## Title
Urethral lichen sclerosus under the microscope: a survey of academic pathologists.



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## Authors
Erickson, Bradley A
Tesdahl, Brennan A
Voznesensky, Maria A
et al.

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## Infections/Inflammation/Cystic Disease of the Genitourinary Tract: Prostate & Genitalia II

## Moderated Poster 11

**Friday, May 12, 2017** **1:00 PM-3:00 PM**

### MP11-01
### ROLE OF CHRONIC INFLAMMATION IN PROSTATE CANCER: A STUDY ON NEEDLE BIOPSY SPECIMENS

*Shardul Soni*, Michael Glover, Qinghu Ren, Gregory MacLennan, Pingfu Fu, Sanjay Gupta, Cleveland, OH*

INTRODUCTION AND OBJECTIVES: The relationship between inflammation and prostate cancer has not been established, although chronic inflammation has frequently been identified in prostate biopsies, radical prostatectomy specimens and tissue resected for treatment of benign prostatic hyperplasia. In the peripheral zone of the prostate, sometimes adjacent to foci of high-grade PIN and cancer, certain morphologic changes are often identified, which may represent active and terminal phases of chronic inflammation. These changes are designated, respectively, proliferative inflammatory atrophy (PIA) and post atrophic hyperplasia (PAH), and their morphology is well documented in pathologic literature. In our previous studies, we have identified chronic inflammation as a putative contributor to neoplastic progression in prostate epithelial cells, and hypothesized that its adverse effects were related to an increase in Bcl2, a survival protein involved in cell survival and carcinogenesis. We hypothesize that changes in the stromal microenvironment, characterized by infiltration of immune cells, with generation of reactive oxygen and nitrogen species, can induce oxidative stress in the surrounding proliferating epithelium and cause permanent genomic alterations. Here we focused on several key proteins involved in the inflammatory process, COX2 and iNOS; cell survival, Bcl2 and GSTPΠ; and evaluated expression of alpha-methylacyl coenzyme A racemase (AMACR) and basal cell-specific markers 34βE12 and/or p63 to evaluate possible neoplastic alterations in epithelial cells in an inflammatory environment.

METHODS: We evaluated 16 prostate core needle biopsy specimens that exhibited the presence of chronic inflammation as well as PIA and PAH lesions. Immunohistochemical staining for P63/34βE12/AMACR cocktail, iNOS, COX2, GSTΠ, and Bcl2 was performed in each set of biopsies.

RESULTS: The integrity of the basal layer was maintained in the area of chronic inflammation with high to moderate expression of p63 in 72% of these cells. Approximately 68% of luminal cells expressed high to moderate levels of iNOS and COX-2, whereas 55% of these cells express modest levels of GSTΠ and Bcl2. We found that basal cells near areas of chronic inflammation in the PIA lesions exhibit high AMACR expression and weak to no p63 expression. Loss of p63 and increased AMACR expression in the basal cells was associated with increased expression of the inflammatory markers COX2 and iNOS, as well as loss in pro-survival signal GSTP1 and Bcl2 in the adjacent luminal cells. These neoplastic alterations were observed in 6/16 (38%) of the needle biopsy specimens.

CONCLUSIONS: Our findings suggest that basal cells undergo alterations in a setting of chronic inflammation. This is important because basal cells are considered to be progenitor cells capable of differentiating into secretory luminal cells, but under the influence of chronic inflammation, they may instead transform into the neoplastic cells that characterize high grade prostatic intraepithelial neoplasia and prostatic adenocarcinoma.

**Source of Funding:** Department of Defense grant W81XWH-15-1-0558, USPHS R21CA193080, R03CA186179 and VA Merit Review 1I01BX002494 to SG.

### MP11-02
### URETHRAL LICHEN SCLEROSUS UNDER THE MICROSCOPE

*Brennan Tesdahl*, Maria Voznesensky, Iowa City, IA; Nejd Alsikafi, Maywood, IL; Benjamin Breyer, San Francisco, CA; Joshua Broghammer, Kansas City, KS; Jill Buckley, San Diego, CA; Sean Elliott, Minneapolis, MN; Christopher McClung, columbus, OH; Jeremy Myers, Salt Lake City, UT; Thomas Smith III, Houston, TX; Alex Vanni, Burlington, MA; Bryan Voelzke, Seattle, WA; Lee Zhao, New York City, NY; William Brant, Salt Lake City, UT; Bradley Erickson, Iowa City, IA*

INTRODUCTION AND OBJECTIVES: Lichen sclerosus (LS) is an inflammatory dermatologic condition that involves squamous epithelium. Genitourinary LS (GLS), historically known as balanitis xerotica obliterans (BXO), is thought to involve the urethra, a stratified/pseudostratified columnar and urothelial lined organ. Given the poor understanding of the pathophysiology of LS and a lack of accepted definitive diagnostic criteria, we proposed to survey pathologists regarding their understanding of LS. We hypothesized that significant disagreement about GLS will exist.

METHODS: All urologists participating in the Trauma and Urologic Reconstruction Network of Surgeons identified genitourinary (GUP) and dermatopathologists (DP) at their respective institutions who were then invited to participate in an online survey regarding their experience with diagnosing LS, LS pathophysiology and its relationship to urethral stricture disease. Statistical comparisons between responses provided by DPs and GUPs were performed using the Fischer's exact test.

RESULTS: There were 23 (12 DP, 11 GUP) pathologists that completed the survey. Overall, 90% still use BXO when describing GLS and 66% require a clinical history. The most agreed upon criteria for diagnosis were dermal collagen homogenization (85.7%), loss of the normal rete pattern (33.3%) and atrophic epidermis (28.5%) - thus no single criteria was deemed necessary for diagnosing GLS by all pathologists. Only 1 pathologist routinely graded GLS severity. The average number required findings for diagnosis was $2.1\pm1.09$ (GUP $2.1\pm1.27$ v DP $2.1\pm1.0$; $p = 0.96$). No pathologists believed GLS had an infectious etiology (19% maybe, 42% unknown) and 19% believed GLS to be an autoimmune disorder (42% maybe, 38% unknown); 19% believed LS to be premalignant, but 52% believed it was associated with cancer; 80% believed that LS could involve the urethra (DP (92%) v GUP (67%); $p = 0.272$). Of those diagnosing urethral GLS, 80% of DUP believed that GLS must first involve the glans/prepuce before involving the urethra, while all GUP believed that urethral disease could exist in isolation ($p=0.007$).

CONCLUSIONS: There was significant disagreement in this specialized cohort of pathologists when diagnosing GLS. A logical first step appears to be improving agreement on how to best describe and classify the disease and characterize possible differences in histological changes between skin and GLS. Specialty-wide efforts to routinely collect and analyze urethral stricture specimens may aid in understanding pathophysiologies that continue to elude urologists and pathologists.

**Source of Funding:** None

### MP11-03
### HPV PREVALENCE IN MALES IN THE UNITED STATES FROM PENILE SWABS: RESULTS FROM NHANES

*Michael Daugherty*, Timothy Byler, Syracuse, NY*

INTRODUCTION AND OBJECTIVES: Human papilloma virus (HPV) is a common sexually transmitted infection (STI) in the US that can lead to both malignant transformation and genital warts. Recently, a vaccine has been developed against the 4 major strains of HPV. The American Committee for Immunization Practices has given a permissive recommendation for boys aged 11-26 years, but does not place it