

PCa Screening and Prostate Biopsy

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Acknowledgement

- J. Kellogg Parsons, MD, MHS, FACS
 - Professor and Endowed Chair
 - Moores Comprehensive Cancer Center
 - UC San Diego Health System



Disclosures

- MDxHealth
 - Study site investigator urine biomarker trial
- Urogen Pharma Ltd
 - Study site investigator Olympus trial
 - Strategic advisor board
- American Kidney Stone Management (AKSM)
 - Stock ownership



Outline

- Resources for study and AUA publications
- Prostate-specific antigen (PSA) screening
- Prostate biopsy
 - Prophylaxis
 - Technical elements
 - Complications and Prevention



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Resources

- National Comprehensive Cancer Network (NCCN) guidelines
- Diagnosis and Management of PCa
 - https://www.nccn.org
 - Evidence-based, updated annually
 - Committee composition = majority urologists



www.nccn.org

Key AUA Publications

- Early Detection of Prostate Cancer
 - Guideline 2013; reviewed for validity 2018
- Optimal Techniques of Prostate Biopsy and Specimen Handling
 - White Paper 2015
- Prevention and Treatment of the More Common Complications Related to Prostate Needle Biopsy
 - White Paper 2017



Key AUA Publications

- Urologic Surgery Antimicrobial Prophylaxis
 - Best Practice Statement 2008; reviewed for validity 2012
- MRI of the Prostate, Standard Operating Procedure
 - Policy Statement 2017



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(Basic) Principles of Screening

Early Detection of Prostate Cancer: AUA Guideline

H. Ballentine Carter, Peter C. Albertsen, Michael J. Barry, Ruth Etzioni, Stephen J. Freedland, Kirsten Lynn Greene, Lars Holmberg, Philip Kantoff, Badrinath R. Konety, Mohammad Hassan Murad, David F. Penson and Anthony L. Zietman

- 5 Index groups that broadly formulate basis of guideline statements
 - Age-based



- 1. The Panel recommends against PSA screening in men under age 40 years. (Recommendation; Evidence Strength Grade C)
 - Low prevalence of disease



Carter HB et al. J Urol 2013

(Basic) Principles of Screening

- 2. The Panel does not recommend routine screening in men between ages 40 to 54 years at average risk. (Recommendation; Evidence Strength Grade C)
- Some men at increased risk may benefit from screening
 - Positive family history
 - 1st degree male relative
 - African-American or Black race



3. For men ages 55 to 69 years the Panel recognizes that the decision to undergo PSA screening involves weighing the benefits of preventing prostate cancer mortality in 1 man for every 1,000 men screened over a decade against the known potential harms associated with screening and treatment. For this reason, the Panel strongly recommends shared decision-making for men age 55 to 69 years that are considering PSA screening and proceeding based on a man's values and preferences. (Standard; Evidence Strength Grade B)



Carter HB et al. J Urol 2013

(Basic) Principles of Screening

- Shared decision making and weighing risks and benefits of screening for men 55 to 69 years of age
- Panel recognizes that greatest benefit of screening appears to be in men 55 to 69 years



4. To reduce the harms of screening, a routine screening interval of two years or more may be preferred over annual screening in those men who have participated in shared decision-making and decided on screening. As compared to annual screening, it is expected that screening intervals of two years preserve the majority of the benefits and reduce over diagnosis and false positives. (Option; Evidence Strength Grade C)

An interval of 2 to 4 years may be preferred over annual screening in men with normal PSA



Carter HB et al. J Urol 2013

(Basic) Principles of Screening

- No specific screening interval data
- Intervals for re-screening can be individualized by baseline PSA
 - For men > 60 years with PSA < 1.0 ng/mL, 4-year interval unlikely to miss curable cancer
 - Goteberg randomized trial



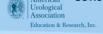
- 5. The Panel does not recommend routine PSA screening in men age 70 years or more, or any man with less than a 10 to 15 year life expectancy. (Recommendation; Evidence Strength Grade C)
- Some men age 70 or greater who are in excellent health may benefit from screening



Carter HB et al. J Urol 2013

(Basic) Principles of Screening

- Additional testing
 - PSA based studies
 - PSA velocity and kinetics
 - PSA density
 - PSA (Free and Total)
 - Ancillary Markers
 - PCA3; PHI; 4K
 - Risk calculators
- Should not be used for primary screening
 - Considered in decision to biopsy or repeat biopsy



Prostate MRI

Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study

Hashim U Ahmed*, Ahmed El-Shater Bosaily*, Louise C Brown*, Rhian Gabe, Richard Kaplan, Mahesh K Parmar, Yolanda Collaco-Moraes, KatieWard, Richard G Hindley, Alex Freeman, Alex P Kirkham, Robert Oldroyd, Chris Parker, Mark Emberton, and the PROMIS study group†

- PROMIS Trial (2017)
 - Multi-center paired cohort trial comparing mpMRI to conventional TRUS biopsy with reference standard being systemic template mapping biopsy



Ahmed HU et al. Lancet 2017

PROMIS Trial (2017)

- mpMRI as a screening modality can
 - Potentially allow over 25% of patients with normal mpMRI to avoid a biopsy
 - Increase diagnosis of clinically significant prostate cancer
 - Reduce likelihood of diagnosing clinical insignificant cancer



Ahmed HU et al. Lancet 2017

Prostate MRI

MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis

V. Kasivisvanathan, A.S. Rannikko, M. Borghi, V. Panebianco, L.A. Mynderse, M.H. Vaarala, A. Briganti, L. Budäus, G. Hellawell, R.G. Hindley, M.J. Roobol, S. Eggener, M. Ghei, A. Villers, F. Bladou, G.M. Villeirs, J. Virdi, S. Boxler, G. Robert, P.B. Singh, W. Venderink, B.A. Hadaschik, A. Ruffion, J.C. Hu, D. Margolis, S. Crouzet, L. Klotz, S.S. Taneja, P. Pinto, I. Gill, C. Allen, F. Giganti, A. Freeman, S. Morris, S. Punwani, N.R. Williams, C. Brew-Graves, J. Deeks, Y. Takwoingi, M. Emberton, and C.M. Moore, for the PRECISION Study Group Collaborators*

- PRECISION Trial (2018)
 - Prospective, randomized, non-inferiority trial of 500 patients undergoing MRI (with or without targeted biopsy) versus conventional TRUS PNB



Kasivisvanathan V et al. N Engl J Med 2018

PRECISION Trial (2018)

- 28% of MRI cohort avoided biopsy due to non-suspicious findings
- Clinically significant cancer in
 - 38% of MRI targeted
 - 26% of standard TRUS PNB



Kasivisvanathan V et al. N Engl J Med 2018

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Prostate Biopsy Prophylaxis

BACTEREMIA AND BACTERIURIA AFTER TRANSRECTAL ULTRASOUND GUIDED PROSTATE BIOPSY

KELLY A. LINDERT, JOHN N. KABALIN AND MARTHA K. TERRIS*

From the Department of Urology, Stanford University Medical Center, Stanford and Section of Urology, Veterans Affairs Palo Alto Health Care System, Palo Alto, California, and Section of Urologic Surgery, University of Nebraska College of Medicine, Scottsbluff, Nebraska

- 50 patients
- No prophylaxis prior to TRUS PNB

Bacteriuria – 44% Bacteremia – 16%



Lindert KA et al. J Urol 2000

Prostate Biopsy Prophylaxis

SINGLE-DOSE ORAL CIPROFLOXACIN VERSUS PLACEBO FOR PROPHYLAXIS DURING TRANSRECTAL PROSTATE BIOPSY

DEEPAK A. KAPOOR, IRA W. KLIMBERG, GHOLAM H. MALEK, JOHN D. WEGENKE, CLAIR E. COX, A. LYNN PATTERSON, EVELYN GRAHAM, ROGER M. ECHOLS, EDWARD WHALEN, AND STEVEN F. KOWALSKY

BJU International (2000), 85, 682-685

Antibiotic prophylaxis for transrectal needle biopsy of the prostate: a randomized controlled study

M. ARON, T.P. RAJEEV and N.P. GUPTA
Department of Urology, All India Institute of Medical Sciences, New Delhi, India



Kapoor DA et al. Urology 1998 Aron M et al. BJU Int 2000

Prostate Biopsy Prophylaxis

Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis

J. Stuart Wolf, Jr., Chairman, $^\circ$ Carol J. Bennett, $^\uparrow$ Roger R. Dmochowski, ‡ Brent K. Hollenbeck, Margaret S. Pearle § and Anthony J. Schaeffer

AUA (updated 1/1/2014)

- All regimens ≤ 24 hours
- First line
 - Oral fluoroquinolone
 - IV / IM 1st / 2nd / 3rd gen. cephalosporin
- Alternatives
 - Oral TMP-SMX (as of 1/1/14)
 - IV / IM aminoglycoside or aztreonam

n & Research, Inc.

Wolf JS et al. J Urol 2008

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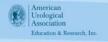


Prostate Biopsy Technique

Optimization of Initial Prostate Biopsy in Clinical Practice: Sampling, Labeling and Specimen Processing

Marc A. Bjurlin, H. Ballentine Carter, Paul Schellhammer, Michael S. Cookson, Leonard G. Gomella, Dean Troyer, Thomas M. Wheeler, Steven Schlossberg, David F. Penson and Samir S. Taneja*

- Minimum of 10 to 12 cores
- Evidence does not support > 12 cores for initial biopsy
 - May be considered for repeat biopsy.



Bjurlin MA et al. J Urol 2013

Prostate Biopsy Technique

- Apical sampling critical
 - Entire apex composed of peripheral zone
 - Increases detection rate and reduces repeat bx
- "Far-lateral" zone
 - Laterally directed biopsies improve cancer detection and NPV



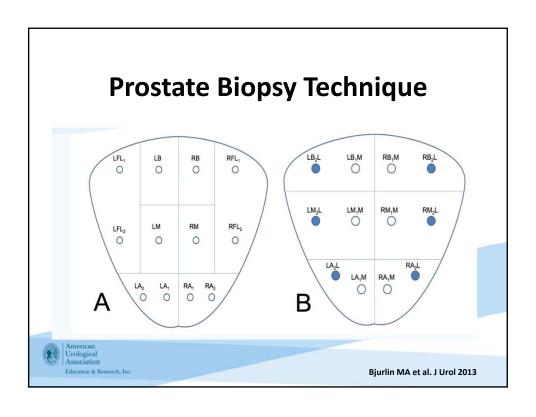
Bjurlin MA et al. J Urol 2013

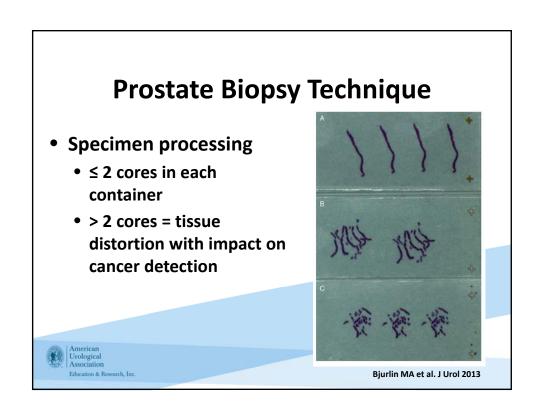
Prostate Biopsy Technique

- Location of cancer in cores
 - Does <u>not</u> predict <u>exact</u> location of pT3 (EPE) or site of positive margin
 - Does predict laterality of disease
- Questionable benefit of transition zone bx



Bjurlin MA et al. J Urol 2013





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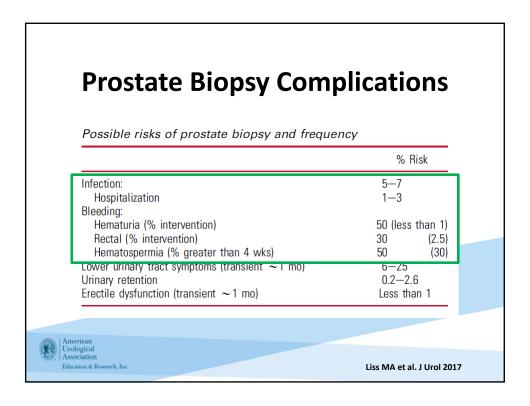
Prostate Biopsy Complications

Possible risks of prostate biopsy and frequency

	% Risk
Infection:	5—7
Hospitalization	1-3
Bleeding:	
Hematuria (% intervention)	50 (less than 1)
Rectal (% intervention)	30 (2.5)
Hematospermia (% greater than 4 wks)	50 (30)
Lower urinary tract symptoms (transient ~1 mo)	6-25
Urinary retention	0.2-2.6
Erectile dysfunction (transient ~ 1 mo)	Less than 1



Liss MA et al. J Urol 2017



Prostate Biopsy Complications

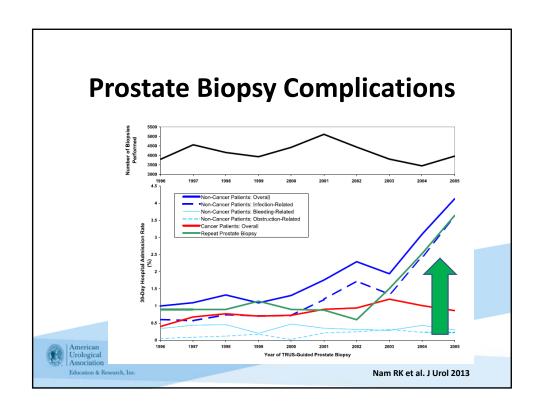
Increasing Hospital Admission Rates for Urological Complications After Transrectal Ultrasound Guided Prostate Biopsy

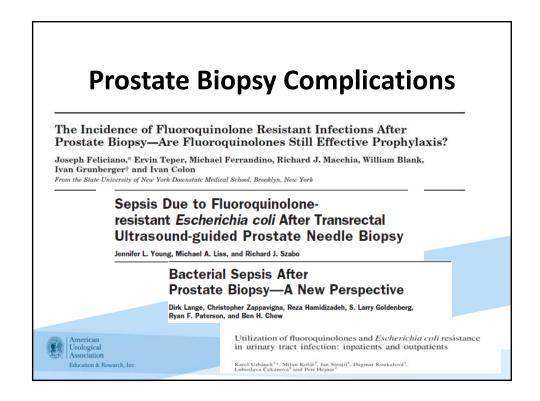
Robert K. Nam,*,† Refik Saskin,† Yuna Lee,† Ying Liu,† Calvin Law,† Laurence H. Klotz,‡ D. Andrew Loblaw,† John Trachtenberg,† Aleksandra Stanimirovic,† Andrew E. Simor,† Arun Seth,† David R. Urbach† and Steven A. Narod†

- 75,190 men undergoing TRUS PNB in Canada between 1996 - 2005
- Hospital and cancer registries for admission and mortality data



Nam RK et al. J Urol 2013





Prevention of PNB Complications

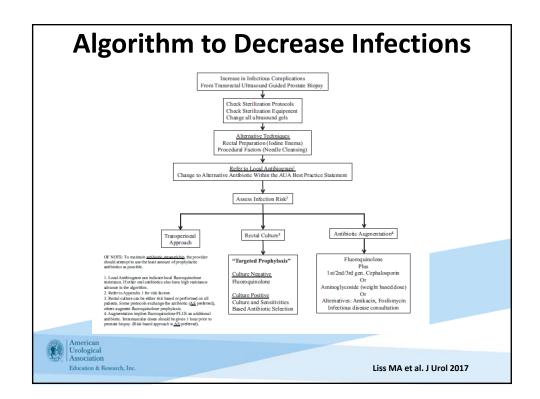
An Update of the American Urological Association White Paper on the Prevention and Treatment of the More Common Complications Related to Prostate Biopsy

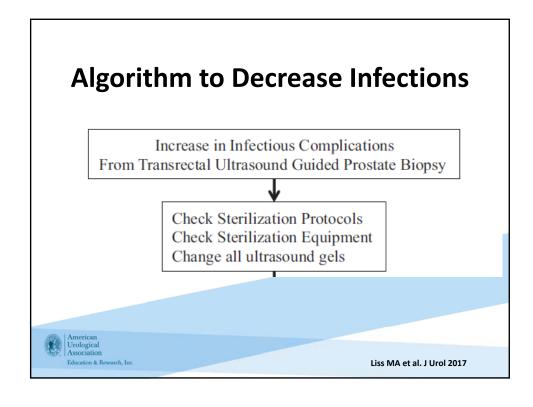
Michael A. Liss,* Behfar Ehdaie, Stacy Loeb, Maxwell V. Meng, Jay D. Raman, Vanessa Spears and Sean P. Stroup

From the University of Texas Health Science Center San Antonio, San Antonio, Texas (MAL); Memorial Sloan Kettering Cancer Center (BE) and New York University (SL), New York, New York; University of California San Francisco, San Francisco, California (MVM); University of Pennsylvania, Philadeliphia, Pennsylvania (UDR); Society of Urologic Nurses Association, Pitman, New Jersey (VS); and Naval Medical Center San Diego, San Diego, California (SPS)



Liss MA et al. J Urol 2017





Does Disposable Needle Guide Minimize Infectious Complications After Transrectal Prostate Needle Biopsy?

Altug Tuncel, Yilmaz Aslan, Tezcan Sezgin, Omur Aydin, Umit Tekdogan, and Ali Atan

Lower rates of bacteriuria and clinical infections in cohort undergoing biopsy with disposable biopsy needles (p < 0.001)



Tuncel A et al. Urology 2008

Infection prevention and control in ultrasound - best practice recommendations from the European Society of Radiology Ultrasound Working Group

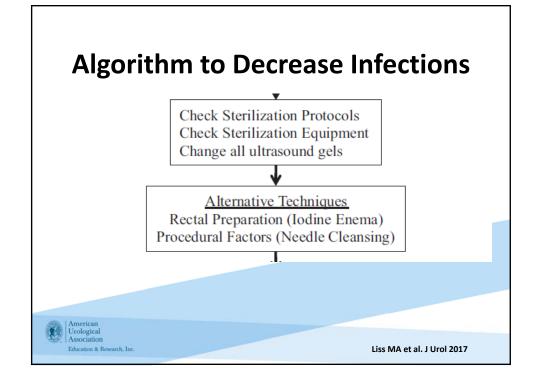
Christiane M. Nyhsen ¹ • Hilary Humphreys ^{2,3} • Roland J. Koerner ⁴ • Nicolas Grenier ⁵ • Adrian Brady ⁶ • Paul Sidhu ⁷ • Carlos Nicolau ⁸ • Gerhard Mostbeck ⁹ • Mirko D'Onofrio ¹⁰ • Afshin Gangi ¹¹ • Michel Claudon ¹²

Single use recommended over multiple use bottles due to contamination

If multi-use, change daily



Nyhsen CM et al. Insights Imaging 2017



Peri-procedural povidone-iodine rectal preparation reduces microorganism counts and infectious complications following ultrasound-guided needle biopsy of the prostate

Justin R. Gyorfi · Christopher Otteni · Kevin Brown · Amar Patel · Kathleen Lehman · Brett E. Phillips · Kalyan Dewan · Girish Kirimanjeswara · Jay D. Raman

Povidone iodine can reduce colony counts in the rectal vault by 97% within 5 minutes of instillation



Gyorfi JR et al. World J Urol 2014

Algorithm to Decrease Infections

Decrease in Infection Rate Following Use of Povidone-Iodine During Transrectal Ultrasound Guided Biopsy of the Prostate: A Double Blind Randomized Clinical Trial

Mahyar Ghafoori 1,2*, Madjid Shakiba 1, Hamidreza Seifmanesh 1, Kamal Hoseini 3

A Prospective Randomized Trial of Povidone-Iodine Prophylactic Cleansing of the Rectum Before Transrectal Ultrasound Guided Prostate Biopsy

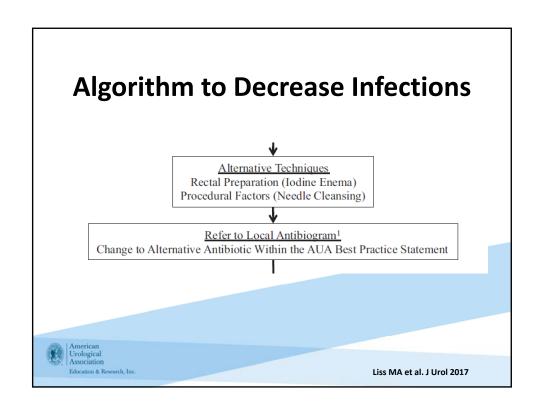
Zeid AbuGhosh,* Joseph Margolick,* S. Larry Goldenberg,† Stephen A. Taylor,* Kourosh Afshar,* Robert Bell,* Dirk Lange,* William R. Bowie,* Diane Roscoe,* Lindsay Machan‡ and Peter C. Black*,§

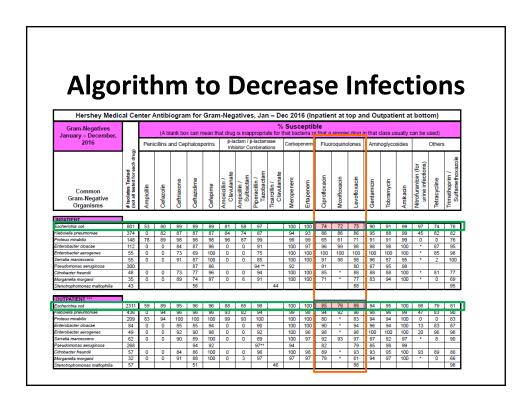
Randomized trials show promise but are not conclusive

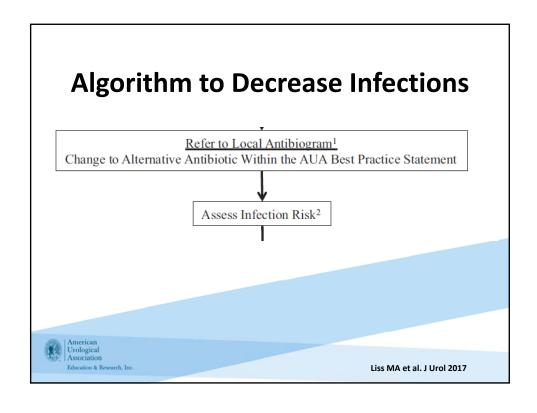


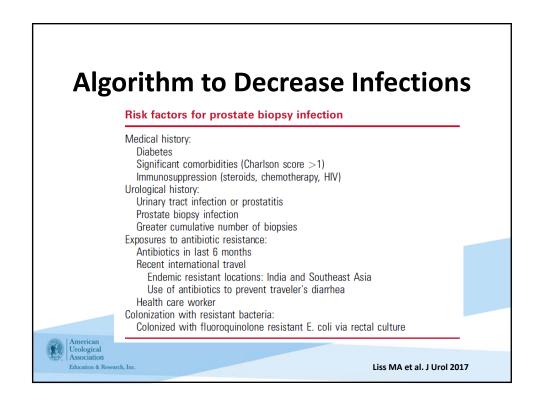
Low risk intervention

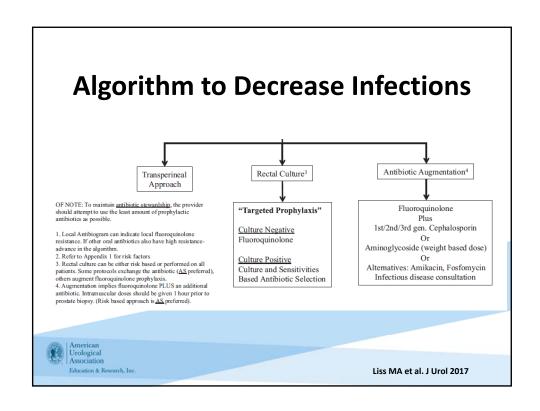
Ghafoori M et al. Iran J Radiol 2012 AbuGhosh Z et al. J Urol 2013

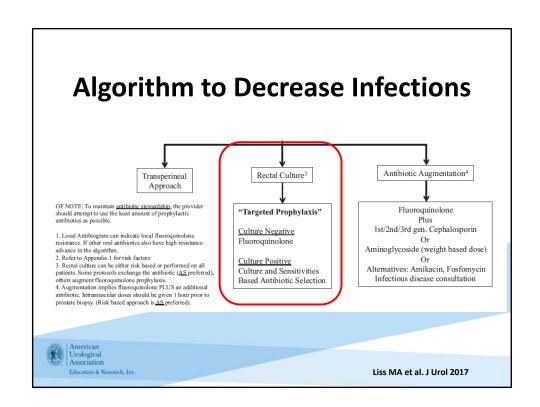












Rectal Cultures Before Transrectal Ultrasound-guided Prostate Biopsy Reduce Post-prostatic Biopsy Infection Rates

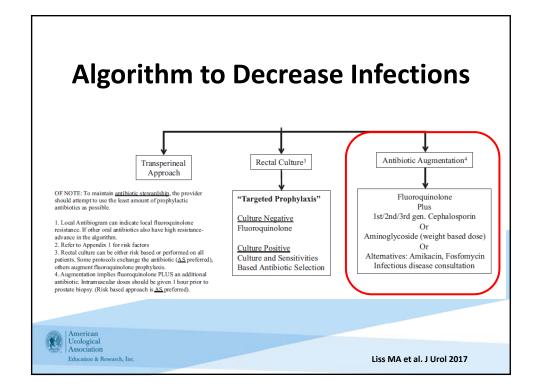
Christopher A. Duplessis, Mary Bavaro, Mark P. Simons, Charles Marguet, Michael Santomauro, Brian Auge, Daniel A. Collard, Joshua Fierer, and James Lesperance

Targeted Antimicrobial Prophylaxis Using Rectal Swab Cultures in Men Undergoing Transrectal Ultrasound Guided Prostate Biopsy is Associated With Reduced Incidence of Postoperative Infectious Complications and Cost of Care

Aisha K. Taylor, Teresa R. Zembower, Robert B. Nadler, Marc H. Scheetz, John P. Cashy, Diana Bowen, Adam B. Murphy, Elodi Dielubanza and Anthony J. Schaeffer*,†



Duplessis CA et al. Urology 2012 Taylor AK et al. JUrol 2012



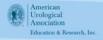
Intramuscular Gentamicin Improves the Efficacy of Ciprofloxacin as an Antibiotic Prophylaxis for Transrectal Prostate Biopsy

Henry SS Ho, ¹MRCS, MMal, FLMS (Urolog), Lay Guat Ng, ¹MBS, FRCS, FLMS (Urolog), Yeh Hong Tan, ¹MBS, FRCS, FLMS (Urolog), Mavis Yeo, ²DIMB, Dip Bosteriolog, FRCP4, Christopher WS Cheng, ¹MBS, FRCS, FLMS (Urolog))

Combined Ciprofloxacin and Amikacin Prophylaxis in the Prevention of Septicemia After Transrectal Ultrasound Guided Biopsy of the Prostate

Elijah O. Kehinde,* May Al-Maghrebi, Mehraj Sheikh and Jehoram T. Anim

From the Departments of Surgery (Division of Urology) (EOK), Biochemistry (MAM), Radiology (MS) and Pathology (JTA), Faculty of Medicine, Kuwait University, Kuwait



Ho HSS et al. Ann Acad Med Singapore 2009 Kehinde EO et al. JUrol 2013

PNB Bleeding Complications

- Hematuria
 - Typically transient & self-limiting
 - Risk factors
 - Large prostate volume & large transition zone
- Blood Per Rectum
 - Typically transient & self-limiting
 - Risk factors
 - Increased # of cores and anticoagulation



Liss MA et al. J Urol 2017

PNB Bleeding Complications

- Hematospermia
 - Occurs in over 90% of biopsy pts
 - Long duration
 - 1/3 still present at 4 weeks post-PNB
 - Risk factors
 - Age, higher prostate volume, prior TURP



Liss MA et al. J Urol 2017

PNB Anticoagulation

Anticoagulation and Antiplatelet Therapy in Urological Practice: ICUD/AUA Review Paper

Daniel J. Culkin,*,† Emilio J. Exaire, David Green, Mark S. Soloway, Andreas J. Gross,‡ Maheshbhai R. Desai, James R. White§ and Deborah J. Lightner

Health Sciences Center, University of Oklahoma (DJC, EJE), Oklahoma City, Oklahoma, Northwestern University (DG), Chicago, Illinois, University of Miami (MSS), Bal Harbour, Florida, Urologische Abteilung (AJG), Hamburg, Germany, Muljibhai Patel Urological Hospital (MRD), Nadiad, India, Baltimore, Maryland (JRW), and Mayo Clinic (DJL), Rochester, Minnesota

Anticoagulation recommendations are discussed for PNB in setting of all urologic procedures



Culkin DJ et al. J Urol 2014

PNB Anticoagulation

- Aspirin, NSAIDS
 - Appear to be safe to continue
- Anti-platelet agents and Coumadin
 - Data too limited to draw conclusions
 - Most studies recommend discontinuation 5-7 days prior
 - Coumadin interacts with quinolones, macrolides, and cephalosporins



Culkin DJ et al. J Urol 2014

PNB Urinary Retention

- Pelvic pain (rectum, suprapubic, glans)
- Risk factors
 - Larger volume prostate, IPSS > 19, increased transition zone volume
- Alpha-blocker x 7 days may decrease risk
 - Begin 1 day prior to biopsy
- 5-7 days catheter drainage



Liss MA et al. J Urol 2017

ARS Q1:

Which of the following is the most significant risk factor for urosepsis following transrectal prostate needle biopsy?

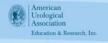
- a) Diabetes
- b) Immunosuppression
- c) Number of prior biopsies
- d) History of antibiotics in last 6 months
- e) Recent travel to Southeast Asia



Answer: D

D. History of antibiotics in last 6 months

All of these patient factors are associated with increased risk of post-biopsy, but the <u>most significant</u> is antibiotic use in the previous 6 months



ARS Q2:

A 59 year-old white man with a history of well-controlled hypertension is referred to you for PSA = 6.0 ng/mL. He has no urinary symptoms. DRE is unremarkable. The next best step is:

- a) Informed discussion of risks and benefits of prostate cancer diagnosis
- b) Ciprofloxacin x 4 weeks, then re-check PSA
- c) Recheck PSA with % free fraction
- d) MRI of pelvis/prostate
- e) Prostate biopsy



Answer: A

A. Informed discussion of risks and benefits of prostate cancer diagnosis

Prior to prostate biopsy, all patients—even those with PSA > 4 ng/mL—should be counseled as to the potential risks and benefits of prostate cancer diagnosis, including overtreatment. Antibiotics are not recommended for asymptomatic PSA elevations. Free PSA, PSA density, and MRI are reasonable secondary tests after an informed discussion.



ARS Q3:

The following patient(s) that should be offered prostate cancer screening through informed discussion is:

- a) 39 year-old African-American man
- b) 78 year-old African-American man with history of insulin-dependent diabetes and coronary artery disease
- c) 39 year-old Hispanic man with father and older brother diagnosed with aggressive prostate cancer
- d) Both a and c
- e) None of the above



Answer: E

E. None of the above

Prostate cancer screening should not be offered to men < 40 years of age. For those ages 40 to 55 years, screening can be considered in African-Americans and those with a family history of prostate cancer. Screening should not be routinely offered to men \ge 70 years or those with \le 10 to 15 life expectancy.



ARS Q4:

Prior to TRUS-guided prostate biopsy, your routine practice is Ciprofloxacin 500 mg po once. You note a substantial increase in post-biopsy urinary infections over a 6-month period. The next best step is:

- a) In addition to ciprofloxacin, administer gentamicin1.5 mg/kg IM once prior to biopsy
- b) Verify equipment sterilization protocols
- c) Change antibiotic prophylaxis per local antibiogram
- d) Initiate iodine enemas prior to biopsy
- e) Perform transperineal prostate biopsies



Answer: B

B. Verify equipment sterilization protocols

If an increase in post-biopsy infections occurs, the next step is to verify equipment sterilization protocols, check sterilization equipment, and change all ultrasound gels. Changes in technique—including iodine enemas and biopsy needle cleaning with formalin—may then be considered, followed by antibiogram-directed prophylaxis. Antibiotic augmentation and transperineal biopsy are reasonable options, but only after completion of risk assessment.



ARS Q5:

For initial diagnostic prostate biopsy, proper technique includes all of the following components except:

- a) Routine transition zone sampling
- b) Laterally-directed samples
- c) Apically-directed samples
- d) No greater than 2 core samples placed in each individual specimen jar
- e) Minimum of 10 to 12 separate core samples obtained



Answer: A

A. Routine transition zone sampling

Transition zone sampling does not improve cancer detection in initial diagnostic biopsy. Proper technique involves lateral and apical samples; ≤ 2 samples placed in each specimen jar; and a minimum of 10 to 12 cores.

