Prostates, Pokes, and “Primum non Nocere”

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57-yo Man with F/C/N/V/HA

3d Hx of fever, chills, nausea, anorexia, & backache

Past 2d: HA, emesis -> admitted to hospital

Family, social Hx: non-contributory

PMH:
- Harrington rods (remote)
- HTN, nephrolithiasis, MI
- BPH
Recent Medical Events

8 wks ago: prostate Bx
Rising PSA (to 9.4) despite $\alpha$-blocker, course of cipro
TRUS “multiple suspicious hypodense areas
TRUSP Bx
- 3d cipro Px, starting AM of Bx (pre-Bx)
Histopathology
- moderate chronic prostatitis
- no CA
PSA SCREENING

1,410 Men

48 Cancers Found

1 Life Saved Over 9 Years

Source: New England Journal of Medicine
Screening for Prostate Cancer: U.S. Preventive Services Task Force Recommendation Statement

DRAFT

The U.S. Preventive Services Task Force (USPSTF) recommends against prostate-specific antigen (PSA)-based screening for prostate cancer.

This is a Grade D recommendation.

This recommendation applies to men in the general population that do not have symptoms that are suspicious for prostate cancer, regardless of age, or family history. The Task Force did not consider the use of the PSA test as part of a diagnostic strategy in men with symptoms that are highly suspicious for prostate cancer. This recommendation also does not consider the use of the PSA test for surveillance after diagnosis and/or treatment of prostate cancer.
Patient’s Post-Bx Problems

5 days post-TRUSP Bx:
- Bilateral scrotal swelling
- Local ED: PO levo (no better) -> amoxi-clav (no better)
- Left testicle: progressive pain, swelling -> admitted

During 1st hospital admission (7 wks ago):
- Empirical IV levo + gent
- Scrotal US: left testicle w/o abscess; w/o blood flow
- Transferred to regional center -> urgent L orchiectomy
- OR: testicular ischemia 2° to severe epididymo-orchitis
Post-Bx Admission

Recovered uneventfully

Discharged on POD #3 with 5d PO levo

Intraoperative cultures grew *E. coli*

- Resistant to amp, gent, FQs (pt’s only Rx to date)
- o/w susceptible

Pt. lost to f/u…

Until present admission
Back to Present: Current Admission

History as described initially (5d F/C/N/V/HA)

ROS: mild photophobia

PE
- Mild distress (from HA); o/w healthy appearing
- VSS normal
- Remainder of PE normal; no nuchal rigidity

Labs
- WBC 10.0 (85% PMN), creat 1.1, LFTs normal
- UA: pyuria, hematuria, bacteriuria
Current Admission (2)

Empirical Rx: IV levofloxacin (750 mg/d)

Day 2: persistent HA -> LP done

CSF formula:
- 1,000 WBC (100% PMN); 2,000 RBC
- Protein 140, Glucose 9
- Gram stain: GNRs seen

UCs x 2 -> GNRs
UC -> GNRs

Day 3 ID consult: “D/C levo; start ceftriaxone”
Current Admission (3)

UC, BCs, CSF all grew *E. coli*
- same sensi’s as previous orchiectomy isolate
- R to amp, gent, FQs; o/w susceptible

MRI of brain negative

Pt. received 2 weeks CTX (2gm IV q24h)
Uneventful recovery
Infectious complications

TRUSP Bx
Prostate Bx & Infections

Prostate CA: 240,000 new cases in 2011 in US
Most are diagnosed by TRUSP Bx
TRUSP Bx positive rate (for CA): 25-30%
Infection rate historically < 1% with FQ Px
Rising infection rate over past decade
- now 2.5 - 10% (despite FQ Px)
Presentation: prostatitis, febrile UTI, sepsis
Mostly *E. coli*, mostly FQ-R -> *E. coli* ST131
Intercontinental emergence of *Escherichia coli* clone O25:H4-ST131 producing CTX-M-15

Marie-Hélène Nicolas-Chanoine¹,²*, Jorge Blanco³, Véronique Leflon-Guibout¹, Raphael Demarty¹, Maria Pilar Alonso⁴, Maria Manuela Caniça⁵, Yeon-Joon Park⁶, Jean-Philippe Lavigne⁷, Johann Pitout⁸ and James R. Johnson⁹

(EID 2008)

*Dissemination of Clonally Related Escherichia coli Strains Expressing Extended-Spectrum β-Lactamase CTX-M-15*

Teresa M. Coque,*†‡ Ángela Novais,*†‡ Alessandra Carattoli,§ Laurent Poirol,‖ Johann Pitout,‖‖ Luisa Peixe,‖ Fernando Baquero,*†‡ Rafael Cantón,*†‡ and Patrice Nordmann‖

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The CTX-M-15-producing *Escherichia coli* diffusing clone belongs to a highly virulent B2 phylogenetic subgroup

Olivier Clermont¹†, Marie Lavollay²†, Sophie Vimont²,³, Catherine Deschamps¹,⁴,
Rising % ST131 Over Time Among Type O25 *E. coli*

![Graph showing the percentage of ST131 among Type O25 E. coli over time.](image)

- **1967-1987**: n = 86
- **1988-1997**: n = 65
- **1998-2007**: n = 106
- **2008-2009**: n = 21

*P < .001*
Recent Rising % ST131 Within TRUST Collection

2002-2008: Occurrence of ST131

For linear trend: P = .019
Prevalence of *E. coli* ST131 at 10 VAMCs
Redominance of ST131 Among the Elderly: 2011 (Olmsted Cty, MN)
8 men with community-onset *Escherichia coli* bacteremia

88% = post-TRUSP Bx

Post-TRUSP Bx cases more often ICU admit, MDR

7% of post-TRUSP *E. coli* BC isolates = ST131
136 men pre-TRUSP
21%: FQ-R rectal E. coli
70% of FQ-R Ec = ST131
15 PFGE types overall
968 (n = 7) & 800 (n = 4) dominate
Both = ST131
Both dominate globally among clinical isolates
Patient’s *E. coli* Isolate

- **MLST:** ST131
- **Multiple virulence genes**
  - Adhesins, capsule, siderophores, toxins
  - Typical for ST131
- **Pulsotyope 968**
  - Most common ST131 pulsotyope globally
Issues in Antimicrobial Px for TRUSP Bx in the ST131 Era

Culture-guided vs. broader empirical Px?
- “One size fits all” -> selection pressure, miss rate
- Culture: logistics (culture, getting results, Rx), misses

Duration & timing of Px?
- Single vs. multiple doses
- If multiple, beginning how long pre-Bx? how long after

Prostate drug levels? (vs. blood)

Dose size? (e.g., CTX 250 mg, vs. 1 gm)

What agent(s) and route?
Antimicrobial Selection Issues

Spectrum
- FQ-R *E. coli* co-resistance: 30% gent, 10% CTX

Prostate penetration
- Fair-poor: aminoglycosides, cefpodoxime
- Adequate: cefixime, cefuroxime, ceftriaxone
- Good: azithro, doxy, mino; also clinda (but GNRs R)

Route and tolerability
- IM painful for patient, cumbersome for clinic (lidoca
- Volume of IM injection (dose-dependent)
- Time to peak: longer for PO (1-5h), vs. IM (30-60 min)
TRUSP Bx at MVAMC

- 400-500 per year (2/3 by Urology, 1/3 by IR)
- 10-14 cores per Bx
- Yield: ~30% prostate CA Dx
- Conventional prep:
  - cipro 500 mg PO 1-2 h pre-Bx
  - no enema
- Recently: 3 pts septic with FQ-R *E. coli*
  - 2 isolates available for testing: both = ST131
- 4th pt recurrent post-TRUSP sepsis: ST131
New VA Approach to Pre-TRUSP Bx Prophylaxis (5/2012)

Multi-disciplinary ad hoc working group
- Urology, IR, ID, Epi, pharmacy, micro lab, nursing

Basic regimen:
- PO cipro 500 mg + PO cefuroxime 1 gm, 2-3h pre-Bx

If patient forgets:
- PO cipro + IM ceftriaxone 250 mg (lidocaine), 1h pre-Bx

If serious β-lactam allergy:
- PO cipro + IM gent 80 mg
And at UM?

*E. coli* susceptibility:
- Cipro: 86%
- Ceftriaxone: 97%
- Gent: 94%

Number of TRUSP Bx’s: 120-145 per year
Number of post-TRUSP Bx sepsis cases: ?
Yesterday's home runs don't win today's games”

Babe Ruth
Internists As “Pitcher”: How Can We Do Better?

• Don’t do PSA screening
• If an elevated PSA is discovered, don’t reflexively refer for TRUSP Bx
• If TRUSP Bx is to be done, ensure that appropriate prophylaxis is used
The U.S. Preventive Services Task Force (USPSTF) recommends against prostate-specific antigen (PSA)-based screening for prostate cancer.

This is a Grade D recommendation.

Don’t screen--don’t biopsy
Urologist and USPSTF member discuss PSA screening
“We made too many wrong mistakes”

Yogi Berra
Internists As “Catcher”: How Can We Do Better?

• For post-TRUSP Bx infections, esp. if FQ Px was used
  – Empirical FQ Rx a BAD idea (ED, clinics, wards)
  – Addition of (or reliance on) gent also risky

• Anticipate FQ + gent resistance
  – Pip-tazo, carbapenem, 3rd gen cephs usually OK
  – But if ESBLs are prevalent, use a carbapenem
  – For “non-sick” patient: fosfomycin
Why fosfomycin trometamol as first line therapy for uncomplicated UTI?

G.C. Schito *


In vitro activity of fosfomycin against Gram-negative urinary pathogens and the biological cost of fosfomycin resistance

Anna Marchese *, Laura Gualco, Eugenio A. Debbia, Gian Carlo Schito, Anna Maria Schito


Fosfomycin in the treatment of extended spectrum beta-lactamase-producing Escherichia coli-related lower urinary tract infections

Husnu Pullukcu a, Meltem Tasbakan a, Oguz Resat Sipahi a,*, Tansu Yamazhan a, Sohret Aydemir b, Sercan Ulusoy a

Review


Fosfomycin for the treatment of infections caused by multidrug-resistant non-fermenting Gram-negative bacilli: a systematic review of microbiological, animal and clinical studies

Matthew E. Falagas a,b,c,*, Antonia C. Kastoris a, Drosos E. Karageorgopoulos a, Petros I. Rafailidis a,b
Fosfomycin

Fosfonic acid derivative (*Streptomyces* spp.)

Inhibits cell wall synthesis -> bactericidal

Broad GNR, GPC activity; no cross-resistance

5% orally bioavailable; 6h half-life; excreted unchanged in urine

FDA: 3gm SDT for acute cystitis in women

But--can be dosed repeatedly q48h for other indications (e.g., complicated UTI, prostatitis)

Blood levels insufficient for invasive infection
Take-Home Points

- FQ no longer OK for pre-TRUSP Bx Px
  - Need a different plan based on local sensi’s and practice patterns (urology, IR, ID)
- For post-TRUSP Bx infections, esp. if FQ P
  - Empirical FQ Rx a BAD idea (ED, Urol, clinics, ward)
  - Addition of (or reliance on) gent also risky
- Anticipate FQ + gent resistance
  - Pip-tazo, carbapenem, 3rd gen ceph are usually OK
  - But if ESBLs are prevalent, carbapenem (fosfomycin)

- Don’t screen PSA, don’t refer for TRUSP Bx
Primum Non Nocere

Don’t check my PSA!