What I’ve Learned
Studying ID in EM

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Financial Disclosure

- Allergan - Research grant (decrease SSTI admits)
- Light AI, Inc. - Research grant (handheld device for strep)
- Shinogi - Research grant (bacterial resistance in urosepsis)
- CDC - Research grant (as above)
- PCORI - Research grant (non-operative treatment of appendicitis)
Let’s Discuss…

- Bites
- Relationship in vitro to in vivo
- MRSA
- Abscess and cellulitis
- Pneumonia
- Superbugs
- UTIs
- Surviving Sepsis Campaign/1-hour bundle

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Bacteriologic Analysis of Infected Dog and Cat Bites

David A. Talan, M.D., Diane M. Citron, B.S., Fredrick M. Abrahamian, D.O., Gregory J. Moran, M.D., and Ellen J.C. Goldstein, M.D., for the Emergency Medicine Animal Bite Infection Study Group

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Face, scalp, or neck</td>
<td>16/2 75%</td>
<td>12/20 46%</td>
<td>90/60 20%</td>
<td>63%</td>
<td>46%</td>
</tr>
<tr>
<td>Trunk</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shoulder, arm, or forearm</td>
<td>12/20</td>
<td>46%</td>
<td>4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand</td>
<td>90/60 20%</td>
<td>63%</td>
<td></td>
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<tr>
<td>Thigh or leg</td>
<td>16/2</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Feet</td>
<td>4/3</td>
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1999
Comparison of Ciprofloxacin (7 Days) and Trimethoprim-Sulfamethoxazole (14 Days) for Acute Uncomplicated Pyelonephritis in Women
A Randomized Trial

David A. Talan, MD
Walter E. Stamm, MD
Thomas M. Hooton, MD
Gregory J. Moran, MD
Thomas Burke, MD
Abdollah Iravani, MD
Jonathan Reuning-Seherer, PhD
Deborah A. Church, MD

Context The optimal antimicrobial regimen and treatment duration for acute uncomplicated pyelonephritis are unknown.

Objective To compare the efficacy and safety of a 7-day ciprofloxacin regimen and a 14-day trimethoprim-sulfamethoxazole regimen for the treatment of acute pyelonephritis in women.

Design Randomized, double-blind comparative trial conducted from October 1994 through January 1997.

Setting Twenty-five outpatient centers in the United States.

Patients Of 378 enrolled premenopausal women aged at least 18 years with clinical diagnosis of acute uncomplicated pyelonephritis, 255 were included in the analysis.

In Vitro Resistance and Cure Rates for TMP/SMX-Treated Pyelonephritis

% clinical cure

92% 35%

Susceptible Resistant

p < 0.0001
ED Sentinel Surveillance and Research of Emerging Infections: EMERGEncyID NET

- Large patient numbers
- Acute and severe presentations
- Clinical syndrome case definitions, e.g. SSTIs
- Community-acquired infections
- At-risk populations
- Real-time, prospective data collection
- Hospital lab availability

EMERGEncy ID NET: 1995-

1 million visits/year
Methicillin-resistant *Staphylococcus aureus* in Community-acquired Skin Infections

Gregory J. Moran,*† Ricky N. Amii,* Fredrick M. Abrahamian,*† and David A. Talan*†

US Skin Infection Epidemic

Methicillin-Resistant *S. aureus* Infections among Patients in the Emergency Department

Gregory J. Moran, M.D., Anusha Krishnadasan, Ph.D., Rachel J. Gorwitz, M.D., M.P.H., Gregory E. Fosheim, M.P.H., Linda K. McDougal, M.S., Roberta B. Carey, Ph.D., and David A. Talan, M.D., for the EMERGEncy ID Net Study Group®

MRSA Prevalence among U.S. ED Patients with Purulent SSTI 2004

59%

“The article by Moran et al. in this issue of the Journal describes a landmark study that defines the amazing extent to which community-associated MRSA, particularly the USA300 clone, has spread through the U.S. population.”

Concordant antibiotics

2004 – 43%
2008 – 98%

*N Engl J Med. 2006*
**STOP MRSA Trials**

Strategies using Off-Patent antibiotics for Methicillin-Resistant *Staphylococcus aureus* ("STOP MRSA")
A Phase IIIB, multi-center, randomized, double-blind clinical trial

**uSSTI**

- **Abscess**
  - Incision & Drainage
  - TMP/SMX 2 DS BID x 7d
  - Placebo
- **Infected Wound**
  - TMP/SMX 2 DS BID x 7d
  - Clindamycin 300 mg QID x 7d
- **Cellulitis**
  - Cephalexin/Placebo
  - Cephalexin/TMP/SMX

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**NEJM Case - 2008**

20-year old basketball player with 5X3 cm buttock abscess, + subjective low-grade fevers. Temp 37.7°C.

- I&D only
- I&D and antibiotic

Trimethoprim–Sulfamethoxazole versus Placebo for Uncomplicated Skin Abscess


Table 3. Cure Rates among Patients with a Drained Cutaneous Abscess in Three Trial Populations.

<table>
<thead>
<tr>
<th>Trial Population</th>
<th>Cure of Abscess</th>
<th>Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trimethoprim–Sulfamethoxazole</td>
<td>Placebo</td>
<td>percentage points</td>
</tr>
<tr>
<td></td>
<td>no./total no. (%)</td>
<td>no./total no. (%)</td>
<td></td>
</tr>
<tr>
<td>Modified intention-to-treat 1</td>
<td>507/630 (80.5)</td>
<td>454/617 (73.6)</td>
<td>6.9 (2.1 to 11.7)</td>
</tr>
<tr>
<td>Per-protocol:</td>
<td>487/524 (92.9)</td>
<td>457/533 (85.7)</td>
<td>7.2 (3.2 to 11.2)</td>
</tr>
<tr>
<td>FDAGEEP</td>
<td>218/601 (36.3)</td>
<td>204/605 (33.7)</td>
<td>2.6 (~3.0 to 8.1)</td>
</tr>
</tbody>
</table>
Table 4. Secondary Outcomes in the Per-Protocol Population. *

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Trimethoprim-Sulfamethoxazole</th>
<th>Placebo</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite clinical cure by test-of-cure visit (%)*</td>
<td>36.5</td>
<td>74.1</td>
<td>12.2 (-7.2 to 17.1)</td>
</tr>
<tr>
<td>Additional surgical drainage procedure (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By test-of-cure visit</td>
<td>3.4</td>
<td>8.6</td>
<td>-5.2 (-8.2 to -2.2)</td>
</tr>
<tr>
<td>By extended follow-up visit</td>
<td>8.0</td>
<td>13.0</td>
<td>-4.9 (-8.8 to -1.1)</td>
</tr>
<tr>
<td>Hospitalization by test-of-cure visit (%)</td>
<td>3.6</td>
<td>6.4</td>
<td>-2.8 (-5.6 to 0.1)</td>
</tr>
<tr>
<td>Recurrent skin infection at original site (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By test-of-cure visit</td>
<td>2.1</td>
<td>3.0</td>
<td>-0.9 (-3.0 to 1.2)</td>
</tr>
<tr>
<td>By extended follow-up visit</td>
<td>5.0</td>
<td>4.3</td>
<td>0.7 (-2.3 to 3.4)</td>
</tr>
<tr>
<td>New skin infection at a different site (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By test-of-cure visit</td>
<td>3.1</td>
<td>10.3</td>
<td>-7.2 (-10.4 to -4.1)</td>
</tr>
<tr>
<td>By extended follow-up visit</td>
<td>10.9</td>
<td>19.1</td>
<td>-8.3 (-12.7 to -3.9)</td>
</tr>
<tr>
<td>Similar infection in household member (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By test-of-cure visit</td>
<td>1.7</td>
<td>4.1</td>
<td>-2.4 (-4.6 to 0.2)</td>
</tr>
<tr>
<td>By extended follow-up visit</td>
<td>3.8</td>
<td>6.2</td>
<td>-2.4 (-5.2 to 0.4)</td>
</tr>
<tr>
<td>Presence of swelling or induration (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By visit during therapy</td>
<td>50.3</td>
<td>52.7</td>
<td>-2.4 (-3.7 to 3.8)</td>
</tr>
<tr>
<td>By end-of-therapy visit</td>
<td>11.4</td>
<td>15.0</td>
<td>-3.6 (-7.9 to 0.7)</td>
</tr>
<tr>
<td>Presence of tenderness (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By visit during therapy</td>
<td>49.0</td>
<td>55.9</td>
<td>-6.9 (-13.2 to -0.8)</td>
</tr>
<tr>
<td>By end-of-therapy visit</td>
<td>6.0</td>
<td>10.0</td>
<td>-4.1 (-7.5 to -0.6)</td>
</tr>
<tr>
<td>Change in mean area of erythema from baseline (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By visit during therapy</td>
<td>-25.5±88.4</td>
<td>-22.2±82.6</td>
<td>3.3 (-13.7 to 7.0)</td>
</tr>
<tr>
<td>By end-of-therapy visit</td>
<td>-30.8±77.5</td>
<td>-48.7±66.0</td>
<td>-21 (-10.8 to 6.7)</td>
</tr>
<tr>
<td>Days missed from normal activities§</td>
<td>2.0±3.1</td>
<td>2.6±1.3</td>
<td>-0.5</td>
</tr>
<tr>
<td>Days missed from work or school§</td>
<td>2.2±3.1</td>
<td>2.4±3.4</td>
<td>-0.2</td>
</tr>
<tr>
<td>Days that analgesics were used§</td>
<td>6.0±4.9</td>
<td>6.4±4.9</td>
<td>-0.4</td>
</tr>
</tbody>
</table>

* Favors Antibiotics

**Difference in Cure Rates (%)**

***Maximum Abscess Dimension (cm)**

I & D Better Than Needle Aspiration

<table>
<thead>
<tr>
<th>Date of follow-up</th>
<th>Incision and Drainage (%)</th>
<th>Ultrasonographically Guided Needle Aspiration (%)</th>
<th>Difference Between Groups, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>2 of 54 (4)</td>
<td>28 of 47 (60)</td>
<td>56 (41 to 62)</td>
</tr>
<tr>
<td>Day 2</td>
<td>4 of 49 (8)</td>
<td>3 of 18 (17)</td>
<td>9 (~6 to 25)</td>
</tr>
<tr>
<td>Day 7</td>
<td>4 of 43 (9)</td>
<td>1 of 11 (9)</td>
<td>2 (~22 to 10)</td>
</tr>
<tr>
<td>Total</td>
<td>10 of 49 (20)</td>
<td>32 of 43 (74)</td>
<td>54 (35 to 69)</td>
</tr>
</tbody>
</table>

*Data are presented as failures (number of patients) of total number (number of patients). Patients who failed at a previous point are not included in the denominator for later points. Loss to follow-up occurred on day 2 (incision and drainage n=3, aspiration n=1) and at day 7 (incision and drainage n=2, aspiration n=2).
Inability of Polymerase Chain Reaction, Pyrosequencing, and Culture of Infected and Uninfected Site Skin Biopsy Specimens to Identify the Cause of Cellulitis

Jonathan G. Crisp, Sukhjit S. Takhar, Gregory J. Moran, Anusha Krishnadasan, Scot E. Dowd, Sydney M. Finegold, Paula H. Summanen, and David A. Talan; for the EMERGency ID Net Study Group
New IDSA CAP guidelines

IV: Ceftriaxone/azithromycin IV
Oral: β-lactam/azithromycin

Fluoroquinolone Side Effects
CNS side effects (seizures, neuropsych)
Tendonitis/rupture (age, steroids)
Hypoglycemia (age, diabetes)
Peripheral neuropathy
Aortic dissection (age)

Lefamulin
Omadacycline
Ceftaroline
Characteristics associated with MRSA pneumonia:

- Hx MRSA
- Nursing home residence
- Close contact with someone with a skin infection
- CXR with multiple infiltrates and/or cavities
- Coma
- Intubation
- Pressors

Gram-negative bacteria

- FQ-resistant
- ESBLs (cephalosporin-resistant)
- CREs (carbapenem-resistant)
Prevalence and Risk Factor Analysis of Trimethoprim-Sulfamethoxazole- and Fluoroquinolone-Resistant *Escherichia coli* Infection among Emergency Department Patients with Pyelonephritis

David A. Talan,1,2 Anusha Krishnadasan,3 Fredrick M. Abrahamian,4 Walter E. Stamm,5 and Gregory J. Moran,6,7 for the EMERGEncy ID NET Study Group8

Fluoroquinolone-Resistant and Extended-Spectrum β-Lactamase-Producing *Escherichia coli* Infections in Patients with Pyelonephritis, United States1

David A. Talan, Sukhjit S. Takhar, Anusha Krishnadasan, Fredrick M. Abrahamian, William R. Mower, Gregory J. Moran; EMERGEncy ID Net Study Group

Fluoroquinolone-Resistant *E. coli* among U.S. ED Patients with Pyelonephritis 2013-14

2000-4: 3.9%
2013-14: 11.7% (UP 0-23%/CP 0-50%/site)

IDSA guidelines
10-20% resistance: add 2nd abx
>20% resistance: no longer use
ESBL-Producing *E. coli* among U.S. ED Patients with Pyelonephritis 2013-14

2000-4: 0.0%

2013-14: 2.6% (UP 0-8%/CP 0-17%/site)

3/4ths – treated with inactive abx
1/3rd – no abx resistance risk

Dramatic Decrease in Antibiotic Drug Approvals

Source: Spielberg, OD 2004: Modified

"the emergence of high rates of fluoroquinolone resistance and ESBL producers causing acute pyelonephritis in US communities indicates the necessity for the IDSA and other organizations to urgently update their relevant treatment guidelines"
Urinary Tract Infection

- **Cystitis**: Macrobid (5d) or Cephalexin (7d) ESBL - Fosfomycin
- **Pyelo**: Ceftriaxone or Aminoglycoside (1st dose) Ciprofloxacin (7d) or Cephalexin (14d) ESBL - Ertapenem or Amikacin/ Cefixime + Amox-clav.
- **Urosepsis**: Carbapenem, Piperacillin-tazo, Ceftaz-avibactam Meropenem + Vancomycin

Analysis of Emergency Department Management of Suspected Bacterial Meningitis

- Time to Antibiotics (h)
No change in sepsis-related outcomes until >5 hours


How the Surviving Sepsis Campaign got almost everything wrong

Challenging the One-Hour Bundle Goal for Sepsis Antibiotics

David A. Talan, MD*; Donald M. Yealy, MD

*From the Department of Emergency Medicine, University of Washington School of Medicine, Seattle, WA.