



TRUS and Prostate Biopsy Sepsis

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Why this topic and why now?

- Perception that increased numbers of patients being admitted for post-TRUS and Bx sepsis
- Concern of increasing ciprofloxacin resistance
 - Do we need to change our antibiotic prophylaxis?
- Changes in practice without evidence to support use
 - IV broad-spectrum antibiotics pre-Bx?

Learning Objectives

- Review patterns of antibiotic resistance
- Review of nosocomial infections
- Review of antibiotic prophylaxis
- Review of role for pre-biopsy enema
- Quality assurance audit results at VGH and relevance to the community urologist

Provide knowledge to help docs
agree on common protocols



VGH Urologists dividing operating room time

Antibiotics and the Prostate

Antibiotics and the Prostate

- Delivery of antibiotics into prostate a passive process; diffuse into/concentrate in prostate
- High lipid solubility and minimal binding to serum proteins required to penetrate prostate
- Animal models- improved penetration of quinolones into prostate and seminal fluid
- Chronic bacterial prostatitis studies support improved eradication with quinolones

Urology 66:2-8, 2005

J Urol 103:187-194, 1970

Int J Antimicrob Agents 26:1-7, 2005

Campbell's Ninth Edition

Antibiotics and Resistance

- Trimethoprim/Sulfamethoxazole
 - ® Enterococcus and pseudomonas sp.
- Nitrofurantoin
 - ® Proteus, pseudomonas sp.
- Cephalosporins
 - ® Enterococcus, pseudomonas sp.
- Fluoroquinolones
 - ® most anaerobic bacteria, streptococci
- Aminoglycosides (Gentamicin)
 - ® anaerobic bacteria

Abx requirements for a GU tissue infection/bacteremia

- Activity against potential uropathogens
- Bacteriocidal
- High serum levels
- High tissue levels
- Minimal toxicity
- ? Long half-life

Campbell's Ninth Edition

Fluoroquinolones (Ciprofloxacin)

- Bacteriocidal; coverage of most gram-negatives
- Excellent oral absorption
- Widely distributed in tissues
- Peak serum levels 1-3 hrs with oral admin
- High urinary/prostatic tissue levels
- levofloxacin and ciprofloxacin have similar bioequivalency between IV and oral formulations
- Mechanisms of quinolone drug resistance
 - Mutation in DNA gyrase-binding site
 - Changes in cell wall porin size (↓ penetration)
 - Active efflux

Evolving Fluoroquinolone Resistance Worldwide

- Up to 30% resistance of *E. coli* to quinolones in Spain
- 3.6% U.S. outpatient *E.coli* samples resistant to quinolones in 2004
- 56% of ESBL-producing strains of *E. coli* resistant to quinolones

Am J Infect Control 32:470-485, 2004

Clin Infect Disease 33:1288-1294, 2001

Risk factors for colonization with a quinolone resistant strain

- Increasing age
- Travel to developing countries
- Prior quinolone use

Br J Hosp Med 67:98-99, 2006
J. Urol. 169:1762-1765, 2003

Antibiotic Resistance Patterns-MDS Burnaby Reference Lab

Urinary Tract Pathogens
January 1, 2005 – December 31, 2005

ORGANISM	Number of isolates tested	ANTIBIOTIC (% susceptible)									
		Ampicillin	Cephalothin/ Cephalexin	Ciprofloxacin	Gentamicin	Nitrofurantoin	Norfloxacin	Tetracycline	Trimethoprim/ Sulfamethoxazole	Ceftazidime	Piperacillin
<i>Escherichia coli</i>	19675	61	60	82	93	96	82	73	78		
<i>Enterococcus</i> spp.	3061	99.6	R	72		97	58	23	N/R	R	
<i>Klebsiella pneumoniae</i>	1679	0	95	97	99	29	98	87	94		
<i>Proteus</i> spp.	755	78	87	87	92	0	94	0	85		
<i>Pseudomonas aeruginosa</i>	294	R	R	65	89	R	70	R	R	93	97
<i>Staphylococcus saprophyticus</i>	568			99		99.8	99	94	97	N/R	
<i>Klebsiella oxytoca</i>	242	0	89	99	99	87	99	94	97		

R The organism is inherently resistant to the antibiotic indicated.
 Antimicrobial susceptibility testing not performed.
N/R Not recommended due to poor clinical response and/or poor activity.

Antibiotic Resistance Patterns-MDS Victoria Reference Lab

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		Ampicillin	Cephalothin/ Cephalexin	Ciprofloxacin	Gentamicin	Nitrofurantoin	Norfloxacin	Tetracycline	Trimethoprim/ Sulfamethoxazole	Ceftazidime	Piperacillin
<i>Escherichia coli</i>	10274	65	58	79	96	96	80	78	80		
<i>Enterococcus</i> spp.	1854	98	R	65		94	44	26	N/R	R	
<i>Klebsiella pneumoniae</i>	1125	0	94	95	99	32	95	88	95		
<i>Proteus</i> spp.	308	88	90	96	94	0	100	0	92		
<i>Pseudomonas aeruginosa</i>	259	R	R	69	91	R	70	R	R	98	99
<i>Staphylococcus saprophyticus</i>	347			99.7		99.7	99.7	95	94	N/R	
<i>Klebsiella oxytoca</i>	202	0	77	98	99	80	99	100	96		

R The organism is inherently resistant to the antibiotic indicated.
 Antimicrobial susceptibility testing not performed.
N/R Not recommended due to poor clinical response and/or poor activity.

Are any Post-TRUS and Biopsy
Infections Nosocomial?

Perhaps a Nosocomial Source?

- Multi-drug resistant organism
- Pseudomonas species
- ? MRSA
- ? Coag. negative staph.
- ? Acinetobacter, Enterobacter, Providencia, Serratia

*Campbell's Ninth Edition
Infect Control Hosp Epidemiol. 28:916-919, 2007*

How do we prevent a nosocomial infection with TRUS/Bx?

- Removal of biopsy guide from ultrasound probe prior to cleaning
- Decontamination and disinfection by soaking in metricide® for 10-20 minutes after each use (*avoid Toronto experience!*)
- Double condom (first over ultrasound transducer with second over transducer and needle guide)

Infect Control Hosp Epidemiol. 28:916-919, 2007

Are hospital bacteremias increasing at VGH?

Predominant organisms isolated from true bacteremic events

Organisms	Fiscal 05/06	Fiscal 06/07
Coagulase neg Staphylococci	138 (24.7%)	148 (24.7%)
<i>S. aureus</i>	70 (12.6%)	59 (9.9%)
<i>E. coli</i>	66 (11.8%)	88 (14.7%)
Enterococcus	51 (9.2%)	56 (9.4%)
MRSA	54 (9.7%)	57 (9.5%)
<i>Klebsiella spp</i>	34 (6.1%)	32 (5.4%)
Anaerobes	29 (5.2%)	25 (4.2%)
Yeast	22 (3.9%)	23 (3.8%)
All Others	93 (16.7%)	110 (18.4%)
Total	557	598

VCHA Infection Control Report 2006-2007

Are nosocomial bacteremias increasing at VGH?

Source of nosocomial bacteremias

Source	2005/06	2006/07
Bone/Joint	1 (0.3%)	4 (1.0%)
CVC	45 (12.6%)	38 (9.8%)
GI tract	88 (24.6%)	85 (21.9%)
Respiratory	46 (12.8%)	54 (13.9%)
Wound	30 (8.4%)	35 (9.0%)
Surgical Site	24 (6.7%)	14 (3.6%)
Urine	38 (10.6%)	63 (16.2%)
Vascular	10 (2.8%)	3 (0.8%)
Unknown	76 (21.2%)	92 (23.7%)
Total	358	388

Distribution of bacteremias by ward

Location	Number (%) Bacteremias
BPU	9 (2.3%)
TSCU	5 (1.3%)
CCU	7 (1.8%)
CSI	2 (0.5%)
ICU	91 (23.5%)
T4a/b	36 (9.3%)
T5a/b	15 (3.9%)
T6a/b	9 (2.3%)
T7a/b	16 (4.1%)
T8a/b	23 (5.9%)
T9a/b	44 (11.3%)
T10a/b/d	21 (5.4%)
T10f	2 (0.5%)
T11b/C10a	9 (2.3%)
T11a/d/T6g	19 (4.9%)
T12a/b/s	8 (2.1%)
T14a/b/f/s/C9	15 (3.9%)
T15a/b	43 (11.1%)
T16	4 (1.0%)
C5	1 (0.3%)
C7	0
C8a/b	1 (0.3%)
C8d	0
Other*	8 (2.1%)
Total	388

VCHA Infection Control Report 2006-2007

What about bacteremias from outpatient facilities?

Where Acquired	2005/06	2006/07
BMT daycare	28 (27.2%)	38 (29.7%)
Hemodialysis	31 (30.1%)	28 (21.9%)
Radiology	13 (12.6%)	21 (16.4%)
Other	31 (30.1%)	41 (32.0%)
Total	103	128

Prevention and presentation
of Post-Biopsy Sepsis

Presentation Post-Biopsy Sepsis

- Usual presentation within first 24-72 hours
- May present a week or longer from biopsy (*Aus et al, 1996*)
- Asymptomatic bacteremia more common with bacteroides and enterococcus (*Thompson et al, 1982*)
- Urine culture often *negative*
- ? Profoundly septic patient now

Incidence Infectious Complications post-Bx

Author	Year	Patients (n)	Antibiotic (dose)	Enema	Infection rate (%)
Kapoor et al. [25]	1998	269	Ciprofloxacin (500 mg)	Yes	2
Shandera et al. [10]	1998	150	Ofloxacin (300 mg)	Yes	0.67
Isen et al. [19]	1999	42	Ofloxacin (300 mg)	Yes	4.76
Isen et al. [19]	1999	45	TMP-SMX (800 + 160 mg)	Yes	6.66
Aron et al. [27]	2000	79	Ciprofloxacin (500 mg)	Yes	7.5
Peyromaure et al. [26]	2002	289	Fluoroquinolone	Yes	4.9
Griffith et al. [11]	2002	400	Levofloxacin (500 mg)	No	0.25

2.9-10.4% without Abx

Eur Radiol. 16:939-943, 2006
Br J Urol. 79:777-780, 1997
Int. Urol. Nephrol. 39:897-903, 2007

Risk Factors for Post-Bx Sepsis

- Recurrent bacterial prostatitis, UTIs
- Prebiopsy bacteriuria
- Indwelling catheter
- Diabetes, immunosuppression, steroids
- Recent antibiotic use
- ? Chronic retention

UCNA 35:23-32, 2008
BJU 77:851-855, 1996

Current Antibiotics Regimes

- Single dose fluoroquinolone pre-Bx or post-Bx
 - No difference in bacteriuria (*Int Urol Nephrol 39:897-903, 2007*)
- 3-doses fluoroquinolone pre/post-Bx
- 3-7 day course fluoroquinolone pre/post-Bx
- Single dose to 3 day course SxT

Infectious Complications and Duration of Antibiotics

Author	Abx Regime	Infection Rate
Aron et al, 2002 (RCT)	None	25%
	Single dose	7.6%
	3-day	10.3%
Norberg et al, 1994	1-day	3.5%
	3-day	1.4%
Aus et al, 1996 (RCT)	Two doses	11%
	One week	4.9%
Griffith et al, 2002	Single dose	0.25%
Petteffi et al, 2002 (RCT)	Single dose	23%
	3-day	8%

Arguments against a longer duration of Antibiotics

- Low incidence of post-Bx sepsis
- Sepsis often caused by resistant organism not inadequate duration
- ? Contribute to worsening resistance to chosen antibiotic
 - Quinolones eradicate flora of gut
- Increased cost of antibiotic
 - \$1500 per inpatient day at VGH!

Benefits of pre-biopsy Enema?

Author	N	Complications- Enema	Complications- no enema	P-value
Carey and Korman, 2001	410	4.4%	3.2%	0.614
Lindert et al, 2000 (RCT)	50	*4%	*28%	0.0003
Vallencien et al, 1991	59	20%	9%	?

*transient bacteremia

Should we change to IV Abx prior to Bx?

Author	Antibiotics	Infection rate	P-Value
Cormio et al, 2002 (RCT)	Piperacillin/ Tazobactam IM x 2d	2.8%	P>0.1
	Cipro PO x 7d	4.5%	
Brewster et al, 1995	Piperacillin/ Tazobactam IV x 1 dose	5.5%	P<0.05
	Cefuroxime IV x 1 dose	2%	
Otrock et al, 2004	Cipro PO	5%	P= 0.4
	Cipro PO and Gent IM	8%	
Shivde et al, 2002 (RCT)	SxT PO x 2 doses	1.6%	P= 0.085
	Gentamicin IV or IM x 1	9.4%	

When should IV antibiotics be given prior to TRUS/Bx?

- SBE prophylaxis (mechanical heart valve, recent ortho prosthetic)
- ? Pt within higher risk group
- ? Prior infectious complication of TRUS/Bx
- ? Multiple prior courses of antibiotics (↑risk of resistant organism)

Does Local Anaesthetic Pre-Bx ↑ Risk of Infectious Complications?

- RCT of 100 men randomized to local infiltration v. no anaesthetic
- Preop enema; SxT x 3 days

	No. Anesthesia (%)	No. Controls (%)	p Value
Urethral bleeding:			
No	45 (90)	46 (92)	0.5 (Fisher's exact test)
Yes	5 (10)	4 (8)	
Rectal bleeding:			
None-mild	29 (58)	17 (34)	0.034 (chi-square test)
Moderate	18 (36)	31 (62)	
Severe-prolonged	3 (6)	2 (4)	

	No. Anesthesia (%)	No. Controls (%)	p Value
Serious clinical infection	2 (4)		0.247 (Fisher's exact test)
Fever:			
Less than 37.8C	5 (10)	8 (16)	0.37 (chi-square test)
Greater than 37.8C	5 (10)	1 (2)	0.102 (Fisher's exact test)
Bacteriuria	11 (22)	3 (6)	0.02 (chi-square test)

Obek et al, J Urol. 168:558-561, 2002

Are rebiopsy cases at higher risk of infections?

TABLE 2. *Delayed morbidity of transrectal ultrasound guided biopsy*

	No. First Biopsy (%)	No. Re-Biopsy (%)	p Value
Urinary tract infections	115 (10.9)	93 (11.3)	0.07
Fever	30 (2.9)	19 (2.3)	0.08
Urinary tract infections, fever	22 (2.1)	16 (1.9)	0.02
Urinary retention	9 (0.9)	10 (1.2)	0.09
Hemospermia	103 (9.8)	84 (10.2)	0.1
Recurrent mild hematuria	167 (15.9)	143 (16.6)	0.06
Persistent dysuria	76 (7.2)	56 (6.8)	0.12

Djavan et al, J Urol. 166:856-860, 2001

Quality assurance audit at Vancouver Hospital

Background and Methods

- Retrospective audit of 4749 *outpt* TRUS biopsies performed at VGH/UBC 2001-2006; cross-referenced to *inpt* admissions to VGH/UBC within 30 days of biopsy.
- N= 26
- No administration of pre-biopsy enema
- 3-days ciprofloxacin for prophylaxis

Results- Blood

- median time to E.D. presentation: 2 days
- of 26 blood cultures: 16 were positive for strains of *E. Coli*, 1 was positive for *Morganella Morganii* and 9 were negative.
- ciprofloxacin was the most common antibiotic to exhibit resistance in 16 of the 17 positively cultured patients.
- of positive blood cultures: organisms were most likely to be sensitive to gentamicin (13).
- of positive blood cultures: 7 were sensitive to sulfamethoxazole and trimethoprim (SMX/TMP).

Results-Blood

Antibiotic Susceptible

Of those with microorganism in blood:

- Gentamicin = 13
- Amikacin = 5
- Cefazolin = 13
- Piperacillin = 7
- Imipenem = 3
- Tobramycin = 12
- Cefuroxime = 1
- Ticarillin = 11
- SXT = 7
- Ceftazidime = 1
- Ceftriaxone = 1
- Cipro = 1

Antibiotic Resistant

Of those with microorganism in blood:

- Ampicillin = 12
- Cefazolin = 4
- Ceftazidime = 2
- Ceftriaxone = 2
- Cefuroxime = 3
- Ciprofloxacin = 16
- Piperacillin = 9
- Gentamicin = 4
- SXT = 9
- Doxycycline = 1
- Tobramycin = 2
- Cefotaxime = 1

Results- Urine

- **11 urine cultures positive for *E. Coli*, one for *Enterobacter cloacae*, one for Coagulase (-) Staphylococci and 13 negative cultures.**
- **ciprofloxacin again was the most common antibiotic to exhibit resistance in all 11 instances.**
- **organisms were most likely to be sensitive to nitrofurantoin**

Ciprofloxacin-resistant E. Coli the common culprit

TABLE 2. Bacterial susceptibility to antibiotics

Drug	% All Cultured Bacteria			% Fluoroquinolone Prophylaxis		
	Susceptible	Intermediate	Resistant	Susceptible	Intermediate	Resistant
Penicillins:						
Ampicillin	25	–	75	18.2	–	81.8
Ampicillin/clavulanate	93.3	–	6.7	90	–	10
Piperacillin	50	37.5	12.5	57.1	28.6	14.3
Piperacillin/tazobactam	100	–	–	100	–	–
Cephalosporins:						
Cefazolin	50	37.5	12.5	25	50	25
Cephalexin	25	25	50	16.7	16.7	66.7
Cephalothin	50	16.7	33.3	33.3	33.3	33.3
Cefuroxime	100	–	–	100	–	–
Cefotaxime	100	–	–	100	–	–
Ceftriaxone	100	–	–	100	–	–
Ceftazidime	90.9	9.1	–	90	10	–
Cefepime	100	–	–	100	–	–
Carbapenems:						
Imipenem	100	–	–	100	–	–
Meropenem	100	–	–	100	–	–
Monobactam: aztreonam	80	20	–	77.8	22.2	–
Aminoglycosides:						
Gentamicin	75	–	25	72.7	–	27.3
Amikacin	100	–	–	100	–	–
Tobramycin	90	–	10	83.3	–	16.7
Fluoroquinolones:						
Ofloxacin	20	–	80	–	–	100
Ciprofloxacin	20	–	80	9.1	–	90.9
Norfloxacin	33.3	–	66.7	–	–	100
Other:						
Nitrofurantoin	100	–	–	100	–	–
Nalixidic acid	14.3	–	85.7	–	–	100
Trimethoprim/sulfamethoxazole	31.3	–	68.8	9.1	–	90.9
Tetracycline	–	–	100	–	–	100
Minocycline	20	–	80	16.7	–	83.3

J. Urol. 169:1762-1765, 2003

Recommendations

- Urosepsis following TRUS biopsy is a rare event; case finding difficult with potential for significant under-reporting
- Urosepsis following TRUS biopsy typically occurs within 1-2 days following biopsy.
- resistance of common uropathogens to ciprofloxacin in this select population

Recommendations

- **Antibiotic resistance patterns in this highly selected population suggest anti-microbial prophylaxis practices should be reevaluated.**
- **consideration of combination therapy pre-biopsy of SXT (or Septra) and ciprofloxacin at our center**
- **based on VGH culture results, gentamicin use in patients presenting with urosepsis post biopsy is recommended at our center**

Response to the Results at our Center

- Increased attention to R/O preBx bacteriuria
- Reintroduction of enemas prior to biopsy (not evidence-based)
- Revision of post-biopsy instructions to patient warning of symptoms of urosepsis and need for immediate action
- Letters to local emergencies warning about the possibility of ciprofloxacin-resistant urosepsis after Bx

Thank you!



VGH Medical Staff Meeting