arthritis with *H. flu* and *S. aureus* respectively
  - Might shorten acute symptoms

#1 DB-RCT of Dex Vs Placebo: SA
- 50 evaluable children >6 months in each arm
- Dexamethasone 0.2 mg/kg IV q 8h X4 days
- First dose 15-20 minutes before antibiotics
  - Uniform antibiotics, differing by age
- Follow up: end of rx, 6,12 months
- Baseline characteristics no different for age, duration of sx, prognostic score, jt involved, jt fluid, bone involved, CRP etc
Pathogens

- 80% pathogen recovery

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Dex (%)</th>
<th>Placebo (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>68</td>
<td>66</td>
</tr>
<tr>
<td>H. flu</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Other*</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

*Other = GAS, S.pneumo, CONS

Clinical Outcomes: % Normal

<table>
<thead>
<tr>
<th></th>
<th>Dex</th>
<th>Placebo</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day to po</td>
<td>7.2</td>
<td>10</td>
<td>0.05</td>
</tr>
<tr>
<td>End of rx</td>
<td>96</td>
<td>68</td>
<td>0.000068</td>
</tr>
<tr>
<td>6 mo</td>
<td>98</td>
<td>62</td>
<td>0.00007</td>
</tr>
<tr>
<td>12 mo</td>
<td>98</td>
<td>74</td>
<td>0.00053</td>
</tr>
</tbody>
</table>

Majority of sequelae in placebo group were in the hip


#2 DB-RCT of Dex Vs Placebo: SA

- 49 evaluable children >3 mo: 24 dex, 25 placebo
- Dexamethasone 0.2mg/kg IV q 8h X 4days
- First dose 30 min before to 2 hrs after antibiotics
- Follow up: end of hospital rx, 2 6, 12 months
- Baseline characteristics similar
- **Only 35% with micro dx:
  - K.kingae (41%)
  - S.aureus (18% or 6% of cohort)

Short term Outcome

<table>
<thead>
<tr>
<th></th>
<th>Dex</th>
<th>Placebo</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days to no pain</td>
<td>1.68</td>
<td>2.83</td>
<td>0.021</td>
</tr>
<tr>
<td>Days to nl ROM</td>
<td>7.00</td>
<td>12.24</td>
<td>0.030</td>
</tr>
<tr>
<td>Days to nl CRP</td>
<td>3.09</td>
<td>5.48</td>
<td>0.029</td>
</tr>
<tr>
<td>Days of IV</td>
<td>9.91</td>
<td>12.6</td>
<td>0.007</td>
</tr>
</tbody>
</table>
Long term Outcome

- Follow up at 3 visits: 45, 39, and 29 (17 dex grp)
- No patients had adverse outcomes
- Phone follow-up found no adverse outcomes
- Difference between studies possibly related to
  - Pathogens*
  - Bones involved


UCSF Protocol

**OB**

**Protocol**

- Obtain baseline CBC with differential, blood culture, ESR and CRP
- Obtain joint aspiration BEFORE giving steroids and antibiotics!**

** If joint aspiration cannot be performed immediately, strongly consider postponing antibiotics until after the procedure. If antibiotics are to be given prior to joint aspiration, give steroids prior to antibiotics, (they can always be discontinued). Remember that many patients, with or without bacterial infection, will feel better with steroids. Therefore, it is important to aggressively pursue diagnosis prior to initiation of therapy.

** Administer IV dexamethasone BEFORE administering IV antibiotics
  - (ideally 30 minutes prior; may also be given concurrently, or up to 2 hours after antibiotics)
  - Dose: IV dexamethasone 0.15 mg/kg/dose IV q6 hours x 4 days

- Administer IV antibiotics

NOTES
- Consult your friendly ID service early! We prefer to be involved from the outset, so please do not hesitate to call.
- Discontinue steroids if osteomyelitis or another serious infection is ruled in
- Grade of evidence IIc